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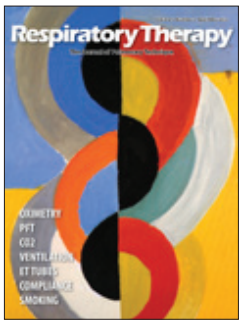

Respiratory Therapy™
The Journal of Pulmonary Technique

Vol. 7 No. 2
April-May 2012

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Editorial

Re-Search

In researching an article about plagiarism for my other job as a writing teacher, I came across a piece by the novelist Jonathan Lethem, which has implications for medical research. He points to a phenomenon "identified about twenty years ago by Don Swanson, a library scientist at the University of Chicago. He called it 'undiscovered public knowledge.' Swanson showed that standing problems in medical research may be significantly addressed, perhaps even solved, simply by systematically surveying the scientific literature. Left to its own devices, research tends to become more specialized and abstracted from the real-world problems that motivated it and to which it remains relevant. This suggests that such a problem may be tackled effectively not by commissioning more research but by assuming that most or all of the solution can already be found in various scientific journals, waiting to be assembled by someone willing to read across specialties. Swanson himself did this in the case of Raynaud's syndrome, a disease that causes the fingers of young women to become numb. His finding is especially striking—perhaps even scandalous—because it happened in the ever-expanding biomedical sciences."*

Swanson's method is called "Swanson linking." It's a term that refers to connecting two pieces of knowledge previously thought to be unrelated. For example, it may be known that illness A is caused by chemical B, and that drug C is known to reduce the amount of chemical B in the body. However, because the respective articles were published separately from one another (called "disjoint data"), the relationship between illness A and drug C may be unknown. Swanson linking aims to find these relationships and report them. If you want to read Swanson's article, google "Fish oil, Raynaud's syndrome, and undiscovered knowledge." The piece appeared in the Autumn 1986 issue of Perspectives in Biology and Medicine. Swanson wrote: "It seems inevitable that, within the abstract world of objective knowledge, other implicitly existing hypotheses await discovery, and that such hypotheses have not yet been discovered because the logically related parts that make them obvious have never been retrieved and assembled – they have never all become known to any one person."

He developed his theory in a paper called Undiscovered Public Knowledge, which appeared in Library Quarterly. In an update to the original article, he wrote: "Two literatures or sets of articles are complementary if, considered together, they can reveal useful information of scientific interest not apparent in either of the two sets alone. Of particular interest are complementary literatures that are also mutually isolated and noninteractive (they do not cite each other and are not co-cited). In that case, the intriguing possibility arises that the information gained by combining them is novel."

For respiratory therapists, and those doing research in the field, the implication is to attempt what might be called a holistic approach to solving problems, looking for connections where they might not at first seem obvious.

Les Plesko

* Jonatham Lethem's article, titled "The Ecstasy of Influence," appeared in the February 2007 issue of Harper's.

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ISSN 2152-355X
Published six times each year by
Goldstein and Associates, Inc.
10940 Wilshire Blvd., Suite 600
Los Angeles, CA 90024 USA
Tel: 310-443-4109 · Fax: 310-443-4110
E-mail: s.gold4@verizon.net
Website: www.respiratorytherapy.ca
Publisher Steve Goldstein
Editor Les Plesko
Associate Editor Jordana Hammeke
Assistant Editor Laszlo Sandor
Design & Production www.accugraphics.net

Circulation, Coverage, Advertising Rates: Complete details regarding circulation, coverage, advertising rates, space sizes, and similar information are available to prospective advertisers. Closing date is 45 days preceding date of issue.

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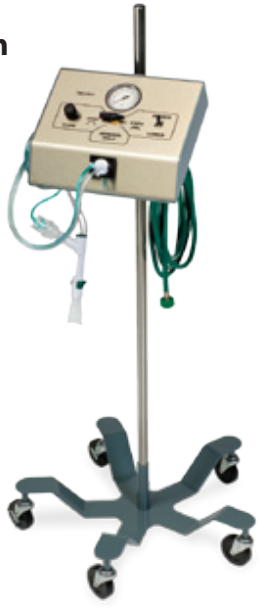

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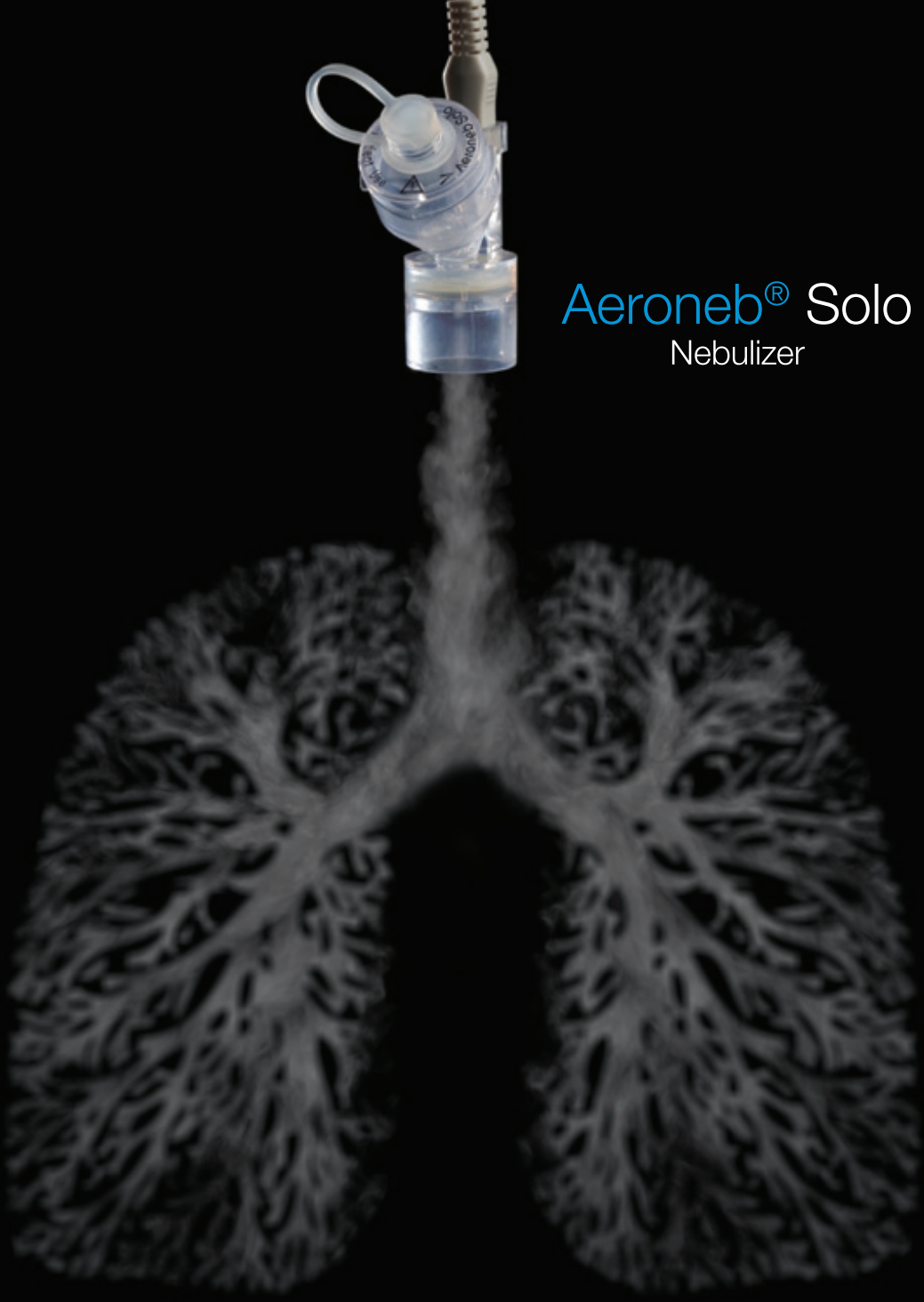

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News

☐ April-May 2012

CORRECTION

Regarding our Feb/March article Advances in Awareness, Research and Optimal Treatment for COPD, by Scott Cerreta, BS, RRT, the author requested we replace the section COPDGene Study, page 30, with the following: The COPDGene Study is one of the largest studies ever to investigate the underlying genetic factors of COPD. The Study has enrolled over 10,000 individuals, and its goals are to identify inherited or genetic factors that make some individuals more likely than others to develop COPD. Each of the subjects enrolled has undergone a clinical evaluation including spirometry, a six-minute walk test, respiratory and quality of life questionnaires and the elements for a BODE score (body mass index, degree of airflow obstruction, degree of dyspnea and exercise capacity). In addition, the subjects have undergone both inspiratory and expiratory chest CT scans and have donated about 30cc of blood for genetic analysis. Because not all smokers develop COPD, and only 15-20 percent of smokers develop severe lung impairment, researchers are looking for associations between genes across the entire human genome that affect the development of COPD. A genome-wide analysis has been done on all subjects in the COPDGene cohort using the Omni Express Chip, which assesses approximately 1 million SNPs (single nucleotide polymorphisms) across the entire human genome. This GWAS data is currently undergoing analysis and will be used to establish genetic regions for detailed sequencing analysis to identify specific genes that associate with risk for COPD. Genetic findings arising from the COPDGene study will be validated in multiple other cohorts to confirm their association with, and importance in, COPD. Ultimately, the results of this study have the potential to lead to better treatments and improved outcomes for patients.

ASBESTOS

The Mesothelioma Center at www.asbestos.com is an advocacy group that promotes awareness on asbestos-related diseases such as mesothelioma and asbestosis. It provides informational materials and its patient advocates work one-on-one with patients to help them find local doctors, treatment centers and support groups. All of its services are free of charge. Additionally it has a full staff of writers and its website is HON code certified with over 3,000 pages of the most up to date content on asbestos and all of its negative health effects. The most common form of mesothelioma cancer is pleural mesothelioma. It develops in the lining of the lungs and is caused by asbestos exposure. Some of the more prominent pleural mesothelioma symptoms include difficulty breathing and chest pains. Asbestos can damage the lung lining and the lungs themselves by causing scarring, plaque buildup, excessive fluid, and tumor growths. Respiratory therapy may help improve lung function as well as ease the difficulty breathing for those suffering from pleural mesothelioma. Some recommended breathing techniques include: • Pursed-Lip Breathing, • Abdominal/Diaphragmatic Breathing, and • Active Cycle of Breathing Technique. For those with a chronic respiratory illness like mesothelioma, pulmonary rehabilitation may be something to consider. The Mesothelioma Center is the leading resource for mesothelioma and other asbestos-related diseases. For more information regarding the Mesothelioma Center visit at Asbestos.com, Facebook, or Twitter.

FROGGY

Scientists at the Salk Institute for Biological Studies have identified a gene that tells cells to develop multiple cilia, a finding that may help generate new therapies that use stem cells to replace damaged tissues in the lung and other organs. The researchers studied clawed frogs, whose multiple cilia are like those of humans, and which push cerebrospinal fluid through the brain and spinal cord, helping to circulate and replenish this fluid. In the respiratory system, the cilia push mucus that traps dust, pathogens

and other foreign matter from the lung up into the trachea, helping prevent infections. In addition to a previously-identified protein, FoxJ1, the researchers identified a gene that produces a second protein, "multicilin," that tells cells to develop multiple cilia. When cells are exposed to multicilin, their genetic mechanisms for developing multiple cilia are activated. In a developing embryo, the protein instructs certain stem cells that will line the lungs, kidney and skin to develop into multiciliate cells. The scientists found that multicilin is both necessary and sufficient to instruct the development of multiple cilia in cells that line the airways of mice.

WHO SPENDS MOST?

According to a report in the Huffington Post, five percent of Americans accounted for half of the country's health care costs in 2009. Findings by the Agency for Healthcare Research and Quality revealed that a small share of the population is responsible for much of the country's health care costs. One percent of Americans accounted for 22% of costs in 2009. Those between the ages of 45 and 64 and the elderly were overly represented among the top health care spenders. Women and white Americans were additionally overly represented, while children and young adults were disproportionately represented among the bottom half of spenders. The nation's health care spending will comprise a fifth of the US economy by the end of the decade, according to a July report from Medicare's Office of the Actuary, up from the 17% of GDP health care spending accounted for last year. In 2008, Americans spent three times more on health care than what they spent just 18 years before, according to a Kaiser report. Health care costs accounted for more than 15% of US gross domestic product by that time, one of the highest rates of industrialized nations. Meanwhile, the total number of Americans with health insurance fell in 2010 for the first time in decades, CNNMoney reports, with nearly 50-million lacking coverage. Reported by the Huffington Post.

BMC NEWS

BMC Endocrine Disorders, Globalization and Health and Gut Pathogens have recently been accepted for Impact Factor tracking by Thomson Reuters… BMC's supporting data information for authors and editors has been updated to provide even more information on best practice for data citation and linking data to publications, as has its reference style guide. More than 10 journals now encourage or require authors to consistently link publications to supporting data. Recently-reported research has suggested this practice may increase research impact in some scientific fields… Oxfam GB, the leading aid and development charity, recently launched their repository, the Oxfam iLibrary. Hosted by Open Repository, the advanced DSpace repository solution, the iLibrary allows Oxfam to organize, showcase and browse their vital research and policy information in a single, secure location online… Israel Journal of Health Policy Research seeks to promote intensive intellectual interactions among scholars and practitioners from Israel and other countries regarding all aspects of health policy, health services research, public health, health promotion, health economics, health care management, and the ethics, sociology, and political science of health care in Israel. The ultimate aim of these intellectual interactions is to contribute to the development of health policy in Israel and around the

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world… BMC International Health and Human Rights has published a collection of articles: Contextualising rights: the lived experience of sexual and reproductive health rights... BMC Health Services Research has published a collection of articles: Social audit: building the community voice into health service delivery and planning… BMC has noted a featured article: Difference in symptom severity between early and late grass pollen season in patients with seasonal allergic rhinitis, in Clinical and Translational Allergy 2011, 1:18. The article notes: Hay fever sufferers report more severe symptoms during early pollen season compared to late season, despite similar pollen count levels. This variation is not accounted for by differences in medication or other concurrent allergies.

EFFECTIVE TREATMENT

An international team of scientists have found that the protein SAA plays a key role in chronic inflammation and lung damage in COPD and also inhibits the natural effort of the lung to repair itself after smoking has stopped. SAA is normally made in the liver, but the researchers found that very high levels were made in the lungs of COPD patients, confirming that SAA not only caused inflammation but hindered natural healing in the lung. This explained why inflammation in COPD never resolves despite stopping smoking. The discovery could lead to the development of a dual treatment by firstly, targeting SAA to switch off its function in the lung and secondly, adding a synthetic form of the natural healing agent to boost lung healing. The combined treatment could also improve the effectiveness of steroid treatment for COPD, which is effective in treating other lung diseases such as asthma.

DANGEROUS

Insights, a publication of the American Society of International Law reports: In the last months of 2011, a controversy emerged involving research on highly pathogenic avian influenza A (H5N1) undertaken in The Netherlands and the United States. The projects produced H5N1 strains more transmissible among mammals. These results alarmed those worried about bioterrorism and accidental release of dangerous pathogens. A US federal advisory body recommended that aspects of the research not be published. The controversy drew attention to governance of research designed to protect health but that creates biological agents, knowledge, and/or scientific methodologies potentially dangerous to national security and public health. Insight describes this controversy and identifies international legal issues it highlights. Insights author David P. Fiedler writes: In September 2011, scientists announced that independent experiments produced H5N1 strains with enhanced transmissibility in mammals. The projects sought to generate information about the H5N1 virus given concerns about potential mutations. The research caused national security and public health anxieties and produced controversy about whether the findings should be fully published. The National Science Advisory Board for Biosecurity recommended that the researchers and journal editors publish the general conclusions highlighting the novel outcome but not include the methodological and other details that could enable replication of the experiment by those who would seek to do harm. DHHS agreed with these recommendations, but neither the researchers nor the publishers are legally bound to follow them. However, experts raised concerns that such research potentially also threatens public health through accidental release, escape, or theft of the research strains because of inadequate biosecurity and biosafety in laboratories, leading to arguments that these strains should be destroyed. The scientific journals in question have agreed not to publish the research findings in full, but the matter is far from resolved, especially in terms of what should happen to the H5N1 strains produced by the research and who should have access to the full findings. More generally, the controversy generated questions about the prudence of conducting this kind of research, the standards under which it is undertaken and managed, disclosure of findings and methodologies, and post-research handling of more dangerous strains produced through research. The controversy's international dimensions fostered calls for strengthened cooperation given perceived weaknesses in international governance. The World Health Organization captured the conundrum when it expressed concern about potentially adverse consequences of the H5N1 research but stressed that research continue "so that critical scientific knowledge needed to reduce the risks posed by the H5N1 virus continues to increase." The WHO has agreed to facilitate negotiations to identify the key issues and work towards solutions. These negotiations have to address issues related to the Dutch and American research, including what should be done with the H5N1 research strains and who can get access to the full research findings. Longer-term challenges involve developing rules and processes for better handling the scientific, public health, and national security interests affected by risky research on pathogens. The foregoing is abridged from Insights, copyright 2011 by The American Society of International Law ASIL. The author, David Fiedler, is the James Louis Calamaras Professor of Law at the Indiana University Maurer School of Law.

CHILDHOOD ASTHMA

A study from the Norwegian Mother and Child Cohort Study (MoBa) suggests that children delivered by cesarean section have an increased risk of asthma at the age of three, especially among children without a hereditary tendency to asthma and allergies. Data from more than 37,000 participants were used to study the relationship between delivery method and the development of lower respiratory tract infections, wheezing and asthma in the first three years of life. Children born by cesarean section were compared with those born vaginally. Children born by caesarean section have a slightly elevated risk for asthma at three years, but have no increased risk of frequent lower respiratory tract infections or wheezing. The increased risk of asthma among children delivered by cesarean section was higher among children of mothers without allergies. Researchers said that these kids may have an increased risk of asthma due to an altered bacterial flora in the intestine that affects their immune system development, or because children born this way often have an increased risk of serious respiratory problems during the first weeks of life.

PERSISTENT

Many patients with mild to moderate asthma suffer from persistently non-eosinophilic disease, which may stay unresponsive to currently available anti-inflammatory treatments, according to the Asthma Clinical Research Network. Just under a thousand individuals with asthma were enrolled in 9 human trials. Researchers discovered that sputum eosinophilia was detected in 36% of asthma patients who don't use an inhaled corticosteroid and 17% of asthmatics who use an ICS. Sputum eosinophilia was found in 15% of patients who did not achieve good asthma control, in comparison to 26% of asthmatics who achieved good asthma control. Researchers also found that 22% of asthmatics not taking ICS who had repeated induced sputum

samples had persistent eosinophilia; 47% were persistently non-eosinophilic; and 31% had eosinophilia on at least one occasion. In participants with eosinophilia asthma, 2 weeks of therapy with a combination of anti-inflammatory medications resulted in considerable improvements in airflow obstruction. However, these improvements were not observed in participants with persistently non-eosinophilic asthma, although in participants with eosinophilia and non-eosinophilic asthma, bronchodilator responses to albuterol were comparable. The researchers noted that prevalence estimates for non-eosinophilic asthma in earlier studies were based on single sputum samples. They showed for the first time that sputum eosinophilia is persistently absent in a large percentage of patients with mild/moderate asthma when sputum is analyzed repeatedly over time. The researchers also found that treatment responses in patients with persistent eosinophilia and intermittent eosinophilia were similar. Reported by Grace Rattue, Medical News Today, copyright Medical News Today.

ROLL ANOTHER ONE

Marijuana tokers may have stronger lungs than non-smokers, according to researchers at UC San Francisco and The University of Alabama. They found evidence that occasional marijuana use can cause an increase in lung airflow rates and lung volume. The study spanned two decades and involved 5,000 participants. The researchers noted that even at one joint per day over seven years, people were not seeming to have any degradation of lung capacity or function. The harm from cigarettes showed up clearly while those smoking a joint a day and not smoking tobacco did not show the degradation. Even one joint per week for twenty years did not appear to have significant effect. It's known that THC, one of the main active cannabis oils, has anti inflammatory properties that may help to soothe the lungs. Rupert Shepherd, writing in Medical News Today, noted, "A part of the increased capacity was put down to the way pot smokers usually take deep breaths when they smoke, but one joint per day is hardly giving your lungs great exercise." He noted that it would be "interesting to see results of lung tests in communities such as Jamaica and the Himalayas where smoking pot is endemic and done in larger daily volumes." Information copyright Medical News Today.

NO HELP, BUT HARM

Pirfenidone inhibits the development of inflammation and fibrosis in pulmonary tissue and has been approved for the treatment of mild to moderate idiopathic pulmonary fibrosis (IPF) since the beginning of 2011. An early benefit assessment by the German Institute for Quality and Efficiency in Health Care has examined the extent of added benefit of pirfenidone. Treatment with pirfenidone was compared with the appropriate comparator therapy, best supportive care; that is, therapy that provides the patient with the best possible individually optimized supportive therapy to alleviate symptoms and improve quality of life. Pirfenidone gave minor added benefit with respect to patients' exercise tolerance, but greater harm was also proven: Study discontinuations and unfavorable effects on the gastrointestinal tract were more frequent than with comparator therapy. The extent of this greater harm was classified as minor, though harm to the skin was considerable and more frequent. Therefore, the scientists concluded that the extent of added benefit from pirfenidone should be classified as "no proven added benefit." To reach this conclusion, one group of study participants was treated with pirfenidone in combination with best supportive care and the comparator group was treated with best supportive care alone. No added benefit could be proven for the outcomes "mortality," "health-related quality of life" and "morbidity," as measured by dyspnea and supplemental oxygen treatment. The patients' exercise tolerance is an aspect of morbidity and was examined using the 6-min walk test. The proportion of the participants for whom the distance walked in 6 min decreased by more than 50 m in the course of the study, and was statistically significantly lower under pirfenidone treatment than under best supportive care alone, though this criterion was specific post hoc. The greater harm under pirfenidone treatment was established for non-serious adverse events. The proportion of patients who discontinued treatment for this reason was greater under pirfenidone.

ACCELERATED APPROVAL

The FDA has approved Prevnar 13, a pneumococcal 13-valent conjugate vaccine, for use on people over 50. The vaccine can prevent pneumonia and disease caused by Streptococcus pneumonia, which typically causes pneumococcal pneumonia and can become more invasive, entering the

spinal fluid or blood. Prevnar 13 is made by Pfizer while GlaxoSmithKline markets a similar product under the name of Synflorix. These have already been approved for use in children ages 6 weeks through 5 years. In randomized, multicenter studies, people 50 and older received either Prevnar 13 or Pneumovax 23, a licensed pneumococcal vaccine also approved for this age group. Prevnar 13 induced antibody levels that were either comparable to or higher than the levels induced by Pneumovax 23. The terms of the FDA's accelerated approval means that the product can be more widely used while full clinical trials are conducted. Reported by Rupert Shepherd in Medical News Today, Copyright Medical News Today.

ASTHMA CODE

Researchers at Johns Hopkins have embarked on a four-year effort to map the genetic code of a thousand people of African descent, in an effort to find genetic variations underlying asthma and to explain why the disease disproportionately afflicts blacks. The researchers contracted with a San Diego, CA company to create a commercially available, customized gene chip, or DNA microarray test, dubbed the "African power chip," to quickly find single mutations in genetic materials from blacks that may be associated with heightened disease risk. Researchers plan to sequence the genomes of blacks selected from among an international group of people participating in existing genetic studies.

PTSD AND RESPIRATORY PROBLEMS

Researchers at Stony Brook University School of Medicine have found a link between two health problems among WTC first responders: respiratory illness and post-traumatic stress disorder. The researchers used data from 8,508 traditional responders, primarily police officers, and 12,333 non-traditional responders, including maintenance and transportation workers, and found a definite correlation between PTSD and respiratory symptoms, with evidence that PTSD might play a mediating role in the exposure-symptom relationship. The researchers found lower rates of probable PTSD among police (5.9%) than non-traditional responders (23%). Somewhat fewer police (22.5%) suffered from respiratory symptoms than non-traditional responders (28.4%). Pulmonary function test results were similar in both groups. Statistical analyses showed that PTSD and respiratory symptoms were moderately correlated, and PTSD was potentially mediating the relationship between WTC exposure and respiratory symptoms in both groups.

NO KIDDING

Diesel exhaust particulates and house dust extract cause pulmonary inflammation that aggravates asthma, according to researchers at Boston University School of Medicine. Exposure to both HDE and DEP demonstrated increased mucus production and higher airway resistance compared to exposure to only HDE. Pulmonary inflammation was measured by oxidative stress, respiratory physiological features, inflammatory cell recruitment and local CXC chemokine production, or soluble mediators of inflammation. The research showed a direct link between air pollution and exacerbation of pre-existing pulmonary diseases, like asthma.

ANOTHER REASON

Adults with aspirin-exacerbated respiratory disease are three times more likely to have been exposed to second-hand smoke during their childhood compared with those without the condition, according to the American College of Allergy, Asthma and Immunology. About 10% of asthma sufferers and a third of asthmatics with chronic sinus inflammation are affected by aspirin-exacerbated respiratory disease (AERD). Most are unable to take aspirin without suffering an attack or other respiratory symptoms, even though they were able to take it previously. Researchers surveyed 260 couples where one partner suffered from asthma and AERD. Those suffering from AERD were over three times more likely to have been exposed to secondhand smoke as children, and five times as likely to have been exposed as children and adults. Smokers had a one-and-a-half times higher risk of AERD compared with those who never smoked. Information reported by Petra Rattue, Medical News Today, copyright Medical News Today.

TAKE AS PRESCRIBED

A quarter of severe asthma attacks could be prevented if patients took their medication as prescribed, according to researchers at Henry Ford Hospital. They noted that their study was the first time that asthma medication use has been tracked closely over time and related to the likelihood of severe asthma attacks. The researchers measured changes in medication use over time and estimated the effect of ICS use on asthma attacks among 298 patients, who were followed for two years and had 435 asthma attacks during that time. Every 25% increase in ICS adherence was associated with an 11% decrease in asthma attacks. Causal use of medications was not enough, especially among patients whose asthma was not controlled.

WHOA THERE

A trial evaluating the intravenous infusion of salbutamol in patients with ARDS was stopped after patients receiving the drug had increased mortality and showed no improvement in outcomes. Researchers with the BALTI-2 study said that routine treatment of ARDS using such β-2 agonists cannot be recommended. An earlier BALTI study said that intravenous salbutamol reduced extra vascular lung water and plateau airway pressure in ARDS patients. The BALTI-2 study was designed to assess the effects of salbutamol on clinical outcomes, including mortality, in a much larger patient population. In a randomized controlled trial on 326 intubated and mechanically ventilated patients with onset of ARDS within 72 hours, researchers randomly assigned 162 patients to receive salbutamol and 164 patients to receive placebo for up to 7 days. The primary outcome was defined as death within 28 days of randomization. However, recruitment was halted due to safety concerns following the second interim analysis. The researchers noted an increased mortality rate in the salbutamol group, with 55 (34%) of 161 patients dying in the salbutamol group compared with 38 (23%) of 163 patients in the placebo group. This translates into an increased death risk of 47% for those in the salbutamol group. The researchers also discovered reduced ventilator-free days and organ failure-free days in the salbutamol group compared with the placebo group. The researchers reported: "Treatment was poorly tolerated because of tachycardia, arrhythmias, and lactic acidosis. These findings were unexpected... Routine use of β-2 agonist therapy in mechanically ventilated patients with ARDS cannot be recommended." Information is reported from an article written by Petra Rattue, Medical News Today, copyright Medical News Today.

CONTROLLED BURN

Lung function decreased with successive days of exposure to smoke among firefighters working prescribed burns, according to researchers at the University Of Georgia. Their study

was designed to investigate whether firefighters experienced a decrease in lung function working at prescribed burns compared with days they spent away from the fires. Previously, researchers had looked only at changes in lung function of wildland firefighters on days with exposure to smoke. Over a 10-week season, the respiratory functions of 26 firefighters who were studied slowly declined.

SUGAR CLOCK

Researchers at the Salk Institute for Biological Studies have found a link between the body's biological clock and sugar metabolism system, which may help avoid the serious side effects of drugs used for treating asthma, allergies and arthritis. It was discovered that the proteins known as cryptochromes, which control the body's biological rhythms, also interact with metabolic switches that are targeted by certain anti-inflammatory drugs. The finding suggests that side effects of current drugs might be avoided by considering patients' biological rhythms when administering drugs, or by developing new drugs that target the cryptochromes. The researchers noted that glucocorticoids, which regulate sugar in blood, also play a role in regulating inflammation and are used as anti-inflammatory drugs for diseases caused by an overactive immune system, such as allergies, asthma and rheumatoid arthritis. However, they can disrupt normal metabolism, resulting in dangerous side effects, including excessively high blood sugar levels, insulin resistance and diabetic complications. Cryptochromes interact with glucocorticoid receptors, helping to regulate how the body stores and uses sugar. They regulate glucocorticoid action, and thus are central to how the biological clock interacts with the daily metabolism of nutrients. By taking into account the daily rise and fall of cryptochrome levels doctors might be able to better time administration of glucocorticoid drugs to avoid certain side effects related to sugar metabolism. This research may also explain the connection between sleep and nutrient metabolism, including why people with night jobs are at higher risk for obesity and diabetes.

HOW LUNGS GROW

Not like we thought, according to researchers at the University of Leicester. They've discovered that alveoli are constantly being formed, not just that they develop before birth and quit increasing at about three years. It was believed that there was no further increase in the number of alveoli beyond that age, and that the existing alveoli just expanded as the lungs grew bigger until final adult size was reached. The researchers studied over 100 healthy volunteers aged between 7 and 21 years. Each volunteer had a range of breathing tests and then an MR scan, during which they breathed in hyperpolarized helium and held their breaths. The helium is hyperpolarized so that the molecules all line up in one direction and it then behaves like a magnetized gas. Within the scanner, researchers could measure how the magnetism decays, and this in turn depends on the size of the alveoli, which contain the helium. The researchers studied small children, whose lungs contain approximately one liter of air, and full-grown adults with lung volumes of around four liters, and found very little difference in the size of the alveoli across everyone studied. If the size of the alveoli were hardly changing, this could only mean that as lungs increase in size, people must be growing new alveoli.

PLAGUE!

New research from the University of North Carolina at Chapel Hill School of Medicine has revealed some info on how the plague bacterium Yersinia pestis goes undetected in the initial day of lung infection. Most infectious microbes trigger an antimicrobial response within a few hours after infection. However, with Y. pestis, nothing is apparent for about 36 hours, even though the bacteria reproduce rapidly, and death comes in a day or two. The researchers wanted to find out if the organism was avoiding detection or if it was suppressing the immune responses of the lungs, and the researchers said their findings suggest the latter. The researchers mixed a fully virulent Y. pestis strain and a mutant strain known not to be infectious and the mix was given to a lab animal. The non-virulent strain grew nearly as well as the non-virulent strain. The researchers tried other microbes as well, but as long as the virulent bacteria were present, the non-virulent organisms grew. Thus, researchers said that looking at the genetic differences between the two species of Y pestis may reveal the mechanism responsible for the microbe's exclusive phenomenon.

CAT

A study by University College London revealed that the COPD Assessment Test (CAT) can accurately evaluate exacerbation severity in individuals with

COPD. The researchers noted that incorporating CAT scores into the assessment of COPD patients may provide a standardized objective method for assessing symptom severity in both clinical practice and clinical trials. An eight-item CAT questionnaire was completed by 161 COPD patients and by 75 patients during 152 treated COPD exacerbations. Participants who experienced frequent exacerbations had considerably higher baseline CAT scores than patients with infrequent exacerbations. In the 152 exacerbations evaluated, CAT scores increased considerably from an average baseline value of 19.4±6.8, to a value of 24.1±7.3 at exacerbation. CAT score from baseline to exacerbation onset were weak and considerably associated to change in CRP, but not to change in fibrinogen. The team found that increases in CAT score at exacerbation were linked to decreases in forced expiratory volume in one second (FEV1). Using symptom diary cards, the researchers determined median recovery time was considerably associated to the time required for CAT scores to return to baseline. Therefore, the researchers noted that the CAT can be used as a score of the multi-dimensional nature of COPD exacerbation severity. Information above was written by Grace Rattue for Medical News Today, copyright Medical News Today.

POLLUTED KIDS

An international study of asthma at the University of Massachusetts Amherst has incorporated incidents caused by air pollution and reveals that the costs for childhood asthma have risen sharply. The overall financial burden of asthma caused by pollution is substantially higher than originally indicated by traditional risk assessments. Researchers conducted their study in Long Beach and Riverside, CA, communities with high regional air pollution levels and large roads close to residential neighborhoods. The total additional asthma-specific costs at the study site due to traffic-related pollution amounts to approximately $18 million per year, with nearly half of the cost accounting for new asthma cases caused by pollution. The findings revealed that a single incident of bronchitic symptoms cost an average $972 in Riverside and $915 in Long Beach. People living in cities with high traffic-related air pollution bear a higher burden of these costs, compared with those in less polluted areas, with the total annual cost for a typical asthma case at $3,819 in Long Beach and $4,063 in Riverside. The largest share of the cost of an asthma case was the indirect cost of asthma-related school absences, which also caused parents to miss work. The researchers concluded that traditional risk assessment methods for air pollution have underestimated both the overall burden of asthma and the cost of the disease associated with air pollution. Information for the above is from an article written by Petra Rattue for Medical News Today, copyright Medical News Today.

BIG AND ASTHMATIC

Accelerated growth in the first three months of life, though not fetal growth, is associated with an increased risk of asthma symptoms in young children, according to a new study from Erasmus Medical Center in the Netherlands. Researchers followed 5,125 kids from fetal life through four years old. Accelerated weight gain from birth to 3 months following normal fetal growth was associated with increased risks of asthma symptoms, including wheezing, shortness of breath, dry cough, and persistent phlegm. The associations between accelerated infant growth and risk of developing asthma symptoms were independent of other fetal growth patterns and tended to be stronger among children of atopic mothers. The researchers speculated that accelerated weight growth in early life might adversely affect lung growth and might be associated with adverse changes in the immune system.

BACK TO NATURE?

With wood-burning stoves a popular source of heating in many countries, a Norwegian researcher with the country's Institute of Public Health has studied the influence of combustion conditions on the emissions and their health effects. The physical and chemical properties of particulate matter from wood-burning have great influence on how these particles may affect our health, and worsening of cardiovascular diseases and respiratory diseases such as asthma and chronic obstructive pulmonary disease was the researcher's main concern. During good combustion conditions with sufficient oxygen supply and high temperature, most potentially harmful organic substances will be burnt in the stove. Wood-burning particles can be split into three classes. Those emitted from poor combustion conditions ("smouldering" combustion) contain relatively large amounts of unburned organic substances from the wood, some of which may be carcinogenic, such as polycyclic aromatic hydrocarbons (PAHs). These particles are water soluble and are assumed to be removed relatively quickly from the lungs. With improved combustion conditions (burning with flames), carbon particles with an insoluble core are formed. Depending on how good the combustion conditions are, the carbon particles have varying amounts of organic compounds on the surface. These particles are likely to remain in the lungs for longer periods of time since they are insoluble. With complete combustion, for instance in pellet stoves, all the organic material in the wood is broken down in the combustion chamber. Any particles like potassium sulphate will dissolve quickly in the lung lining fluid and thus be removed. It was recommended that old stoves be replaced with cleaner-burning new ones. Some recommendations: use dry wood; light the fire on top so gases will rise, meet the flame, and ignite. Also, heating efficiency is thus gained.

SMOKIN'

A Loyola University Chicago Stritch School of Medicine study found that burn patients who died from injuries had lower inflammatory responses in their lungs than patients who survived. Researchers followed 60 burn patients in Loyola's Burn Center. Patients with the worst combined burn and smoke-inhalation injuries required more time on the ventilator, in the intensive care unit and in the hospital. They also were more likely to die. Also, patients who died were older and had larger injuries than patients who survived. Researchers measured concentrations of 28 immune system modulators in fluid collected from the lungs of patients within 14 hours of burn and smoke-inhalation injuries, which are proteins produced by leukocytes and other cells, including those that line the airway. Some of the modulators recruit leukocytes to areas of tissue damage or activate them to begin the repair process that follows tissue injury. The researchers had expected to find higher concentrations of modulators in patients who died, because sicker patients tend to have more active inflammatory responses, but they found the opposite: patients who died had lower concentrations of these modulators in their lungs. The researchers concluded that the immune response to injury remains incompletely understood and additional effort is required to further improve survival of the burn-injured patient.

PRODUCTS

CLEARED

Masimo announced FDA 510(k) clearance and full market commercial launch of the Masimo Pronto-7, a palm-sized handheld device designed for quick and easy noninvasive spot-checking of total hemoglobin (SpHb), SpO2, pulse rate, and perfusion index. It was hailed as a "potential game-changing technology" by Dr Andrew J. Schuman, adjunct assistant professor of pediatrics at Dartmouth Medical School, contributing editor for Contemporary Pediatrics, and a practicing pediatrician in New Hampshire, who reviewed the device prior to FDA clearance. He said the new Pronto-7 is so innovative it has the "potential for significantly improving pediatric practice… [and] can help healthcare providers expedite the diagnosis and treatment of anemia in children and adolescents. Not only does it represent an exciting medical advancement in point-of-care testing, but it also provides pediatricians with a high-tech alternative to painful venipuncture or finger stick blood sampling that, until now, has been the only way to measure hemoglobin levels in our young patients. Parents and pediatricians will also appreciate our new ability to screen without the scream." With FDA 510(k) clearance and full commercial availability of the new Pronto-7 device, which includes expanded sensor size options to accommodate a wider range of finger sizes and the addition of a Max Sensitivity Mode, clinicians throughout the United States will be able to quickly and conveniently measure total hemoglobin, SpO2, pulse rate, and perfusion index without removing a drop of blood. The Pronto-7 offers a breakthrough solution for measuring hemoglobin in less than one minute without the needles, risk of blood contamination, hazardous medical waste, laboratory analysis, and patient discomfort associated with traditional blood tests. With dimensions of just 13 cm x 7.2 cm x 2.5 cm (5.1" x 2.8" x 1") and weight of 296 grams (10.5 ounces), the palm-sized Pronto-7 puts the power of noninvasive hemoglobin spot-check testing, along with SpO2, pulse rate, and perfusion index, into any clinician's hands in various clinical settings, including physician offices, hospitals, and clinics. Because of the device's embedded 802.11 b/g and Bluetooth communication capability, wireless printing or emailing of test results is enabled and future upgrades will allow for wireless transmission to electronic health record (EHR) systems. Masimo is the first company to commercially introduce continuous and spot-check noninvasive total hemoglobin devices. Prior to the introduction of the Pronto-7, Masimo received FDA 510(k) and CE mark clearance and first introduced the ability to noninvasively and continuously measure total hemoglobin (SpHb) in 2008 using its Radical-7 bedside Pulse CO-Oximeter. In 2009, Masimo launched Pronto, its first handheld noninvasive spot-check device for point-of-care hemoglobin, SpO2, and pulse rate testing. Contact masimo.com.

INNOVATIVE PRODUCTS

Respiralogics, based in San Marcos, CA and owned and operated by the management team of David Thompson and Beth Keifer, collectively brings more than 60 years of clinical, educational and technical expertise in the critical care field. The longtime partners' goal is to free clinicians to focus on patient care. The company's suite of products focuses on the respiratory care field. Respiralogics' product line includes: Babi.Plus Bubble nCPAP System for delivery of non-invasive respiratory support for premature and small infants; Sil.Flex Stoma Pad and Sil.Flex TC Pad, ergonomically designed cushions intended to redistribute pressure at stoma sites, improving patient comfort and minimizing skin breakdown; Danny Ties, unique tracheostomy tube holders with a softer and more comfortable fit around the neck for patients of all ages; and Venti.Plus Test Lungs and Babi.Plus nTest Lung, great tools to simulate the respiratory system that demonstrate mechanical ventilator applications and perform ventilator circuit testing prior to clinical use. (Babi.Plus, Sil.Flex and Venti.Plus are trademarks of A Plus Medical. Danny Ties is a trademark of Leckie Medical Products, Inc.) Visit www.respiralogics.com.

REGISTERED

Discovery Laboratories, Inc announced AFECTAIR is now registered with the FDA and cleared to be marketed in the US. AFECTAIR is a proprietary patient interface technology that simplifies delivery of aerosolized medications to patients requiring ventilator support. AFECTAIR originates from the AEROSURF development program and is a proprietary disposable ventilator circuit/patient interface connector that simplifies the delivery of aerosolized medications to critical-care patients requiring ventilatory support from either intermittent

mechanical ventilation or continuous positive airway pressure. To date, in vitro studies suggest that the AFECTAIR technology may be an effective new solution for delivering aerosolized medicine to patients receiving ventilator support while providing healthcare professionals with a simplified alternative to current practices. Discovery Labs is also pursuing a European Conformity (CE) marking for commercialization of the initial AFECTAIR products in the European Union (EU) and believes that it may be in a position to initiate the commercial introduction of the initial AFECTAIR products in EU in late 2012. Contact discoverylabs.com.

READY TO GO

Neotech Products, Inc (Valencia, CA), announced that the Neotech RAM Cannula is available for sale and trial. The Neotech RAM Nasal Cannula is a simple, revolutionary interface for nasal respiratory support, specifically designed for premature babies or critically ill babies in the neonatal intensive care unit (NICU). The Neotech RAM Cannula has been clinically proven as a safe, effective and gentle method for delivering CPAP, PPV, IMV and continuous oxygen, as well as many other modes of respiratory support. This unique cannula has a universal 15mm adapter, soft, curved prongs, and is currently available in three sizes with more sizes for larger patients in development. The shorter, kink-resistant tubing allows for better pressures, better flows, and less dead space. The Neotech RAM Cannula is compatible with HFOV, T-Piece resuscitators, traditional wall oxygen, most ventilators and Bubble CPAP. Also available is an optional oxygen adapter that allows for the transition from NCPAP or NIPPV to oxygen support without having to change the cannula. To date, the cannula in clinical trial has been used for more than 3,000 patient hours. The device allows nurses and respiratory therapists to deliver the therapy required for their babies in a gentle and effective manner. It's also great for parents because they can see their baby's face, and they can hold their baby much easier during Kangaroo Care. Contact ramcannula.com or call (800) 966-0500.

BREATH DELIVERY

The Philips Respironics V60 ventilator has expanded its breath delivery options to include proportional pressure ventilation (PPV). This innovative mode delivers pressure and flow in proportion to the patient's effort,[1] enabling the patient to more efficiently adjust their breathing to meet their changing requirements. Patients receive the breathing support they need when they need it. Proportional assist modes have been shown to lower peak pressures as compared to pressure support and may improve patient comfort.[2] Patient comfort leads to therapy compliance, which may improve the success of noninvasive ventilation. PPV mode allows the clinician to decrease support via one parameter adjustment, PPV%, when the patient is ready to take on a greater proportion of the work of breathing. This new mode is distinctive as it can be used noninvasively, taking NIV even further while also being available for invasive ventilation. [1. Gay P., Hess D., and Hill N. Noninvasive proportional assist ventilation for acute respiratory insufficiency comparison with pressure support ventilation. Am J Respir Crit Care Med. 2001; 164:1606-1611. 2. Younes M. Proportional assist ventilation, a new approach to ventilatory support. American Review of Respiratory Disease 1992; 145(1):114-120.]

REAL-TIME

Respiratory Technology Corporation (Restech) announced the launch of its Primus Probe for the Dx-pH Measurement System, adding to the world's first and only system for monitoring real-time aerosolized pH currently used throughout the United States and in thirty countries worldwide. With a 25% smaller tip and softer polymer catheter than the standard Restech Dx-pH Probe, the Primus is ideal for patients who are more sensitive or have less nasopharyngeal clearance. The tip of the probe is less than 2.4 millimeters in diameter and the smooth, flexible catheter allows for easy insertion through a small naris. Visual placement in the oropharynx guided by a blinking LED eliminates the need for manometry, fluoroscopy, or x-ray. Because it sits comfortably in the airway, the Primus Probe does not interfere with speaking or swallowing while the patient continues with his or her normal daily routine. The Dx-pH Measurement System measures pH in the airway. The small pH sensor at the tip of the probe is unique in its ability to measure pH in a non-liquid environment, such as the oropharynx. By monitoring the pH levels in the pharynx, the Dx-System enables physicians to assess presence of laryngopharyngeal reflux and evaluate it as a possible contributor to their patients' symptoms. The Dx-pH Probe and Primus Probe house a micro sensor at the end of a catheter. The probe is placed posterior to the uvula in the oropharynx. Because it sits high in the airway, swallowing and speaking are not impeded. The small size and minimally invasive position allow patients to carry on normal, everyday activities including eating, talking, and sleeping with more comfort than conventional esophageal pH probes. The measurements taken by the pH sensor is sent wirelessly to a recording device which the patient carries throughout the study period. Upon completion of the study (usually 24 hours), the patient returns to the physician's office where the data is downloaded and presented graphically for analysis using Restech's custom DataView software. Contact restech.com, (800) 352-1512.

APPROVED

Uptake Medical announced that it received Australian Therapeutic Goods Administration (TGA) approval for its InterVapor System for endoscopic lung volume reduction for the treatment of severe emphysema. InterVapor is the first non-surgical, endoscopic lung volume reduction system for the treatment of severe emphysema that uses the body's natural healing processes without leaving implants or foreign materials in the lung. This announcement follows the procedure's receipt of the CE mark in September, 2011 and the first commercial procedure in Germany in November. Clinical efficacy of InterVapor has been established by the multi-center VAPOR trial which showed a reduction in lung volume as well as statistical and clinical significance in lung function improvement (FEV1) and health-related quality of life (SGRQ) at six months. In clinical studies, InterVapor has demonstrated clinically meaningful improvements in breathing function, exercise capacity and quality of life. Contact uptakemedical.com.

POINT OF CARE

MediPurpose, a master distributor and manufacturer of medical products, announced its continued partnership with point-of-care (POC) diagnostic equipment manufacturer EKF Diagnostics. MediPurpose supplies SurgiLance safety lancets for use with EKF Diagnostics' POC blood analysis equipment, used in tests for glucose, lactate, hemoglobin, hematocrit and HbA1c. EKF Diagnostics manufactures a range of equipment that analyzes vital organ function through blood values. Its latest offering is the Quo-Lab, which tests the HbA1c levels in the bloodstream. HbA1c values are the best long-range indicators of elevated blood glucose levels and are used in both the detection of pre-

diabetes, as well as in monitoring blood sugar control in Type 1 and Type 2 diabetes patients. SurgiLance is currently available in six models, ranging from 18–26 gauges and 1.0–2.3 mm penetration depths. EKF Diagnostics Holdings, PLC specializes in the development, production and distribution of near-patient analyzers for use in the detection and management of diabetes, anemia, lactate and kidney-related diseases. Founded in 1999, MediPurpose is a leading medical device company headquartered in Singapore, with offices in the United States and Europe, known for its babyLance heel incision device, SurgiLance safety lance and MediPlus advanced wound care products. Contact medipurpose.com/surgilance or ekfdiagnostics.com.

SHOW US YOUR PAPERS

Itamar Medical Ltd's recent newsletter presented info on a number of papers related to its PAT (Peripheral Arterial Tone) signal technology, including Impact of Acute Smoking on Artery Function in Healthy Chronic Smokers. The PAT signal is a non-invasive "window" to the cardiovascular system and the autonomic nervous system. The company's WatchPAT provides ambulatory diagnosis of sleep-related breathing disorders and sleep architecture. It was named as one of the top 10 medical innovations for 2010 by the Cleveland Clinic. The device is worn on the patient's wrist and uses a noninvasive finger-mounted probe to measure signals that indicate changes in the autonomic nervous system. Contact itamar-medical.com.

HIRED

Mada International Limited announced the hiring of Rafael Bassi as International Sales Manager for Latin America. Rafael is a native of Colombia, SA and earned his BBA degree from Corp Universitaria Simon Bolivar in Barranquilla. He brings over 10 years of sales experience focused on Latin America. Mada International offers a wide range of ventilation and respiratory care products. Contact madainternational.com.

TAKING THE LEAD

Dräger Medical, Inc has introduced a new single-patient use ECG leads that help reduce the risk of nosocomial infections that are on the rise in hospital environments. The high-quality disposable leads support hospital guidelines for hygiene and help reduce the cost of care related to hospital acquired infections. Available as 3- and 5-lead standard color coded sets, the single-patient use leads are fully shielded and provide signal quality equal to reusable leads. Complementing the existing portfolio of reusable leads, the single-patient use leads have been extensively tested and certified for use with the Dräger Infinity patient monitoring product range. The single-patient use ECG leads are easily applied and eliminate the need for time-consuming preparation. The flexible ribbon cable also provides more comfort for patients and caregivers. The flexible cables also have a unique ability to adapt to patient size. Contact draeger.com.

RENEWED

CareFusion and Fisher & Paykel Healthcare announced a three-year renewal of their longstanding agreement providing CareFusion the exclusive right to distribute Fisher & Paykel Healthcare products into the US hospital market. Under the agreement, CareFusion, through its Air*Life* Respiratory Consumables business, will continue to serve as the exclusive US distributor of Fisher & Paykel Healthcare's extensive portfolio of respiratory consumable products, including the MR850 Heated Humidification System with Evaqua circuit technology, AIRVO high flow device, Optiflow nasal cannula, and FlexiFit non-invasive interfaces. CareFusion employs more than 14,000 people across its global operations, and Fisher & Paykel Healthcare's products are sold in more than 120 countries. Contact carefusion.com or fphcare.com.

ON THE GO

Philips Respironics, a unit of Royal Philips Electronics is introducing its latest advancement in oxygen therapy. SimplyGo is the only portable oxygen concentrator (POC) to offer continuous flow (up to 2 liters per minute) and pulse-dose delivery in a single device weighing 10 pounds or less. With this combination of capabilities, the SimplyGo POC helps homecare providers manage the therapy and lifestyle needs of nearly all oxygen users. SimplyGo is different from smaller devices because it is also capable of delivering oxygen continuously, similar to stationary concentrators used at home. With oxygen output of up to four times that of some lightweight POCs, SimplyGo can meet the portable needs of nearly all oxygen users including those who are highly active or require continuous flow. Philips designed its latest portable oxygen concentrator with a long-life compressor, high-impact resistant design and oversized cart wheels. SimplyGo was tested and subjected to extreme conditions, including impacts, vibrations and temperatures, to deliver reliable performance day in and day out in real-life conditions experienced by oxygen users. Contact philips.com/simplygo.

CLEARED FOR TRANSPORT

Hamilton Medical, Inc has received FDA 510(k) clearance on the Hamilton T1 Transport Ventilator. The Hamilton T1 ventilator features a compact, powerful design that increases the availability of appropriate modes of therapy for ventilated intensive care patients outside the hospital. Small enough to fit into any mobile ICU environment, the Hamilton T1 covers the full range of clinical requirements including ventilation with closed loop ventilation, Adaptive Support Ventilation (ASV) and non-invasive ventilation (NIV). The Hamilton T1 delivers an ICU ventilation solution in a transportable platform, appropriate for pediatric to adult patients. The T1 delivers reliable data and easy-to-follow user guidance for improved patient outcomes, together with low operating costs throughout the working life of the investment. Contact hamilton-medical.com.

OXIMETRY ROUNDTABLE

Nonin Medical, Inc

Tell us about your oximetry products currently available.

Nonin Medical, Inc is the inventor of finger pulse oximetry and a global leader in designing and manufacturing noninvasive physiological monitoring solutions. The Nonin name and Onyx brand are recognized worldwide as the gold standard in pulse oximetry. Our branded and OEM offerings include pulse oximeters, sensors, software and accessories. During the past five years, Nonin has expanded its monitoring solutions to include capnographs and cerebral tissue oximeters, which are used in perioperative procedures. Nonin offers a variety of SpO2 professional and consumer finger pulse oximeters, tabletops, handhelds and wrist-worn devices. Our newest professional finger oximeter is the **Onyx Vantage 9590 Finger Pulse Oximeter**. It is the only finger pulse oximeter brand with scientifically proven accuracy in the most challenging cases, including patients with low perfusion or dark skin tones. The proven PureSAT technology provides accuracy in the widest range of patients and settings, and one unit

works from pediatric to adult patients. The Onyx Vantage has 6,000 spot checks on two AAA-batteries and a four-year warranty. Visit www.OnyxVantage.com for more information. For patient home use, the **Nonin GO_2** finger pulse oximeter (available with a physician prescription) provides highly accurate, quick and easy pulse rate and SpO2 measurements. The GO_2 is a helpful tool to use to evaluate vital signs during activities and at rest, helping patients take control and live life to the fullest. Visit www.go2nonin.com for more information.

What oximetry products do you have in development?
Nonin Medical is continually leading the advancement and implementation of new physiological monitoring technologies designed to improve patient care. Technologies that are versatile and can work on the broadest base of patients are in highest demand. Nonin has products today that meet these needs, and we continue to design products that simplify the exchange of information, which should ultimately result in lower healthcare costs and improved patient care. We are continuing innovation on our key technologies so they are more sensitive and work on more patients and more parameters. Additionally, we are looking to advance our technologies by combining and integrating technologies and looking towards communication of devices not just among a single manufacturer or platform, but interconnectivity.

Discuss the range of your oximetry products' applications, and where your product can be used.
Our quality, cost-effective and highly accurate noninvasive monitoring devices address patients from neonatal to adult, chronic respiratory to acute disorders, continuous monitoring to individualized spot checking and even direct to the patient population and sleep assessments. Nonin has continued to expand its parameter offerings, including exhaled CO_2 measurements of respiratory distress and tissue oximetry that can be used in a variety of applications. Our products are used in hospital, physician's offices, long-term acute care, skilled nursing facilities, sleep, emergency medical services, and homecare settings. We continue to develop technologies that can meet the needs and demands for continuum of care – from the hospital to the home. Nonin prides itself on our products' accuracy and ability to work where you need, it when you need it – including patients with low perfusion. Most brands of oximetry devices can take an accurate reading on a healthy patient, but it is when you get a more challenging situation that Nonin's ability to provide reliable readings in the widest range of patients and settings really stands out.

What type of customer assistance and/or training do you offer?
Nonin has been a leader in our proactive approach with educational materials and clinical support. Throughout the years, we have worked with key clinicians in developing or supporting the creation of educational materials. For example, Nonin was the sponsor of the WONCA/International COPD Coalition's "Clinical Use of Pulse Oximetry: Pocket Reference" to expand knowledge about the clinical applications and benefits of pulse oximetry. We worked with Dr Thomas L. Petty to create the booklet titled, "Your Personal Oximeter: A Guide for Patients." We supported the efforts of Dr Brian Tiep in the creation of a patient education video on pulse oximetry. All of these resources, along with many others, are available on www.nonin.com to help educate and support clinicians and customers. (Nonin can also be contacted at (800) 356-8874.)

Finally, we are the only oximetry company to support GOLD (Global Initiative for Chronic Obstructive Lung Disease) and the December 2011 revision "Global Strategy for Diagnosis, Management and Prevention of COPD." Nonin believes in providing clinical support and outstanding products for clinicians and patients.

FOCUS PREVIEW

Ambulatory Monitoring Inc

Booth 811

Since actigraphy is a cost-effective and important component in respiratory care and sleep medicine, be sure to visit Ambulatory Monitoring Inc's Booth #811 to see our latest **Motionlogger Actigraph** models and meet our personnel, who will be happy to discuss your actigraph needs and answer any questions you may have.

Caire SeQual

Booth 819

What products will you be showing?
Caire SeQual manufactures oxygen therapy systems for the home healthcare industry. Caire's core product lines include liquid oxygen bases, ranging in size from 10-60 liters, giving patients the option of filling easily at home or on the go, and portable units, with sizes ranging from 4-8 lbs and estimated operation from 7-34 hours at 2 LPM. The **SeQual Eclipse** POC meets the ambulatory and round-the-clock oxygen needs of LTOT patients with technology that makes them smaller, quieter, and more reliable. We will be showing all of our signature products at the Focus exhibition. For any product-related questions, please call our customer service at (800) 482-2473.

Discuss educational/training materials you'll be distributing or promoting.
We offer a variety of educational materials regarding our various product lines. These include, but are not limited to, a variety of clinical studies and informational materials geared to both providers and patients.

Why should Focus visitors stop by your display?
The addition of the SeQual Eclipse and **SeQual Integra** market-leading portable and stationary oxygen concentrators to Caire's LOX solutions has broadened and complemented our portfolio. With product lines of the Eclipse, Stroller, HELiOS, Companion and Liberator, Caire SeQual has become the one source for a provider's oxygen needs. Caire SeQual is in booth 819, and at table #35 at the Manager's Reception.

Dräger

Booth 417

What products will you be showing?
The Dräger ventilation portfolio has been transformed with newly released products to address each area of specialty care. Our newest critical care ventilator is the Evita Infinity V500, and our infant-specific ventilator is the Babylog VN500. In addition to the new V-series ventilators, Dräger introduced its newest turbine-driven ventilator, the Savina 300 and newest transport

ventilator, the Oxylog 3000 plus during the AARC this past November. **The Evita Infinity V500** is a comprehensive critical care workstation that can provide for the needs of neonatal, pediatric, and adult populations. Newest features include a "Smart Pulmonary View," standardized nomenclature, PC-APRV with auto-release, and customizable weaning protocols. The **Babylog VN500** is a neonatal-pediatric specific ventilator which offers a wide array of therapies including oxygen therapy, non-invasive ventilation, and invasive modes. Critical to ventilating premature infants is proper monitoring and compensation; the VN500 provides for effective leakage identification and compensation and has the option to volume ventilate small babies to a TV of 2 cc's. The **Savina 300** focuses on the essential elements of ventilation. Whether in volume or pressure ventilation, the Savina 300 provides for both adult and pediatric patients in settings such as acute, emergency, sub-acute, or post-operative care areas. Both invasive and non-invasive ventilation is available to provide clinicians a greater degree of flexibility for patient care. The **Oxylog 3000 plus** is a compact transport ventilator that can provide for adult and pediatric patients down to 50 cc's tidal volume. In addition to an array of volume, pressure, and spontaneous modes of ventilation, the Oxylog 3000 plus can provide AutoFlow as well. Additionally, the Oxylog 3000 plus can provide for integrated capnography and data management/export.

Discuss educational/training materials that you'll be distributing or promoting.
Throughout the year webinar training on contemporary issues is provided to all interested clinicians. The most recent web-training sessions included such topics as APRV by Dr Nader Habashi and Neonatal Ventilation by Dr Martin Keszler. A complete series of monthly webinars will be offered throughout 2012 to all Dräger customers through www.intensivecareonline.com.

Why should Focus attendees visit your display?
Our 10x20 foot inline booth will showcase our entire portfolio of new products. Whether you are an adult critical care therapist, neonatal therapist, chronic care or focused on transport – there is something new to preview. Stop by and see the latest innovations in respiratory care.

Philips Respironics

Booth 403

Philips Respironics brings a patient's journey from the hospital to the home to the forefront at Focus 2012 with its solutions pathway—an interactive showcase of the latest advances for diagnosing, treating and managing long-term respiratory and sleep-disordered breathing illnesses. Attendees will walk through the unique patient-care model and progress from diagnosis to therapy and ultimately to compliance. The pathway features several "stops" that each include large, vertical monitors displaying videos of patients with commentary delivered by an on-screen healthcare professional. An aisle-facing video at the start of the pathway introduces patients and connects attendees to the patients and their conditions. Once inside the booth pathway, attendees follow each patient's story from hospital to home, highlighting the products relevant to each patient and disease state. A professional staff of docents engages booth visitors and helps guide them along the journey. Upon leaving the pathway, visitors will have an opportunity to visit product stations for hands-on demonstrations of our complete line of respiratory products, including noninvasive ventilators, oxygen delivery, respiratory drug delivery devices, and sleep diagnostic and therapy systems.

Philips Respironics, a global leader in the sleep and respiratory markets, is passionate about improving the quality of people's lives with solutions designed around the needs of customers and patients. That's why we align with caregivers to establish healthier living and healthier practices. Philips Respironics first considers the needs of our customers, their patients and caregivers and then introduces simpler and more intuitive innovations that consistently revolutionize the areas of sleep, oxygen therapy, ventilation and respiratory drug delivery. As a result, Philips Respironics is recognized worldwide as a pacesetter and as a valuable ally in better sleep and breathing.

MEDGRAPHICS

Booth 2018

What products will you be showing?
We will feature MEDGRAPHICS recent product developments and technology advancements, including **BreezeSuite WebReview** for test interpretation anywhere, anytime; **Platinum Elite Plethysmograph** and **Ultima Series** with Real Time Diffusion (RTD) MultiGas Technology, delivering clinically significant graphic data and immediate results; together with our latest version of BreezeSuite software incorporating the latest HIPAA – HITECH Security Safeguards protecting your patient's Identifiable Health Information.

Discuss educational/training materials you'll be distributing or promoting.
MEDGRAPHICS continues to provide educational opportunities with our annual Cardiorespiratory Diagnostics Seminar held in Orlando, FL October 1-3, 2012. Participants will advance their knowledge of diagnostic techniques, performance standards, quality assurance procedures, and clinical applications. The program format includes lectures, hands-on demonstrations and small group discussions – all conducted by a faculty of experts. In addition to our annual events, we sponsor and support numerous state, regional and local respiratory therapy initiatives.

What speakers or papers will your company be featuring?
Carl Mottram, BA, RRT, FAARC will be presenting on Exhaled Nitric Oxide Thursday, May 10th from 2:40 pm - 3:40 pm and Friday May 11th from 2:55 pm - 3:55 pm. He will also be presenting on The Six Minute Walk Test on Saturday, May 12th from 7:30 am - 8:30 am.

Why should Focus visitors stop by your display?
MEDGRAPHICS is a global leader of innovative solutions for diagnosis, monitoring and management of cardio-respiratory disease. With 35 years of leadership and innovation we offer a wide variety of products and services to meet your unique needs.

Neotech

Booth 206

What products will you be showing?
We will be debuting our new **Neotech RAM Cannula**, a simple, effective, safe interface for non-invasive respiratory support. We

will also be displaying our new **Little Sucker Cover**, made for the Little Sucker suctioning device, our most popular product.

Discuss educational/training materials you'll be distributing or promoting.
We'll have some clinical information and brochures to distribute.

Why should Focus visitors stop by your display?
Stop by to learn more about the amazing RAM Cannula and learn what it can do, how it can make your practice more effective, and how it can make your patient more comfortable!

Newport Medical

Booth 617

What products will you be showing?
Stop by the Newport Medical booth #617 to see the next generation of the **HT70** Ventilator family, the HT70 Plus. The HT70 Plus model includes an on-airway flow sensor and expanded capabilities. New features include exhaled volume monitoring, flow triggering and a Waves graphic screen that displays flow/ pressure/ volume waveforms. Both the HT70 and the HT70 Plus can be used in homecare, transport, hospital or longterm care. We'll be happy to give you our "5 minute Demo" that will show you all that the HT70 family of ventilators has to offer. We will also have our critical care ventilator, the **Newport e360T** in the booth to demonstrate our patented "FlexCycle" feature, only available on Newport ventilators. Clinicians will appreciate this feature that automatically adjusts expiratory threshold settings as patient conditions change. Used in conjunction with Automatic Leak Compensation and other patient comfort settings, FlexCycle can help improve synchrony. Sophisticated technology made easy and affordable – that's the e360T ventilator.

Discuss educational/training materials you'll be distributing or promoting.
The safe and effective use of our products is one of our highest priorities. We have a library of online and electronic training programs that we offer to our customers. Our newest addition is the HT70 Interactive Training Program. This module based program provides comprehensive training on the HT70 that the user can review at their own pace. If you own Newport products, stop by the booth, #617 and we'll get you the latest training materials for your ventilator.

Why should Focus visitors stop by your display?
Many visitors to the Focus conference are looking to expand their knowledge of the latest ventilator technology. If you are not familiar with Newport Medical's portable and critical care ventilators, please stop by. You'll find our products not only easy to use but surprisingly affordable. If you own or have owned Newport ventilators you should come to the booth and see the new products and accessories that we have to offer. Newport Medical's booth, 617, will be near the car giveaway display.

Philips Healthcare

Booth 403

What products will you be showing?
From our patient interface line, we will be showing our Respironics **AF531 NIV mask system** with interchangeable elbow connectors that allow one mask to be used for specialized procedures, such as bronchoscopy and medication nebulization. The AF531 also allows the connection of the same mask to dual-limb or single-limb circuits. In addition to the AF531, we will be showing our **XL Respironics PerforMax mask**, designed to better fit larger patients. We also have some new pediatric masks to show. On the ventilator side, we will be showing **VentAssist**, a software option for the NM3 respiratory profile monitor that gives real-time ventilation guidance and support for clinical decisions. We have a triggering mechanism on our V200 ventilator called **IntelliTrak**, which supports patient-ventilator synchrony even in the presence of leaks and dynamic hyperinflation. We will also be showing our **Trilogy 202** ventilator as well as our flagship **V60** ventilator. The V60 also has an exciting proportional pressure ventilation (PPV) option.

Discuss educational/training materials you'll be distributing or promoting.
Our Education Manager will have an internet connection showing clinicians how to access the Philips Online Learning Center to take courses for CEU credit. We will also have clinical pocket guides and interactive CD programs for all of our ventilators and monitors.

What speakers or papers will your company be featuring?
Philips will be providing an educational grant to the conference to be used at will.

Why should Focus visitors stop by your display?
Focus visitors know us as a leader in noninvasive ventilation. We always enjoy visiting with our valued customers and friends and hearing how they are using our products to make a difference in patients' lives. We hope they will enjoy seeing how we continue to take NIV further with our new ventilators, patient masks, and educational offerings.

Ventus Medical

Booth 313

What products will you be showing?
Provent Therapy is an FDA cleared, prescription-only device that utilizes nasal EPAP (expiratory positive airway pressure) to treat all levels of severity of obstructive sleep apnea (OSA) and related snoring. It may be an ideal treatment option for your patient who has rejected or is non-compliant with CPAP. The device consists of a small valve attached externally to each nostril with hypoallergenic adhesive. The valve acts as a one-way resistor, permitting unobstructed inspiration. During expiration, airflow is directed through small air channels, increasing resistance. This increased resistance during expiration creates EPAP which is maintained until the start of the next inspiration. As a result, the device helps pressurize and stabilize the upper airway during the critical end-expiratory period, when the airway has been found to be most narrow in the breaths prior to an apnea. Whereas CPAP provides positive pressure during both inspiration and expiration, EPAP only creates pressure during expiration. The **Provent Nasal Cannula** is a diagnostic tool to be used with the Provent Sleep Apnea Therapy device during sleep studies, enabling practitioners to confirm product efficacy. The Provent Nasal Cannula is indicated for the transmission

of respiratory airflow signals between the Provent Sleep Apnea Therapy device and the pressure transducers used with physiologic recorders during sleep studies.

Discuss educational/training materials you'll be distributing or promoting.
Patient education is important to adherence and compliance with Provent Therapy, and many educational and support materials are provided to healthcare providers and suppliers: • Detailed patient information is included in each Provent Therapy package. This includes steps and visuals on how to apply Provent Therapy, what to expect, and tips to acclimate. • A comprehensive training video that provides application instructions instructs patients on the proper application method, expectations and acclimation tips. • Comprehensive information is available at the Provent Therapy website, www.proventtherapy.com, including a detailed patient video, downloadable tip sheet and instructions. • A Provent Therapy product specialist is available through a toll-free number to patients who have questions about how to apply and get adjusted to using Provent. • A patient acclimation guide is provided to physicians and Provent Therapy suppliers. This acclimation guide contains steps and tips for successful acclimation to Provent Therapy and is a helpful at-home resource.

What papers will your company be featuring?
The device has been evaluated in multiple published studies including a 19 center, randomized controlled trial published in the journal SLEEP. Journal reprints are available at the Ventus Medical booth.

Why should Focus visitors stop by your display?
Visit the Ventus Medical booth to learn more about Provent Sleep Apnea Therapy and how it might benefit your patients. Come by to see the Provent device and pick up a reprint of the published studies.

VORTRAN
Medical Technology 1, Inc
Booth 703

What products will you be featuring?
The **VAR (VORTRAN Automatic Resuscitator)** is a unique single patient use, disposable resuscitator for use with patients weighing (10Kg & above). It provides consistent, reliable, hands free ventilatory support via a mask or endotracheal tube using a continuous gas flow source. The **VORTRAN-APM (Airway Pressure Monitor)** is a battery (9 VDC) operated, portable, self-contained device that is connected to the patient via the connection kits to monitor cycling conditions of resuscitators, such as the VORTRAN Automatic Resuscitator. Monitoring parameters include, Peek Inspiratory Pressure (PIP), Respiration Rate, Peek End Expiratory Pressure (PEEP), Inspiratory Time, and Expiratory Time. The APM also provides 3 alarm limits, High Pressure, High Rate, and a non-cycling alarm which are shown on the LCD display as well as an audible alarm. These settings differ from the adult (RED) and pediatric (BLUE) models for the best clinical practice. The **PercussiveNEB** is VORTRAN's next generation of high frequency intrapulmonary percussive nebulizers. It offers unique single patient, multiple use, with high frequency intrapulmonary percussive treatments. **VORTRAN Test Lung Kit Part # VTL-3600**: The VORTRAN Test Lung (VTL) Kit is ideal for use in training, demonstration, and testing applications to simulate respiratory response for both adult and pediatric. The VTL features a unique independent compliance adjustment for each lung (single and double lungs) and a set of three resistors (Rp5, Rp20 & Rp50) settings providing versatility and performance at an affordable price. The **VORTRAN-IPPB** is a new and unique single patient, multiple use IPPB treatment powered by the Pulmonary Modulation Technology (PMT). The VORTRAN-IPPB is easier to use and more cost effective than a conventional IPPB machine for the delivery of IPPB type treatments in the hospital or home care environment.

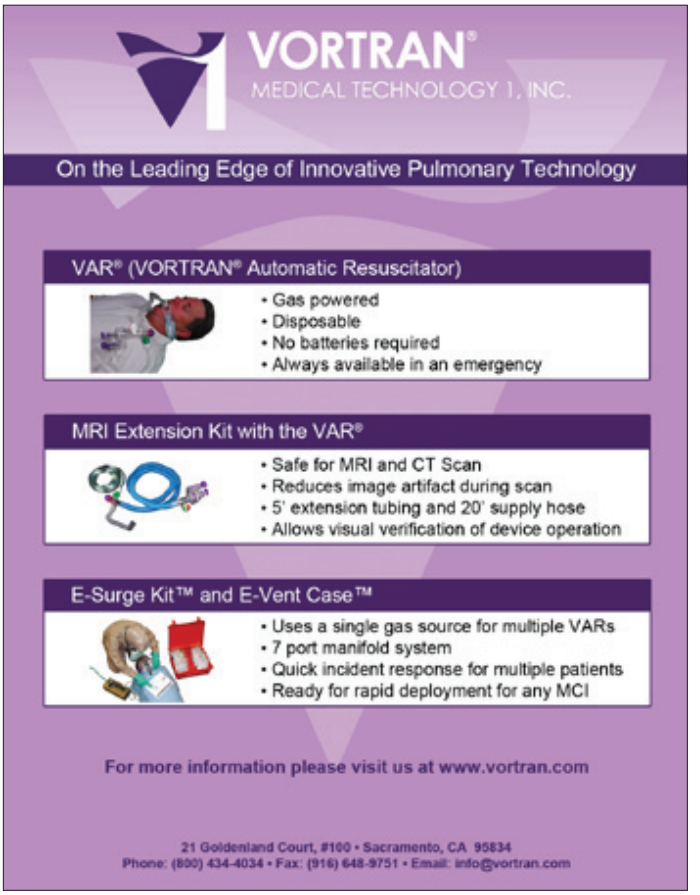
What educational opportunities will you be offering?
We will have a flyer for 3 FREE CEU's to all who visit our booth! Available online.

Why should participants visit your display?
Focus visitors should stop by our booth to play with the new Airway Pressure Monitor to see how they can have a transport vent for under $500.

COMPANY REVIEW

TRACOE medical GmbH

TRACOE medical, a German company, is one of the leading manufacturers of tracheostomy tubes with 60 years of experience and therefore a competent partner for physicians and patients. Special requirements call for special solutions, which is why TRACOE medical offers a complete product line consisting of various product families which complement each other. It starts with an assortment of tracheostomy tubes, and extend to items for postoperative care and rehabilitation. All tubes are



developed by TRACOE medical, as the company has the know-how for innovations to form practice-orientated products. As TRACOE medical distributes their CE-marked products via competent distributors to more than 80 countries worldwide it meets the requirements of the most demanding applications and complies with all relevant national and international guidelines and standards. They are registered and approved in many countries worldwide, including the United States (FDA 21CFR 820) and Canada (CanMDR). With the wide range of products and services, solutions for optimal patient care are provided. The company's international sales team is dedicated to support you with competent advice and assistance. To every problem there is a solution – TRACOE distributors and employees will find this solution together with you!

TRACOE *twist*: The most outstanding feature of TRACOE twist is an anatomically shaped neck flange that moves around two axes: vertically and horizontally (patent-registered). This allows patients to turn their head and neck without the tube exerting pressure on the trachea. TRACOE *twist* tubes are made of tissue-friendly polyurethane (free of DEHP). TRACOE *twist* tubes have very thin walls, which ensure maximum air flow (1/3 as thick as conventional tubes), therefore they are well-tolerated by patients. TRACOE *twist* tubes were originally developed for ventilation but in the meantime they have turned out as an optimal product for therapeutic treatment. Furthermore it is increasingly used by patients at home as well. Your investment is enhanced by a broad range of replacement parts and accessories.

TRACOE *mini*: Sometimes the greatest achievements are made on a small scale. A prime example is the TRACOE *mini* – the product line especially developed for newborns, infants and children. TRACOE *mini* tracheostomy tubes are particularly soft and equipped with a neck flange with a slanted bottom, providing the tube with an optimized and atraumatic fit. These tubes have very thin walls to meet the special requirements of use in small patients, however, they reliably retain their shape at all times. The smooth, funnel-shaped inner design of the 15mm connector allows an easy insertion of suction catheters. The special obturator is extremely practical. The grip on its end makes sure that the tube can be easily and reliably inserted despite its small size. Neck straps and compresses are also available to match. So the best solution can be found for every small patient. TRACOE *mini* is available in 12 different sizes (starting with size 2.5!): 4 for neonates and 8 for pediatric use. In addition custom-made variants are offered in terms of length.

TRACOE *vario*: TRACOE *vario* comes in seven different models: reinforced with a metal spiral or as a clear, nonreinforced version (with an X-ray contrast line). In addition the mentioned products are available as extra-long versions with or without an embedded subglottic suction line. This soft and flexible single lumen tube has a patented, variably adjustable neck flange. The flange can be moved along the tube (distal/proximal) by a simple and easy push-button mechanism on the body of the flange. This allows the medical staff to individually adjust the tube to different patient neck thicknesses or after a post-operative edema. Additionally as an optional precaution, the neck flange can be securely locked by pulling up the orange lever system. There are also flexible wings on the flange that can be rotated independently of one another. This provides additional possibilities for meeting the unique anatomical requirements of each patient.

TRACOE *comfort*: TRACOE *comfort* tubes are mainly used for long-term wearing, ie for ENT patients who have a tracheostoma due to partial or complete removal of the larynx or other reasons. TRACOE *comfort* tracheostomy tubes are made of clear medical-grade polymer material, which makes them both especially soft and very lightweight. They do not have to be removed for X-ray or cobalt therapy. A TRACOE *comfort* tube weighs only about one-third of a silver tube of the same size. Because they are transparent, it is also very easy to ensure that they are perfectly clean. As the name suggests, TRACOE *comfort* tubes are designed to be as comfortable as possible for permanent wearers after tracheostomy or laryngectomy. Their discreet appearance is an added benefit. To ensure optimum quality, they are still made by hand – an extra effort that does a world of good to the patient. In addition custom-made variants are offered in terms of length and fenestration.

TRACOE speaking valves: TRACOE phon assist I is a speaking valve for fenestrated TRACOE *twist* and *twist* plus tracheostomy tubes and stoma buttons and adhesive carrier. This valve has a silicone membrane with a fast occlusion time and side openings to adjust the supply or the expiration of air individually. That means it allows the patient to set any desired resistance to exhalation which improves the respiratory situation. This innovative and unique feature helps on the one side to set the optimum air resistance but also it avoids air trapping especially during the weaning process. Furthermore due to the adjustable side openings the patient will find his voice much easier and the valve can be opened completely without detaching it in case of shortness of breath. It comes with or without and oxygen supply port to allow intermittent oxygen supply for hypoxic or weak patients. In 2006 a clinical study by H. Prigent et al, "Characteristics of tracheostomy phonation valves," was published in the renowned "European Respiratory Journal" and tested six of the most common speaking valves for six of the most important parameters a speaking valve must display. In terms of the four most important parameters: minimal pressure, the resistance, the work of breathing and the time pressure product, ie in four out of six parameters TRACOE came out best.

DEHP-free Products: Like the *twist* and *comfort* range also the *mini* tubes are free of Di(2-ethylhexyl) phthalate (DEHP). In the 2009 published American Academy of Otolaryngology-Head and Neck Surgery Foundation, Asa A. Mair and Eric A. Mair mention in a commentary that "DEHP is a reproductive toxicant that alters the male reproductive system in animals, in vitro tests, and limited human data. DEHP leaches from PVC tracheotomy tubes in children." Furthermore Mair and Mair mention that the "FDA along with other international health boards has issued a Public Health Notification on PVC devices that urges health care professionals to use DEHP-free devices for vulnerable patients, especially the male infant. Many health care systems and hospitals have successfully transitioned away from the use of DEHP." For more contact tracoe.com. The US distributor is Bryan Medical Inc in Mariemont, OH, bryanmedical.net.

Products in Practice: Breathing is Believing – Respironics AF531 at Bert Fish Medical Center

Bert Fish Medical Center is a 116-bed acute medical center service in New Smyrna Beach, FL, that provides Southeast Volusia County with leading, state-of-the-art procedures and a focus on patient-centered care. Patients who require noninvasive ventilation sometimes find it difficult to tolerate the masks required to deliver therapy. The Respironics AF531 mask and accessories aid comfort and compliance with therapy, helping to enhance patient care and potentially avoid intubation and invasive ventilation.

Background

Bert Fish Medical Center provides inpatient, outpatient, diagnostic, and therapeutic respiratory services for a range of patients. The respiratory therapy department performs NIV procedures mainly for chronic obstructive pulmonary disease (COPD) and other respiratory conditions. The facility uses Philips Respironics ventilators, including the Respironics BiPAP Vision and Respironics V60 equipment.

The Respironics AF351 mask provides comfort with ease for patients and clinicians, simplifying delivery of noninvasive ventilation. With CapStrap headgear, the initial fitting is quick and mask removal and re-applications are easy. As patients move from acute to sub-acute settings, the AF531 can be adapted to different ventilation systems without requiring mask replacement.

Kevin Morris, Respiratory Therapy Supervisor, describes the facility's experience with a non-Philips mask previously in use: "We were mostly very satisfied with one particular brand of mask because it seemed to fit the patients well, but its problems were leaking and release," he recalls. "If a mask leaked, we'd have to get another one, and so we went through more masks, which is not good from an economic or workflow point of view. And if we needed to remove the mask in an emergency, it wasn't easy to do."

Putting the AF531 to the test

"I put the AF531 mask on and when you try it yourself, you realize how easy it is to adjust because it slides on the face, but still keeps a seal without being pressed so tightly," he explains. "The double flap design really makes a difference. Because there is less leaking, it doesn't have to be as tight to do the same job efficiently. The airflow is naturally less because the machine isn't trying to constantly compensate for a leak. There's a better flow and a feeling of less pressure on the face," he says.

Patient comfort a priority

"Patient comfort is one of our priorities," Morris continues. "It leads to patients being compliant. If a patient will wear the mask when needed and tolerate it for long enough periods of time, then you can potentially prevent the patient from having to be intubated and ventilated on a ventilator. With the AF531 we found a mask that we felt our patients would actually tolerate well enough so we could do the job we needed to do and keep them off of invasive ventilation when possible," he says.

Aiding reimbursement

Morris says that comfort can also have a direct effect on reimbursement, explaining, "Our reimbursement is based to some extent on patient satisfaction scores. When patients are comfortable, their satisfaction scores go up. That helps from an economic perspective, because we're doing a better job of making the patients happy and comfortable and improving our services to them."

Flexibility and economy in care

Morris explains that because of the mask design, the team is potentially able to use fewer masks per patient, providing a cost savings. "We find we're having to replace fewer masks because there is less opportunity for leaking. Also, the elbow helps make the mask very versatile, he says. "With the AF531 the elbow from the mask to the circuit can be easily changed. For instance, if we need to perform a bronchoscopy on a patient, we can do it directly through the mask with an elbow nose piece, which means the patient can stay on BiPAP. Before if we had to change a patient from BiPAP to a different mode of ventilation, we would have used an entirely new mask. With the AF531 you just change the elbow, which is very economical," he comments.

Workflow advantages

The AF531 is helping smooth workflow at Bert Fish, too. "It makes our job as respiratory therapists a little easier because it does the job it's meant to do. It comes with a sizing gauge that you can use to compare to the patient's face and get a very clear picture of which size you need to use, rather than opening up multiple masks trying to find one that's going to work. That's a big savings because once you've opened a mask, you really can't use it on anybody else," he says. "Getting it on and off is a benefit, too. If you have patients who are a little confused or start pulling on it by accident, it's not going to come off. If a respiratory therapist wants to remove the mask, it is literally the work of a second to get it off a patient's face when needed."

To summarize: "Our patients seem comfortable, which means they get continuous therapy in the beginning and they might not need it for as long a period of time. The support we have from the Philips people is excellent," he concludes.

For more information visit www.philips.com/NIVmasks.

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Pulmonary Function Testing – An Interview with Rodney J. Folz, MD, PhD

Rodney J Folz, MD, PhD is Professor and Chief, Pulmonary, Critical Care and Sleep Disorders Medicine, Distinguished University Scholar, and Director, Adult Cystic Fibrosis Program, University of Louisville Health Sciences Center, Louisville, KY. Questions for this interview were provided by nSpire Health.

Accuracy in the PTF lab:

Being that your laboratory uses systems from nSpire Health, and a critical feature of their HDpft products is a measurement enhancement system called iFlow, how important clinically is a routine improvement of pulmonary function result accuracy from the traditionally accepted 3% to the sub 1% capability provided by the iFlow feature?

There are three sources of variability when performing pulmonary function testing on patients. These include (1) machine variability, (2) biological variability and (3) variability caused by dysfunction or disease. Machine variability relates to technical variation as a result of instrument procedures, calibration, and observer/subject interactions. Whereas biological and disease variability relates to the within subject variability present in healthy and in those with chronic lung disease, respectively. Machine variability encompasses both accuracy, the degree of closeness of that measurement to that of the true value, and precision (the degree to which repeated measurements show the same results). Overall variability may be more appropriately expressed in absolute terms instead of as a percentage. Clinically important thresholds are more difficult to determine. Herpel and colleagues (AJRCCM 2006;173:1106-1113), using standard pulmonary function testing measurements, demonstrated that a change of 225 ml absolute difference in FEV1 was a significant clinical indicator of a true change in respiratory status, whereas it took a change of 325 ml in the FVC. Thus, it stands to reason that improving the accuracy of the spirometric measurement would serve to reduce the absolute change needed in the spirometric measurement to detect a true change in respiratory status. Assuming that the sources of variability are independent and contribute equally to the total variability, then reducing accuracy from 3% to 1% may decrease the absolute change needed from 225 ml to 175 ml for a clinically significant event.

In a research environment, would these tighter tolerances offer the potential for smaller sample sizes to obtain statistically significant results?

Since variance and sample size are proportional, reducing the total variance of a test would have the positive effect of needing a smaller sample size in a study population in order to detect a true difference between the two populations. Thus, implementing tighter tolerances to spirometry testing in clinical trials would likely reduce the study sizes needed to determine meaningful results. Smaller study sizes would result in reduced expenses for performing clinical trials, leading to substantial cost savings.

Web access to data:

Do you see true efficiency gain for a pulmonary medical director, responsible for overseeing results from the PFT lab, being able to log in from anywhere to review the data and send it on to its destination (ie, the permanent medical record)?

Remote access to the PFT lab and the PFT equipment allows the medical director of the pulmonary function lab greater access and enhanced presence in relation to the daily activities performed in the lab. In addition, remote presence allows the pulmonologist to markedly improve the turnaround time for the interpretation and transmission of the final report to the ordering health care providers. Remote presence also has great potential to reduce errors that might arise due to miscommunication, misinterpretation, and other system errors present in systems that rely on multiple intermediate steps before reaching the final product. Remote presence reduces many, if not most, of these errors by eliminating these multiple steps and directly engaging the physician from the initial raw PFT report to the final interpretation and signed report.

Telehealth and remote monitoring:

In a pulmonary practice treating COPD patients, in conjunction with a program that alerted the physician of results below a pre-set threshold, would you consider home testing of FEV1 and/or FEV6 to be helpful in both monitoring treatment and preventing exacerbations?

Here at the University of Louisville, our faculty in the Division of Pulmonary, Critical Care and Sleep Disorders Medicine manage many patients with COPD. These include those with early stage disease (GOLD stage 1 and 2) and those with more advanced stages of disease (GOLD stage 3 and stage 4). We have a comprehensive approach to their care and view COPD as a systemic disease process that encompasses more than just the pulmonary system. Home monitoring of a patient's spirometry metrics, such as FEV1 and/or FEV6, would be an invaluable instrument to help monitor the respiratory health and well-being of our patients, in particular between office visits. Establishing pre-set thresholds which, when crossed, automatically trigger an intervention or response, would lead to more timely institution of medical care earlier in the initial course of an acute COPD exacerbation.

For asthma patients, in conjunction with a program that alerted the physician of results below a pre-set threshold, would you consider home testing of PEF and FEV1 to be helpful in both monitoring treatment and preventing exacerbations?

Home monitoring of spirometry and establishing pre-set thresholds for individuals with asthma could provide significant health benefits. I suspect these potential benefits would be better realized in those with moderate persistent to severe persistent disease or in those who have more difficult to treat asthma and who develop more frequent asthma exacerbations. As in COPD, home testing of PEF and FEV1 in those with asthma would significantly strengthen the healthcare providers' ability to monitor their patients between office visits and allow for much earlier intervention of asthma exacerbations.

The Other Gas – CO2

Joseph Hollowell, RRT, RCP; Ray Braxton, RRT, RCP

Those of you who have recently attended an Advanced Cardiovascular Life Support (ACLS) course utilizing the 2010 American Heart Association (AHA) Guidelines/ Recommendations, have probably found that there is a great deal of interest to provide waveform capnography during cardiopulmonary resuscitation (CPR) efforts and during immediate post-cardiac arrest care measures. AHA published reasoning for this new recommendation which is that end-tidal CO2 (ETCO2) monitoring is a safe and effective noninvasive indicator of cardiac output during CPR and may be an early indicator of return of spontaneous circulation (ROSC) in intubated patients. During cardiac arrest, CO2 continues to be generated throughout the body. The major determinant of CO2 excretion is its rate of delivery from the peripheral production sites to the lungs. In the low flow state during CPR, ventilation is relatively high compared with blood flow, so that the ETCO2 concentration is low. If ventilation is reasonably constant, then the changes in ETCO2 concentration reflect changes in cardiac output.[1]

Over the past twenty years there have been several published studies showing improving outcomes by performing CPR and providing resuscitative measures with the goal of establishing and maintaining ETCO2 > 10 mm Hg. Patients who were successfully resuscitated from cardiac arrest had significantly higher levels of ETCO2. It is suggested that if the partial pressure ETCO2 level is < 10 mm Hg during CPR the provider should try to improve chest compressions and/or consider vasotherapy measures. Abrupt increase to a normal value of 35 to 40 mm Hg is a good indication of ROSC. In fact, this abrupt increase in ETCO2 often occurs before return of palpable pulse or blood pressure (BP) and virtually eliminates the need to stop compressions to check for a pulse.

It was also shown that in patients with ROSC, continuous or intermittent monitoring of ETCO2 provides assurance that the endotracheal tube is maintained in the trachea. The AHA recommends that the providers should observe a persistent capnographic waveform with ventilation to confirm and monitor endotracheal tube placement in the field, in the transport vehicle, on arrival at the hospital, and after any patient transfer to reduce the risk of unrecognized tube misplacement or displacement.

Hollowell is Clinical Specialist, Respiratory Care, Vidant Health Care, Pitt County Memorial Hospital; Braxton is Clinical Support Specialist, Hamilton Medical. This article is from Hamilton Medical's newsletter.

Capnography is an important tool for the respiratory therapist to use to evaluate the adequacy of ventilation, as the obvious goal of ventilation is to remove the CO2 produced by the body's metabolic processes. Over the past 40 years, we have seen the advancement from conventional, time-based capnography to today's volumetric capnography which is an option on the Hamilton Medical G5 ventilator. The figure below depicts data obtained from a typical volumetric capnogram tracing.

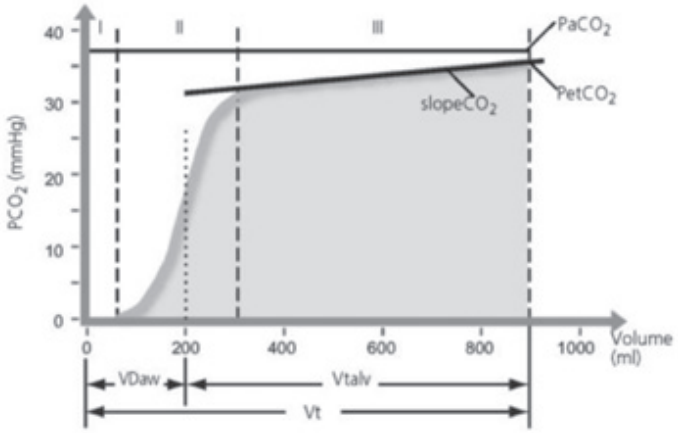

Figure 1. Interpretation of volumetric capnogram.[2]

Volumetric capnography measurements[3] provide us with an assessment of the patient's ventilation, state such as:

- CO2 elimination (V'CO2) - measurement permits assessment of metabolic rate (CO2 production) and efficiency of CO2 elimination
- End-tidal CO2 (PetCO2 and FetCO2) - measurement permits assessment of predicted arterial CO2 or degree of deadspace ventilation if PaCO2-PetCO2 gradient is widened.
- Airway dead space (VDaw) and alveolar minute ventilation (V'alv) - measurement permits assessment of alveolar ventilation (as opposed to minute ventilation)
- Capnogram shape (slopeCO2) - measurement permits assessment of the degree of inefficient ventilation or ventilation/perfusion mismatch as seen in COPD
- Physiological dead space fraction (VD/Vt) - measures the portion of tidal volume (Vt) that does not participate in gas exchange (wasted ventilation).

Another value to capnography monitoring is its ability to display a need for ventilator setting adjustments. Take a moment to

review the following waveforms and see if you can interpret what ventilator adjusted setting is needed.

How many of you were able to detect that the patient is attempting to initiate a spontaneous breath which was not sensed by the ventilator's sensitivity setting (Where the cursor is, the bottom CO2 waveform shows a patient breath not recognized by the ventilator). Adjustment of flow-trigger setting yielded the following results:

Carbon dioxide is the other gas whose measurement and capnogram tracing can provide the respiratory therapist with a wealth of knowledge to aid in improving the performance of CPR, ensuring safety of establishing and maintaining an artificial airway, fine tuning adjustment of ventilator settings, and assessing the patient ventilated state. I suspect we will see a renewed interest in capnography with the recent American Heart Association's guidelines and recommendation for capnography. Take a moment to review further interpretations of capnogram tracings at the following sites: http://www.capnography.com; http:/www.capnography.com/find htm.

References

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2 Astrom E, Niklason L, Drefeldt B, Bajc M, Jonson B. Partitioning of deadspace - a method and reference values in the awake human. Eur Respir J. 2000 Oct; 16(4): 659-664.

3 Hamilton Medical Volumetric Capnography User's Guide (624152/02), Dec 2011.

Optimizing Patient Compliance on Nasal EPAP (Provent Therapy): The Role of the Healthcare Provider

Rajiv Doshi, MD; Debra L. Heller

Abstract
Nasal EPAP (Provent Therapy) represents an important novel treatment option for obstructive sleep apnea (OSA). Published clinical studies and case series of nasal EPAP have demonstrated impressive initial patient acceptance and ongoing compliance through 12 months of treatment. This summary is intended to review published nasal EPAP compliance to date and provide healthcare providers with an understanding of how to optimize nasal EPAP compliance in their practices.

Introduction

Continuous positive airway pressure (CPAP) has historically been the gold standard of therapy for obstructive sleep apnea (OSA). CPAP has been demonstrated to have excellent efficacy in the in laboratory setting. However, many patients either initially reject CPAP or do not use it as frequently as prescribed within the home setting. It has been reported that between 46 to 83% of patients with OSA are non-adherent to CPAP.[1] As a result, other treatment options are needed.

Figure 1: Provent Sleep Apnea Therapy

One such treatment is nasal expiratory positive airway pressure (EPAP). The only FDA cleared nasal EPAP product indicated to treat OSA is known as Provent Therapy (Ventus Medical, San Jose, CA) [See Figure 1]. The device has been evaluated in seven published studies including a 19 center, 250 patient randomized controlled trial. The device has been shown to effectively treat mild, moderate and severe OSA. [See Figure 2]. The device consists of a small valve attached externally to each nostril with hypoallergenic adhesive. The valve acts as a one-way resistor, permitting nearly unobstructed inspiration. During expiration, the airflow is directed through small air channels, increasing the resistance. This increased resistance during expiration creates EPAP which is maintained until the start of the next inspiration. [See Figure 3].

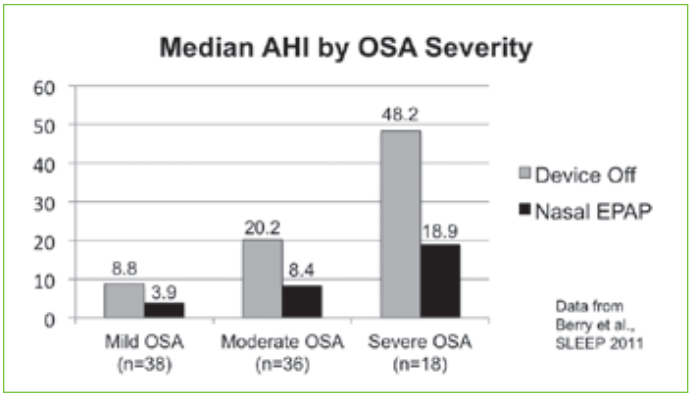


Figure 2: AHI reduction by severity[2]

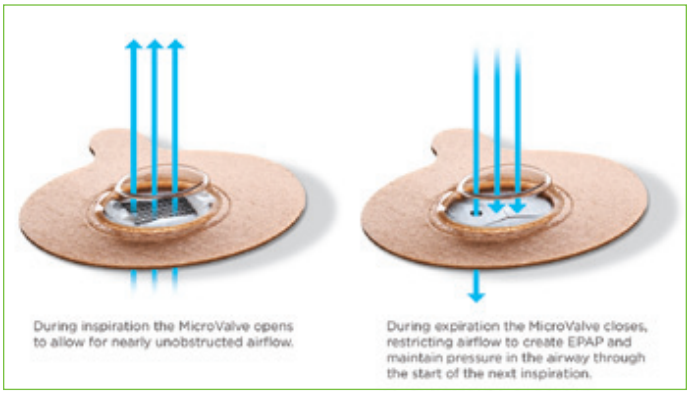


Figure 3: Provent Therapy's valve creates EPAP

The exact mechanism through which nasal EPAP treats OSA is still unclear, but several mechanisms appear most likely:

1) Positive end-expiratory pressure (PEEP) leading to increased end-expiratory lung volumes (or FRC) that increases longitudinal traction on the pharynx, making it less collapsible ("tracheal tug")[3]

The authors are with Ventus Medical, San Jose, CA.

2) Dilatation of the upper airway by EPAP which carries over until the start of the next inspiration[4]
3) Mild hypercapnia due to reduced ventilation which would lead to increased respiratory drive to the upper airway[4]

Recommended patients for Provent nasal EPAP include:

1) Patients (mild, moderate or severe) who have rejected or are non-compliant with prescribed CPAP
2) Newly diagnosed mild/moderate OSA patients without significant co-morbidities
3) CPAP compliant patients seeking alternatives for travel

Review of Compliance from Published Nasal EPAP Studies

Provent Therapy has been studied in a series of longitudinal published clinical studies. Several are highlighted below:

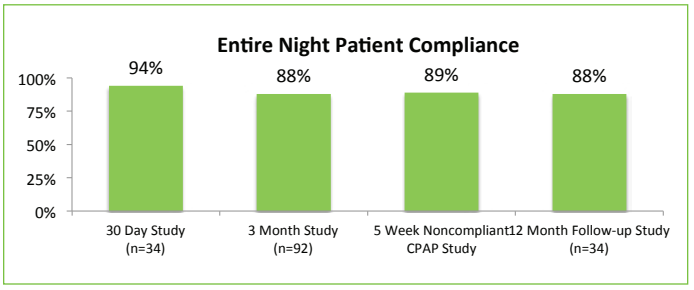


Figure 4: Nightly compliance on Provent Therapy from four published studies[2,5-7]

A novel nasal expiratory positive airway pressure device for the treatment of obstructive sleep apnea: a randomized controlled trial[2]

– Berry RB, Kryger MH, Massie CA. [SLEEP 2011; 34:479-485]

In this 19 center study, 250 OSA patients were enrolled in this prospective, multicenter, parallel-group, sham controlled, randomized double-blind trial with three month follow up. Treatment effect by severity is shown in Figure 2. Provent nasal EPAP reduced the median AHI from 8.8 to 3.9 in mild OSA patients ($p<0.001$), from 20.5 to 8.4 in moderate OSA patients ($p<0.001$) and from 48.2 to 18.9 in severe OSA patients ($p<0.001$). Based on patient self report, the median percentage of nights the EPAP device was used for the entire night was 88.2%.

Long term use of a nasal expiratory positive airway pressure (EPAP) device as a treatment for obstructive sleep apnea[7]

– Kryger MH, Berry RB, Massie CA [Journal of Clinical Sleep Medicine 2011; 7:5:449-453.]

This 13 center study was an extension of the three month (Berry et al) study and designed to evaluate the long-term effectiveness of Provent nasal EPAP after 12 months of follow-up. 41 patients from the Provent arm of the three month study who met adherence and efficacy criteria were continued on therapy and returned for in-lab PSG after 12 months of treatment The median percentage of nights patients reported using the device the entire night was 89.3%.

A convenient expiratory positive airway pressure nasal device for the treatment of sleep apnea in patients non-adherent with continuous positive airway pressure[6]

– Walsh JK, Griffin KS, Forst EH, et al. [Sleep Medicine 2011;12:147-52]

This study focused on OSA patients who were non-adherent to CPAP. Most patients had moderate to severe OSA, with over half of the patients having a baseline AHI ≥30. A total of 59 patients with OSA who refused CPAP or used CPAP for less than 3 hours per night were provided the Provent nasal EPAP device, of which 47 patients (80%) tolerated the device. Device use was reported an average of 92% of all sleep hours.

A multicenter, prospective study of a novel nasal EPAP device in the treatment of obstructive sleep apnea. Efficacy and 30-day adherence[5]

– Rosenthal L, Massie CA, Dolan DC, et al. [Journal of Clinical Sleep Medicine 2009;5:532-37]

This multicenter prospective study was specifically designed to assess adherence over a 30 day period, and also evaluated efficacy based on serial in-lab PSG studies. A total of 34 patients with OSA underwent a 30 day trial of the Provent nasal EPAP device. Participants reported using the Provent nasal EPAP device all night long for 94.4% of the possible nights during the in-home trial.

Retrospective cases series analysis of a nasal expiratory positive airway pressure (EPAP) device to treat obstructive sleep apnea in a clinical practice[8]

– Adams, G. [SLEEP Abstract Supplement, 2011 (34):A146]

This retrospective analysis was completed to evaluate patient acceptance and AHI reduction using Provent nasal EPAP in a real world clinical practice. OSA patients (with AHI >10) received 10 nights of EPAP devices for in-home evaluation. Patients that acclimated returned for efficacy confirmation using standard in-lab PSG. 151 patients sampled nasal EPAP and 131 were in the analysis group. Of the analysis group, 75% acclimated to the device.

Nasal EPAP in the "Real World"

Acceptance and compliance with Provent Nasal EPAP in clinical practice may be more variable than that reported in the published literature. Patients in clinical studies may be more motivated and the level of training provided to them may be more rigorous and standardized than in normal clinical practice. That being said, a recent retrospective case series of 131 real world patients within a community practice demonstrated an impressive 75% acceptance of nasal EPAP after a 10 day trial.[8]

The healthcare provider plays a critical role in educating and motivating the patient to use and acclimate to nasal EPAP. Physicians, respiratory therapists, lab managers, PSG technologists and others that have direct patient contact should be familiar with how to counsel patients about nasal EPAP use and acclimation. A short learning curve is expected for most healthcare providers that begin prescribing nasal EPAP, as expectation setting and acclimation support for nasal EPAP is different from CPAP.

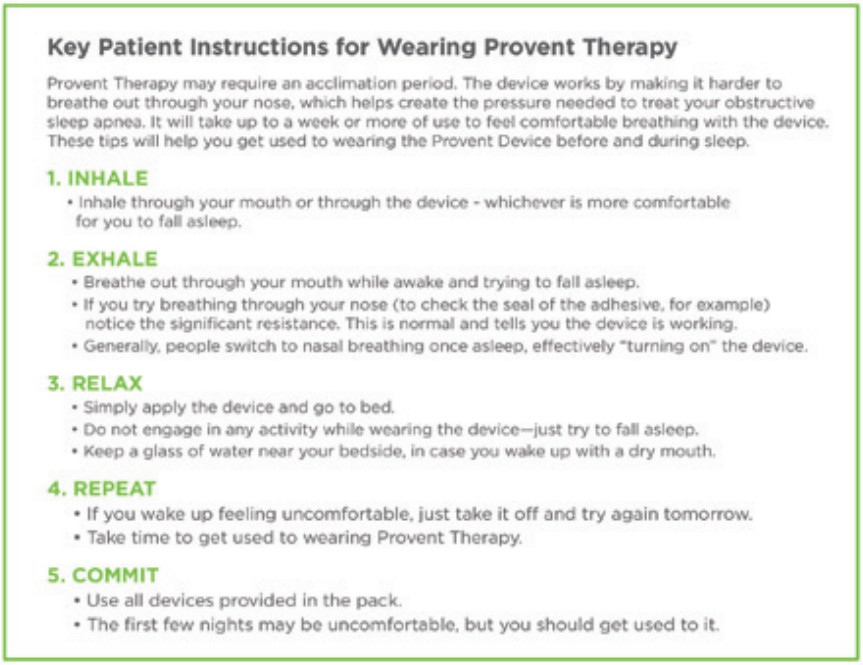
Perhaps the most important messages to provide to the patient is that they need to make sure the device is sealed against the nostril, that they should breathe through the mouth while awake, and that it may take up to a week or longer to adjust to wearing Provent nasal EPAP. Best practices for use of Provent nasal EPAP include:

Set proper expectations while the patient is in the healthcare provider's office:

1) Have the patient apply and then breathe through a Provent EPAP device if available
2) Explain to the patient why Provent works (and reassure that the feeling of expiratory resistance is normal)
3) Instruct the patient to breathe through the mouth (and not the device) while awake to allow comfortable breathing
4) Review all the patient instructions in Figure 5
5) Encourage the patient to read the instruction booklet (included in the box) in its entirety before first at home use of Provent
6) Let the patient know that the first several nights may be uncomfortable, but this should resolve over the next several days. The patient should not give up after a night or two
7) Remind the patient that OSA is a chronic condition that requires treatment every night
8) If the patient is having difficulty, have him/her call the support number on the box to receive individualized training from an acclimation specialist

Other tips

- Cleaning of skin just prior to device application can improve device seal. If skin is oily, apply isopropyl alcohol or witch hazel (an astringent) to ensure good skin contact
- Use a mirror while applying devices
- Prior to applying the device, draw down upper lip over top teeth to stretch out skin under nostril to enable a proper seal
- If a leak is discovered or there are folds or creases present, remove device and re-apply. If this occurs again, remove device and apply new one
- Try briefly breathing out through the device. Notice the resistance. This is normal and means the device has been applied properly
- It may take up to a week or longer to adjust to using the device
- If the patient wakes up during the night and feels uncomfortable, remove the device and try again the next night. This may happen for several nights until they are used to wearing nasal EPAP



Key Patient Instructions for Wearing Provent Therapy

Provent Therapy may require an acclimation period. The device works by making it harder to breathe out through your nose, which helps create the pressure needed to treat your obstructive sleep apnea. It will take up to a week or more of use to feel comfortable breathing with the device. These tips will help you get used to wearing the Provent Device before and during sleep.

1. INHALE
- Inhale through your mouth or through the device - whichever is more comfortable for you to fall asleep.

2. EXHALE
- Breathe out through your mouth while awake and trying to fall asleep.
- If you try breathing through your nose (to check the seal of the adhesive, for example) notice the significant resistance. This is normal and tells you the device is working.
- Generally, people switch to nasal breathing once asleep, effectively "turning on" the device.

3. RELAX
- Simply apply the device and go to bed.
- Do not engage in any activity while wearing the device—just try to fall asleep.
- Keep a glass of water near your bedside, in case you wake up with a dry mouth.

4. REPEAT
- If you wake up feeling uncomfortable, just take it off and try again tomorrow.
- Take time to get used to wearing Provent Therapy.

5. COMMIT
- Use all devices provided in the pack.
- The first few nights may be uncomfortable, but you should get used to it.

Figure 5: Key patient instructions

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1 Weaver TE, Grunstein RR. Adherence to continuous positive airway pressure therapy: the challenge to effective treatment. Proc Am Thorac Soc. 2008;5(2):173.
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7 Kryger. MH, Berry RB, Massie CA. Long-term use of a nasal expiratory positive airway pressure (EPAP) device as a treatment for obstructive sleep apnea (OSA). J Clin Sleep Med 2011; 7:5:449-453.
8 Adams, G. Retrospective cases series analysis of a nasal expiratory positive airway pressure (EPAP) device to treat obstructive sleep apnea in a clinical practice. SLEEP Abstract Supplement, 2011 (34):A146.

The Control of End Tidal CO2

Robert Kohler, EMT-P

Introduction

Pre-hospital care can be defined as efforts to achieve or maintain homeostasis. The ability to monitor and control CO2, a key component of the buffering system, is an essential means to that end. Because CO2, a key component of the buffering system, has a direct effect on the pH of the body, the ability to monitor and control End Tidal CO2 (ETCO2), is essential in order to maintain homeostasis.

Recently the American Heart Association has issued new guidelines defining a narrow range of optimal oxygen saturation for many situations. Based on these recommendations proper patient care mandates that we have the ability to control both components of ventilation. This pilot study examines the feasibility of controlling the End Tidal CO2 during 911 ground ambulance operations.

Materials and Methods

There were 2 ventilation adjuncts available, the choice of either was not defined or dictated by the protocol and was the clinician's choice.

The control: an adult bag valve mask (BVM) as manufactured by Life Support Products #L770 with a bag volume of 1488 ml, valve dead space of 7.8 ml (not including mask) and a patient connection of 22 mm outside diameter, 15 mm inside diameter with no pop off valve.

The study: An oxygen powered disposable PIP cycled automatic resuscitator that regulated: Respiratory Rate, Tidal Volume, Peek Inspiratory Pressure (PIP). Peak End Expiratory Pressure was variable at 20% of the selected PIP. The VAR-Plus model PCM (VORTRAN Automatic Resuscitator) was used.

In December of 2009 Stamford EMS Paramedics began a program of training using manufacturer's competency requirements and guidelines from the FCCS course curriculum. Clinical targets were FiO2 of 100% at a rate of 10-12bpm and a PIP range from 20-25cm/H2O. Paramedics were not restricted to these targets and were instructed to vary settings to meet the patients' needs.

ETCO2 was monitored via Side-Stream filter line capnography as manufactured by Microstream and available on the Lifepak 12s currently in use.

January through September of 2010, 152 intubated patients were reviewed. 46 met the criteria of any patient greater than 10 kg with an intrinsic pulse and in respiratory arrest whether idiopathic or clinician induced as an example from Rapid Sequence Induction. One patient was excluded due to a metabolic aberration. The remaining cases were split, with 1,012 specific ETCO2 samplings evenly distributed over 23 cases using a BVM (as the control) and with 1,270 specific ETCO2 samplings evenly distributed over 22 cases using the VAR. The first 4 minutes of data records from all cases were excluded to compensate for procedural anomalies experienced while securing the airway.

Data for all cases in each group were combined for the calculation of standard deviation (Sd). The Sd was also calculated for each individual case. The difference in the quantity of records had no statistical significance on results in a test analysis.

Results

After 9 months, ETCO2 values in the control group reflected a Standard deviation of 16.97 while the test group ventilated with the VAR reflected a standard deviation of 14.09. In addition the study group trended lower as time progressed while the control group did not.

Conclusion

Although data is still being collected, these initial values show that despite the dynamic environment of the pre hospital setting, with a minimum of additional training the pre-hospital provider can more accurately control ETCO2 with a disposable PIP cycled respirator than with a Bag Valve Mask.

Sources

- Stamford Emergency Medical Services – Stamford CT.
- Vortran Medical Technology 1, Inc – Sacramento CA.
- Fundamentals of Critical Care Support fourth edition – Society of Critical Care Medicine
- Lifepak 12 is manufactured by Physio-Control Inc – Redmond WA.

The author is with Stamford Emergency Medical Service, Stamford, CT. This article was provided by Vortran.

Use of a Non-invasive Open Ventilation (NIOV) System to Assist Mobilization: A Case Study

Robert McCoy, BS, RRT, FAARC; Nishith Patel, BSRC, RRT-NPS, CPFT

Overview

Neuromuscular weakness often occurs as a consequence of the immobility associated with prolonged hospitalization and especially during intensive care treatment, where its negative effects can be persistent and severe. Clinical studies have shown that exercise and early mobilization is beneficial in altering the downward spiral associated with immobility, and in improving muscle strength and physical function.[1] Recently, early mobility studies in the ICU have demonstrated that doing so can be accomplished safely, with reductions in short-term physical impairment.[2-3] However, accomplishing early mobility often requires significant changes in ICU practices, including reduction of sedation, teamwork, and the availability of portable devices.

A portable device that augments ventilation, while supplying supplemental oxygen could improve patient mobility, enhance rehabilitation, and offset some of the functional impairment associated with prolonged immobility and neuromuscular weakness. In this regard, a wearable, non-invasive open ventilation (NIOV) system that delivers oxygen therapy while augmenting ventilation has been developed by Breathe Technologies, Inc and cleared for use by the FDA. The ventilator is light enough (1 lb) to be carried by patients, and uses a proprietary "open" nasal pillow interface (Figure 1). Because of its portability and comfortable nasal interface, the NIOV System is uniquely positioned to provide patients with a means of receiving truly ambulatory augmented ventilation plus supplemental oxygen.

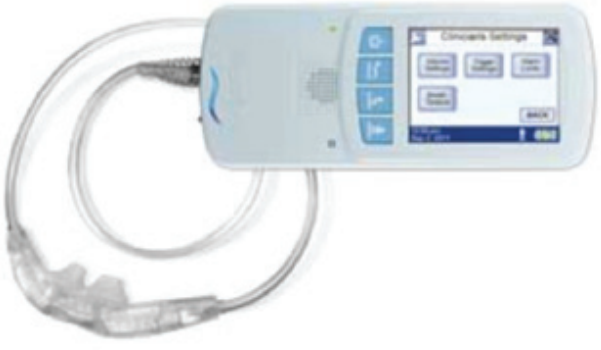

Figure 1. The portable Breathe Technologies NIOV System.

This article was provided by Breathe Technologies.

Potential Benefits of the Breathe NIOV System include:

- A portable method for augmenting ventilation and oxygenation, allowing patients to move from a sedentary situation, build strength and stamina, enhance mobility, and reduce neuromuscular weakness.
- Establishes a foundation of effective ventilation and oxygenation that allows patients to perform basic activities and functions with the intent upon improving cardiopulmonary function.

Patient Case Study

The NIOV System was evaluated in a 71-year-old, male patient chosen by the pulmonary staff with an admitting diagnosis of Waldenström macroglobulinemia (WM). WM is a rare, slow-growing, non-Hodgkin lymphoma. Approximately 18 days prior to the NIOV evaluation, the patient had been directly admitted into the intensive care unit due to failure to thrive. Initially, the patient was placed on a high-flow nasal cannula. Earlier in the week, the ICU staff was able to successfully wean his supplemental oxygen requirement down to a standard nasal cannula at 4-6 lpm. The patient's current chest radiographs revealed moderate bilateral pleural effusions and auscultation revealed coarse crackles bilaterally. The patient complained of moderate-to-severe weakness and fatigue. After conferring with the patient's physician and obtaining a prescription, evaluation of the NIOV System was undertaken to determine whether the patient could benefit from the device.

Summary of Results

Day 1: The patient found the NIOV nasal pillow interface to be comfortable, and he was able to immediately breathe in synchrony with the ventilator. Initial acclimation and titration to the NIOV System resulted in volume augmentation settings of 90 mL, 150 mL, and 180 mL on the low, medium, and high volume settings, respectively. The patient was slowly progressed out of bed, and throughout his first walk using the ventilator, volume augmentation was titrated up three times, with final settings of 180 mL, 200 mL, and 230 mL. During the entire trial session, the patient maintained SpO2 >95% with a maximum respiratory rate of 28/min and maximum heart rate of 91/min. The patient walked a total distance of approximately 70 ft. During the walk, the patient complained of weakness in the legs, and felt that this was the greater limiting factor versus dyspnea in his decision to terminate the walk. The patient commented that the NIOV pillow interface was "more comfortable than all previous nasal [interfaces]" he had been placed on.

Continued on page 40…

Modified Endotracheal Tubes — Do They Make A Difference?

Carl Sprow, RCP; Melissa Turner, BA, RRT

Nosocomial pneumonia is a complication in the ICU ventilator patient and is the most common infection. Factors that play a large role in this complication are the following: the intubation process, micro-aspiration of contaminated secretions past the ETT cuff, and mechanical ventilation. Ventilator Associated Pneumonia, also known as VAP, accounts for 80 - 90% of nosocomial pneumonia in ICU ventilator patients. Patients are at the greatest risk for VAP the first few days of mechanical ventilation and the risk factors increase the longer they are on the ventilator.

There are things that can be done to help with VAP prevention:

- Basic infection control practices implemented by the staff coming in contact with the patient.
- Oral hygiene should be done Q4 hours and prn.
- Keeping the patient properly positioned in bed (ex. Head of the bed at 30 degrees or greater).
- GI prophylaxis.
- Removing the endotracheal tube as soon as possible (ex. Sedation vacation to assess if the patient can be weaned towards extubation).
- Maintenance of cuff pressures and suctioning of secretions above the ETT cuff.

Today there are several different ETT designs that are available to help reduce the mechanism leading to ventilator associated pneumonia. One is the ETT that allows subglottic suctioning to be performed. This can be done with either intermittent or continuous suctioning and prevent micro aspiration from happening. There are the risks of drying out and causing trauma to the mucosa with subglottic suctioning. Another style is a cuff composed of polyurethane or silicone which also helps prevent aspiration and reduces early incidence of pneumonia as the shape of the cuff is tapered to reduce leakage past the cuff. There are also antibacterial-coated tubes that help to limit the bacterial colonization on the lumen of the ETT. Some designs have also changed the shape and inflation features to reduce the amount of secretions that build up on the lumen of the tube.

Of course, there are the costs that are associated with each of the modified endotracheal tubes. Depending on the style of the tube, they can range in price from $30 - $100 per tube. This increased cost might be worth the investment based on how well they work in reducing VAP and the extra costs associated with it. However, there is still insufficient evidence on how well the various tubes work and what risks factors are involved with each.

VAP is a costly nosocomial infection that is directly related to the introduction of the endotracheal tube into the airway. With a wide spectrum approach using infection control practices, oral hygiene, proper patient positioning, and removing the ETT as soon as possible, VAP prevention will probably be most effective when bundled together. Modified ETTs might play an important role in helping prevent micro aspiration but further studies need to be done to prove the efficacy on patient outcomes and safety. The verdict is still out but some recent evidence is promising.

Reference

Steven Deem MD and Miriam M Treggiari MD PhD MPH. New Endotracheal Tubes Designed to Prevent Ventilator - Associated Pneumonia: Do They Make a Difference? Respiratory Care August 2010 Vol.55 No 8.

Editorial Note (by Melissa Turner)

In Carl's article, he mentions some of the newer types of endotracheal tubes (ETT) that have been developed in an attempt to help prevent microaspiration in the critical care patient. Microaspiration from the subglottic space above the ETT cuff has been found to be a primary cause of ventilator associated pneumonia (VAP), so it would stand to conclude that as clinicians we should do all we can to avoid this happening. As Carl mentioned, one way to reduce microaspiration is by using one of the newer ETTs he wrote about. Of course those new ETTs are quite pricey, and although not as pricey as a VAP case would be to a hospital, but a considerably higher cost than what centers are used to paying for regular ETT's at this time.

Let's now consider a study by Sole et al[2] that shows that ETT cuff pressure should be maintained at least at 20 cm H2O pressure. Maintaining the cuff pressure at least at 20 cm is listed as one of the measures shown to reduce VAP because it helps prevent microaspiration of subglottic secretions. In the real world, maintaining cuff pressure can be a significant problem. Nseir and colleagues[3] studied 101 patients and found that of those, 73% had overinflated cuffs and 54% had under-inflated cuffs over 808 hours. In Sole et al's article, it was an average of 8 times per day in which the ETT cuff needed to be manually adjusted to keep the pressure at 20-30 cm.

Sprow is, Clinical Support Specialist, Hamilton Medical, Inc. The editorial note is by Melissa Turner Clinical Support Specialist, Hamilton Medical, Inc. This article is from Hamilton Medical's newsletter.

If clinicians are able to keep the ETT cuffs inflated to the therapeutic range, not only would it prevent damage to the mucosa, but would certainly help to prevent microaspiration shown to cause VAP. One way to do this is to have continuous ETT cuff pressure monitoring and control. Nseir and colleagues[1] showed in their study that continuous cuff pressure monitoring and control resulted in reduced microaspiration and the rate of VAP. If automatic cuff controllers could be used with every patient it is likely that we would see a reduction in VAP as a direct consequence of the reduction in microaspiration of subglottic secretions. One such automatic cuff controller just cleared by the FDA is INTELLiCUFF, which is an option on Hamilton G5 ventilators.

Today, we must be vigilant in the effort to continue to reduce VAP. Hospital costs skyrocket with each new case of VAP that is diagnosed. Knowing that we can reduce microaspiration in the ventilated patient is good news as it is directly linked to the incidence of VAP. Automatic ETT cuff controllers have been studied and have shown that they, in fact, reduce microaspiration. For the number of VAP cases that can be prevented by the continuous control of cuff pressure, it seems as though the cost of these devices is well worth it.

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Day 2: The patient was re-evaluated on the NIOV System with no changes made to the ventilator settings from the previous day. During this trial, the patient was able to increase his total distance walked to 125 ft, while maintaining stable vital signs comparable to Day 1. During both evaluation walks, the patient used a special arm rest walker and was encumbered with a Foley catheter, two intravenous lines, and an arterial line. The NIOV System was on only during activity and the patient was returned to his standard oxygen cannula afterwards.

Discussion

This limited evaluation of the NIOV System is part of an ongoing effort to explore the applications of a unique product. The use of a portable non-invasive open ventilation system in the acute care setting may allow patients with neuromuscular weakness to more easily accomplish early mobilization. If so, this might ultimately result in a reduction in morbidity and complications associated with neuromuscular weakness and immobility. This case study, along with prior clinical trials[4,5] using the NIOV System, support the premise that a truly portable ventilator can provide utility in improving mobility and exercise tolerance. Further clinical evaluations and trials are required to better define NIOV's applications, benefits, and its expected outcomes.

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Reducing Fires and Burns from Smoking While Using Medical Oxygen

Abstract

There is a growing awareness of the incidence of fires due to the misuse of oxygen therapy equipment while smoking. Smoking is by far the leading cause of injuries and deaths in all home fires, whether or not home oxygen is in use. Several studies have revealed an increased incidence of burn injuries associated with home use of medical oxygen, and it is believed that the frequency of fires has been grossly underestimated. Clinicians, providers, manufacturers, and regulators of this equipment share the responsibility to reduce the number of burn injuries and deaths. Responses and recommendations appear to be ineffective because of the lack of communication and a knowledge deficit concerning oxygen fires, particularly the incidence of unreported thermal burns, the ease with which tubing is ignited while oxygen is flowing, and the characteristic burn pattern toward the oxygen supply. This paper discusses the causes of home medical oxygen fires, explains cannula burn patterns and firebreaks, and identifies potential cost-effective solutions.

The Dangers of Smoking

Ninety-five percent of chronic obstructive pulmonary disease (COPD) is caused by smoking, with most smokers eventually developing some degree of pulmonary impairment. COPD may occasionally occur in nonsmokers as a result of environmental factors such as dusts, chemicals, or air pollution; or genetic factors such as alpha-1 antitrypsin deficiency.[1] COPD is the most common reason for long-term oxygen therapy (LTOT) prescriptions.[2] An estimated 182 home fires in the United States (US) involve oxygen therapy equipment each year, resulting in 46 deaths. An additional 1190 thermal burns involving oxygen therapy equipment require treatment each year in emergency rooms, with nearly half resulting in hospital admissions, yet the majority are not reported to fire officials.[3] The National Fire Protection Association (NFPA) estimates that in the US, 30 percent of oxygen patients continue to smoke, with other sources estimating smoking rates up to 50 percent.[4,5] Smoking while on oxygen therapy is responsible for the majority of home oxygen fires and resulting deaths.[3] These incidents involve fire department interaction and are well documented. However, an alarming number of thermal burns in the US caused by patient smoking while using home medical oxygen occur each year that are not reported to fire authorities. It is feared that this number may be greatly underestimated, and will increase as the 50- to 75-year-old population grows, along with their need for oxygen therapy equipment.[3,4]

Oxygen patients have been observed smoking while using their oxygen therapy, and self-report having engaged in this risky behavior repeatedly. Cannula ignition may occur during the initial lighting of the cigarette, bringing the cigarette too close to the cannula tips and having it flare up, or through the relighting of cigarettes, which may be more common now with the expanded use of self-extinguishing cigarettes.

Smoking while using oxygen therapy greatly increases the risk of facial burns. Facial burns account for 89% of all thermal burns, and although the overall burn size is generally small, due to the intense heat of the flame and inhalation of hot toxic smoke, significant injuries may occur to the patient's upper and lower airways that require hospital admission, specialized treatment at burn centers, or even result in death. At least a thousand burn injuries a year happen when cannula tips ignite after coming in close contact with cigarettes, lighters, or matches. In many cases, patients quickly remove the cannula and extinguish the fire, and fire authorities are never notified by the patient or hospital. Oxygen patients may be reluctant to report these occurrences due to embarrassment, or they may not want to take responsibility for the incident, since they were likely informed of the fire danger.

Consequences of these fires can be catastrophic for home oxygen patients, since their health is often already so fragile that even small burn injuries can have very poor outcomes. The disease processes that necessitate oxygen therapy can contribute to mortality from burns that would have been expected to be easily survivable in younger, healthier patients.[4] These patients differ from standard burn patients because they are older, have higher rates of inhalation injury, and require much longer hospitalizations, despite their injuries having a mean total body surface area (TBSA) of only 3 percent.[6] Mortality rates attributed to home oxygen fires may be understated for these compromised patients. Many times these related deaths are assigned natural causes, when in fact, the exacerbation was triggered by the fire injury. Some experts, particularly the Thoracic Society of Australia and New Zealand, feel that the risk of fire for patients who continue to smoke cigarettes while using oxygen therapy offsets the treatment benefits.[7]

Patients may choose to remove the cannula and place it next to them while they smoke. This creates an oxygen-enriched environment, particularly closest to the cannula tips, of bedding and other combustible materials that can create a flash-fire with just an ember. While oxygen itself does not burn, it greatly lowers the ignition point of combustible materials.

Most fire deaths in the bedroom occur as a result of smoke inhalation while sleeping, whether oxygen is involved or not.

Smoking in bed increases the probability of falling asleep, greatly increasing the likelihood of the cigarette touching and igniting the bedding or oxygen tubing. In addition to sleeping, many victims of fires caused by smoking materials are affected by alcohol, drug impairment, or a health condition that limits mobility, cognitive function, or the ability to react prior to the fire. Impairment is much more likely with smoking material fires than with other fires.

The percentage of alcohol involvement among fatal victims was 23 percent for smoking material home fires in 2004-2008, compared to 11 percent for all other home structure fires with a known heat source as the cause of ignition. The percentage with possible other drug impairment during the same time period was 10 percent for smoking material home fires, compared to 4 percent for all other home structure fires with a known heat ignition source. Sadly, in two-thirds of all home fire deaths, smoke alarms are either absent or not working.[3] Anything that causes a delay in reaction time will decrease survival rates.

Cannula Tubing Burn Pattern: Back To The Oxygen Source

Oxygen cannula and tubing made of polyvinyl chloride (PVC) is commonly used to administer oxygen therapy. A cannula refers to a patient interface, which has two vinyl tips, or prongs, for positioning at the base of the nostrils, and attaches to tubing of lengths up to 50 feet (15.2 m). Most homecare companies use cannulas of 4 or 7 feet (1.2 or 2.1 m), and supply ample lengths of additional oxygen tubing in the range of 25 to 50 feet (7.6 to 15.2 m). This allows a patient to move about freely within the home and away from the oxygen supply, which may be heavy and difficult to move. The oxygen equipment may be located in a central position of the home, such as a hallway, living room, bedroom, or even on a different floor or level. Tubing is commonly gathered and coiled up to prevent tripping and clutter while it rests on the floor, as one does with a long extension cord. When a patient moves around the home, the position of the tubing changes and touches combustible materials, such as carpeting, bedding, furniture, curtains, and clothes.

Although the cannula does not easily ignite in room air or with a pulsing oxygen conserving delivery system, when a continuous flow of oxygen passes through it, the cannula tips and tubing will easily ignite when in close proximity to any flame or ember. The nasal cannula tubing, a PVC product, emits an intense flame and thick, toxic black smoke when burning, releasing highly flammable vinyl chloride gas.[5] Although referred to as a cannula fire, a more accurate description is cannula torch or fuse, because of its intense flame and the speed at which it supplies ignition to combustibles as the fire advances up the tubing towards the oxygen supply.

Any portion of the cannula and tubing may ignite from a flame or cigarette ember, and the point of ignition is generally very recognizable, as it presents a delineation between the burned and intact tubing. This flame can travel both externally or internally down the tubing, giving off a loud whistling sound. Once ignited, the fire consumes the tubing, leaving a charred trail of ash and melted tubing as it advances, always toward the oxygen supply.[8] A 4 foot (1.2 m) Salter 1600-4 cannula ignited at the tips takes about 2.5 minutes with a flow rate of 2 liters per minute (LPM), 4.5 minutes with a flow of 3 LPM, and 10 minutes at a flow rate of 5 LPM to burn to the connection. Although, burn times seem counter intuitive for each liter flow listed, results were validated. Higher oxygen flows create a slower moving, more intense fire as it burns back to the oxygen source. As the tubing burns, combustible materials ignite along its path, creating additional fires. The fire may bypass and jump sections of crossed or coiled tubing and continue burning toward the oxygen supply. The tubing may also whip around (in a manner similar to a full flowing, unattended garden hose), fanning its reach to ignite combustibles. If a humidifier bottle is used, it also will readily burn, and may cause additional damage to the device and allow the fire to breach the cabinet, depending on its location. Gathered or coiled oxygen tubing on and around the oxygen supply, particularly an oxygen concentrator, may cause the cabinet of the concentrator to ignite, sustain heavy damage, or even become unrecognizable.

The most common medical oxygen supplied for use in the home is an oxygen concentrator, a machine that separates room air and concentrates the oxygen. A trail of burned tubing outside and downstream of the machine is evidence of oxygen flowing within the tubing and an external ignition source, as fire always advances toward, rather than away from, the oxygen supply. In fact, when PVC tubing was ignited by a fire investigator, it stopped burning within 20 seconds of shutting off power to the oxygen concentrator.[8] Concentrators damaged by fire may incorrectly be identified as the ignition source when this burned tubing is observed by people who are not aware of this specific burn pattern. This may create an erroneous belief that oxygen concentrators are unsafe, when these electromechanical devices do not store oxygen, cannot explode, and stop functioning when fire enters the device. In the rare event that the concentrator is the ignition source, there will be no evidence of burnt tubing leading up to the machine.

Addendum

Prescriber/Educational Checklist

Home Oxygen Hazard Awareness Safety Agreement[5, 22]

Safety Tips

- Never smoke in a room where oxygen is used.
- Post "no smoking" signs in and outside of the room to remind residents and guests not to smoke.
- Smoking cessation is strongly suggested: cessation aides will be prescribed or recommended.
- If unable or unwilling to stop smoking, patient has been instructed/reminded to remove the cannula, shut off the oxygen supply, and leave the room, or if unable/unwilling to leave the room due to physical limitations or inclement weather, wait for 10 minutes for oxygen to dissipate prior to smoking.
- Do not smoke in bed, if sleepy, or if under the influence of alcohol or medications, as this increases the risk of accidental fire.
- If oxygen is used in the home, the amount of oxygen in the air, furniture, clothing, hair, and bedding may increase, making it easier for a fire to start and spread. This means that there is a higher risk of both fires and burns.
- Never put a cannula in bedding to smoke …you might think it is off when it is not and oxygen still may bleed out.
- Do not use petroleum or flammable products on the skin and hair, especially on the face, head and hands, where they may be in close proximity to the cannula tip.
- Never use an open flame, such as candles, incense, matches, wood stoves, and sparking toys, within 5 feet (1.5 m) of the oxygen source, tubing and accessories.
- Make sure that the home has smoke alarms and test them at least monthly.
- Have a fire extinguisher available in the home.
- Have a home fire escape plan with two ways out of every room and an outside meeting place, and practice the plan at least twice a year.
- People who may have difficulty escaping a fire should have a phone near their bed or chair.

Prescribing Clinician Signature: _____ Date: _____

I agree to comply with the above safety guidelines:

Patient Signature: _____ Date: _____

The cause of the fire is frequently misrepresented by grieving family members, but sometimes even experienced fire investigators get it wrong. A malfunctioning oxygen machine was initially believed to be the cause of a tragic blaze that killed four children and an elderly grandmother on LTOT because the machine was found melted in the rubble, and the family reported it to be the ignition source.[9] Later investigation revealed that the family had attempted to move a burning couch outside, but could not get it out the door, and it is now believed that the fire started when the patient was smoking while using her oxygen on the couch.[10] Another grieving family is blaming their loved one's death on an exploding oxygen concentrator, even though her death certificate states that the cannula, the tube which delivers oxygen into the nostrils, ignited.[11] Additionally, in both of these fires, as well as all others, the fire advanced toward the oxygen supply, not away from it, and oxygen flow is needed within the cannula to produce its characteristic burn pattern, providing evidence that the machine was not the starting point.

An even greater hazard is present during fire with liquid oxygen canisters or compressed oxygen gas cylinders. Unlike oxygen concentrators, these oxygen containers may rupture or explode, releasing large quantities of oxygen contents into the room, increasing the rate of combustion, generating more heat, and even causing fragments of the tanks to become projectiles. A recent mobile home fire in Florida caused oxygen tanks to explode, accelerating the fire as well as the danger to firefighters.[12] Two fatal fires caused by LTOT patients smoking in Pitt County, North Carolina, became significantly more dangerous for victims and rescuers when oxygen tanks exploded. Both patients died in the separate incidents nine hours apart, and three firefighters were injured.[13] In yet another incident in Florida, two firefighters and a neighbor were injured in a mobile home fire that ignited medical oxygen tanks, throwing one of the rescuers 15 feet (4.6 m) in the blast.[14] Another explosion during a fatal fire in Washington caused fragments of the pressurized tanks to hit firefighters as they attempted to reach the victim, who had started the blaze by smoking while using medical oxygen.[15]

Firebreaks

Firebreaks are considered secondary prevention measures, as are smoke alarms and fire extinguishers, because they do not prevent fires, but attempt to reduce negative consequences. Firebreaks are devices designed to stop the flow of oxygen along the oxygen supply tubing, preventing the spread of fire past their location. They are used as connectors in the oxygen supply line or at the oxygen source, incorporating a small piece of plastic that holds open a spring-loaded metal ball. When the fire reaches the plastic, it melts, allowing the spring to push the ball shut, stopping the flow of oxygen. They may be installed between the cannula and the oxygen supply tubing and at the oxygen source. They are promoted to provide additional time for evacuation, to prevent the spread of fire upstream to the equipment, and to reduce the probability that the fire will spread further.

While some agency and home care equipment providers view firebreaks as a cost-effective way of improving patient safety, others share an unfavorable view, noting them as only a secondary measure that does not address behavior modification needed to lessen the high occurrence of thermal burns to the face. Others are concerned that firebreaks may send the wrong message to patients: that is smoking while on oxygen therapy is in some way "safer" with the use of these devices. Unfortunately, many incidences of fires and burns while using oxygen therapy remain undocumented, making it difficult to accurately report incidences and properly credit the potentially effective measures. In the United Kingdom (UK), where firebreak use has been required since 2005, a joint working group of oxygen suppliers, Fire and Rescue Services, and health care agencies have undertaken initiatives to raise awareness of the dangers of smoking while using oxygen.[16,17] Unfortunately, according to the Department of Health, the collated smoking-related oxygen fire incidents results are alarming. There was 106 smoking-related fires in the period from April 2010-March 2011.[18]

In considering the use of firebreaks, it is important to consider their placement in the oxygen cannula and tubing, as well as their limitations.

Placement

A firebreak's effectiveness in reducing fire potential is directly related to its proximity to the ignition point.

In the UK, home oxygen installation is rather unique. A house is piped with safety tubing affixed to the wall, with two or more outlets where the cannula is attached. The National Health Service (NHS) Home Oxygen Service Specification (2005)[19] has a requirement for firebreaks. Although not detailed in the requirement, it is largely accepted that firebreaks need to be placed as close to the patient as possible. Other agencies and standards require oxygen concentrators to be fitted with a means of preventing fire from entering the machine.[20] Therefore, there needs to be at least two firebreaks: one close to the patient and another at the oxygen supply. Since humidifiers are highly flammable with oxygen flow, a firebreak would also be needed at this spot, amounting to three firebreaks per installation.

The overwhelming majority of home oxygen fires are started by the patient at the cannula.[3] Currently, there is no firebreak device on the market that fits into the most common point of ignition: the ends of the cannula prongs.

Inner channels are incorporated in most cannulas and tubing as a safety feature, which prevents oxygen flow from occluding when tubing is kinked. These channels prevent the splicing of oxygen tubing to accommodate the firebreak; consequently, the closest opportunity to install a firebreak is at the cannula and its oxygen tubing connection.

Common cannula lengths are four and seven feet (1.2 and 2.1 m), with a seldom used one foot (.3 m) cannula available. The cannula is added to one or more 25 foot (7.6 m) sections of oxygen tubing. While it appears that a shorter length cannula would be safer, a firebreak connected to a one-foot cannula would be easily bypassed by a cigarette dangling from the outstretched arm of a sleeping patient, creating the deadliest of all scenarios.

A firebreak located close to, or at, the oxygen supply has minimal benefit. A fire reaching this point has traveled the length of the tubing, already creating serious damage. There is an elevated risk when gas and liquid oxygen cylinders and canisters are involved: large quantities of oxygen may be released, or the cylinder may rupture or explode with the intense heat of a fire. An oxygen concentrator does not present this danger, as it will stop functioning when fire enters the unit.

Limitations

Firebreaks do not reduce the occurrence of fires or awaken individuals in the event of the deadliest of fires: falling asleep in bed while smoking.

Firebreaks do not extinguish fires. Even if the cannula tubing is no longer burning, combustible items such as clothing, bedding, carpeting, curtains, or furniture already ignited will continue to burn.

Burning cannula tubing, even just a small length, produces large amounts of thick noxious smoke, which injure and overcome patients very quickly, even when firebreaks are in use.

Firebreaks only stop the flow at their position; secondary fires may reignite the oxygen tubing.

Fire can jump sections of coiled tubing and bypass the firebreak.

Firebreaks are directional and may be inserted the wrong way by patients.

Firebreaks create back pressure, resulting in reduced oxygen delivery when using orifice flow controllers, or reduced sensitivity and performance when using oxygen conserving devices. If devices deliver both continuous flow and pulse flow delivery, the firebreak may need to be removed during the pulse flow delivery mode.

Firebreaks built into oxygen concentrators or added to their outlets do not address the humidifiers when used.

Firebreaks only limit fire potential; requirement mandates would add substantial cost without evidence of effectiveness. Of the 1190 thermal burns annually, 1059, or 89 percent, burn the face of the patient. Patients who smoke and set themselves on fire at the cannula pull it off quickly and extinguish the fire. It is unlikely that fire breaks will reduce this type of fire injury or resulting death, since the fire begins proximal to its placement in the tubing.

Effective Solutions For Reducing Fires, Burns, And Deaths While Using Oxygen

The most important solution is a coordinated effort to highlight and stress the dangers of smoking while on oxygen therapy through aggressive patient and caregiver warnings and education by prescribing clinicians and equipment providers.[5]

Smoking cessation is the safest way to reduce the incidence of home oxygen fires. However, this may not be a realistic goal for all, as an estimated 30-50 percent continue to smoke. Many are unable or unwilling to quit at this point in their lives, after decades of smoking. Nicotine addiction is a chronic, relapsing disease, and less than 3 percent of attempts to quit result in sustained, 12-month cessation.[21] LTOT patients who smoke must be offered smoking cessation interventions such as nicotine replacement therapy to prevent nicotine withdrawal.[22]

If patients are going to continue to smoke, it is imperative that they understand the importance of turning off the oxygen, removing their cannula, and leaving the room where their oxygen was in use. These three precautions, in addition to thoroughly explaining the dangers of smoking with oxygen therapy equipment, need to be clearly stated and presented separately from the accompanying user manual. The majority of LTOT patients are elderly, and many have impaired vision, lower reading levels, and even different primary languages. Brochures and educational materials need to include pictures that perhaps realistically depict the results of a cannula fire with facial burns, as this is a very real possibility for patients who smoke while using their oxygen. Educational DVDs should be produced and widely distributed.[23,24]

The prescribing clinician needs to be responsible for discussing and documenting education about the hazards of smoking during oxygen therapy at the initiation of LTOT, and for reviewing this information every six months, or more frequently if a close encounter is reported that is related to smoking.

A signed checklist and agreement to comply with smoking safety guidelines should be completed by the HME provider, and any witnessed violations of safety guidelines, such as smoking while oxygen is in use, should be reported to the prescribing clinician within 48 hours.[25]

Repetition is an effective way to reinforce safety messages. The US Food and Drug Administration (FDA) requires large, graphic warnings about the dangers of smoking on every package of cigarettes,[26] not on the bottom of ashtrays. In the same way, nasal cannulas are disposable items used with all oxygen systems, and require regular replacement. Their user instructions present the best opportunity for a repetitive, highly visual safety message. FDA involvement would be required to implement this intervention.

Clinicians and providers are morally and ethically obligated to fully inform patients and their families of the risks and benefits of oxygen therapy. However, should the patient choose to continue to smoke without taking the necessary precautions, the risk of unsafe oxygen use may lead to a difficult decision of equipment removal, or at the very least, exchanging continuous flow delivery with a pulse-only system.

Conclusion

Regulating agencies, home care providers, manufacturers, and health care providers who prescribe oxygen equipment must all share the responsibility of formulating and recommending effective strategies to reduce the incidence of fires involving home oxygen equipment. These strategies must be effectively communicated to our patients and caregivers. It is dramatic to witness how easily and violently a nasal cannula burns. Perhaps if those who are setting up equipment and taking care of LTOT patients have viewed footage of how these materials ignite and burn, as well as the resulting injury and damage it creates, then this danger would be more thoroughly and emphatically explained to patients and caregivers.

The use of oxygen while smoking is product misuse with deadly consequences. This warrants patient behavior modification through primary prevention measures: education and instruction. Primary prevention is always preferable to secondary prevention when dealing with the health of patients. Education is the key to reducing the impact of unsafe choices and the incidence of fires as a result of this risky behavior. Secondary prevention measures, such as smoke alarms, fire extinguishers and firebreaks are intended to identify and treat fires early that have already occurred, but do nothing to prevent them or reduce the number of occurrences.

Oxygen equipment includes warnings about the dangers of smoking in their user manuals, and the devices are marked with symbols prohibiting smoking; yet, there is no warning on the oxygen cannula. While the industry's objective is no smoking, the reality is that up to 50 percent of LTOT patients continue to smoke. Although patients may have a right to continue to smoke, it is imperative that they turn the oxygen off, remove their cannula, and leave the room where their oxygen was in use.

Smoking is the number one cause of death in home fires for all households in the United States, and 7 percent of the estimated 680 home fire deaths per year are related to the use of oxygen therapy equipment. For the two million households that use home oxygen, there is the added hazard of high concentration oxygen. While the size of the oxygen-enriched environment created by an oxygen concentrator in and around the patient is debatable, what happens when patients bring their cigarette too close to the cannula is irrefutable. Oxygen is not flammable, but it converts cannulas and oxygen tubing into easily ignited fuses set off by cigarettes causing potentially deadly situations for patients and their families. Most of these injuries and deaths are preventable through proper education and instruction.
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Oximetry Roundup – Studies of Interest

Susan Goldstein

Critical Care Medicine reported on "Accuracy of a continuous noninvasive hemoglobin monitor in intensive care unit patients." [Crit Care Med. 2011 Oct;39(10):2277-82, Frasca D., et al] The objective of the study was to determine whether noninvasive hemoglobin measurement by Pulse CO-Oximetry could provide clinically acceptable absolute and trend accuracy in critically ill patients, compared to other invasive methods of hemoglobin assessment available at bedside and the gold standard, the laboratory analyzer. This was a prospective study in a surgical intensive care unit of a university teaching hospital. Sixty-two patients were continuously monitored with Pulse CO-Oximetry (Masimo Radical-7). There were no interventions. Four hundred seventy-one blood samples were analyzed by a point-of-care device (HemoCue 301), a satellite lab CO-Oximeter (Siemens RapidPoint 405), and a laboratory hematology analyzer (Sysmex XT-2000i), which was considered the reference device. Hemoglobin values reported from the invasive methods were compared to the values reported by the Pulse CO-Oximeter at the time of blood draw. When the case-to-case variation was assessed, the bias and limits of agreement were 0.0±1.0 g/dL for the Pulse CO-Oximeter, 0.3±1.3g/dL for the point-of-care device, and 0.9±0.6 g/dL for the satellite lab CO-Oximeter compared to the reference method. Pulse CO-Oximetry showed similar trend accuracy as satellite lab CO-Oximetry, whereas the point-of-care device did not appear to follow the trend of the laboratory analyzer as well as the other test devices. The authors concluded that when compared to laboratory reference values, hemoglobin measurement with Pulse CO-Oximetry has absolute accuracy and trending accuracy similar to widely used, invasive methods of hemoglobin measurement at bedside. Hemoglobin measurement with pulse CO-Oximetry has the additional advantages of providing continuous measurements, noninvasively, which may facilitate hemoglobin monitoring in the intensive care unit.

The journal Anesthesiology reported on the "Impact of pulse oximetry surveillance on rescue events and intensive care unit transfers: a before-and-after concurrence study." [Anesthesiology 2010 Feb;112(2):282-7. Taenzer A.H., et al]. The authors noted that some preventable deaths in hospitalized patients are due to unrecognized deterioration. There are no publications of studies that have instituted routine patient monitoring postoperatively and analyzed impact on patient outcomes. The authors implemented a patient surveillance system based on pulse oximetry with nursing notification of violation of alarm limits via wireless pager. Data were collected for 11 months before and 10 months after implementation of the system. Concurrently, matching outcome data were collected on two other postoperative units. The primary outcomes were rescue events and transfers to the intensive care unit compared before and after monitoring change. Rescue events decreased from 3.4 (1.89-4.85) to 1.2 (0.53-1.88) per 1,000 patient discharges and intensive care unit transfers from 5.6 (3.7-7.4) to 2.9 (1.4-4.3) per 1,000 patient days, whereas the comparison units had no change. The authors concluded that patient surveillance monitoring results in a reduced need for rescues and intensive care unit transfers.

The Journal of Clinical Monitoring and Computing reported on "Developing an algorithm for pulse oximetry derived respiratory rate (RR(oxi)): a healthy volunteer study." [J Clin Monit Comput. 2012 Jan 10. Addison P.S. et al. Source: Advanced Research Group, Covidien Respiratory and Monitoring Solutions, Technopole Centre, Edinburgh, UK.] The authors wrote: The presence of respiratory information within the pulse oximeter signal (PPG) is a well-documented phenomenon. However, extracting this information for the purpose of continuously monitoring respiratory rate requires: (1) the recognition of the multi-faceted manifestations of respiratory modulation components within the PPG and the complex interactions among them; (2) the implementation of appropriate advanced signal processing techniques to take full advantage of this information; and (3) the post-processing infrastructure to deliver a clinically useful reported respiratory rate to the end user. A holistic algorithmic approach to the problem is therefore required. We have developed the RR(OXI) algorithm based on this principle and its performance on healthy subject trial data is described herein. Finger PPGs were collected from a cohort of 139 healthy adult volunteers monitored during free breathing over an 8-min period. These were subsequently processed using a novel in-house algorithm based on continuous wavelet transform technology within an infrastructure incorporating weighted averaging and logical decision making processes. The computed oximeter respiratory rates (RR(oxi)) were then compared to an end-tidal CO2 reference rate. Results ranged from a lowest recorded value of 2.97 breaths per min (br/min) to a highest value of 28.02 br/min. The mean rate was 14.49 br/min with standard deviation of 4.36 br/min. Excellent agreement was found between RR(oxi) and, with a mean difference of -0.23 br/min and standard deviation of 1.14 br/min. The two measures are tightly spread around the line of agreement with a strong correlation observable between them (R (2) = 0.93). These data indicate that RR(oxi) represents a viable technology for the measurement of respiratory rate of healthy individuals.

Pediatric Critical Care Medicine reported on: "Monitoring of standard hemodynamic parameters: heart rate, systemic blood pressure, atrial pressure, pulse oximetry, and end-tidal CO2." [Pediatr Crit Care Med. 2011 Jul;12(4 Suppl):S2-S11. Sivarajan V.B., Bohn D.] The authors stated: Continuous monitoring of various clinical parameters of hemodynamic and respiratory status in pediatric critical care medicine has become routine. The evidence supporting these practices is examined in this review. A search of MEDLINE, EMBASE, PubMed, and the Cochrane Database was conducted to find controlled trials of heart rate, electrocardiography, noninvasive and invasive blood pressure, atrial pressure, end-tidal carbon dioxide, and pulse oximetry monitoring. Adult

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and pediatric data were considered. Guidelines published by the Society for Critical Care Medicine, the American Heart Association, the American Academy of Pediatrics, and the International Liaison Committee on Resuscitation were reviewed, including further review of references cited. The authors noted and concluded: Use of heart rate, electrocardiography, noninvasive and arterial blood pressure, atrial pressure, pulse oximetry, and end-tidal carbon dioxide monitoring in the pediatric critical care unit is commonplace; this practice, however, is not supported by well-controlled clinical trials. Despite the majority of literature being case series, expert opinion would suggest that use of routine pulse oximetry and end-tidal carbon dioxide is the current standard of care. In addition, literature would suggest that invasive arterial monitoring is the current standard for monitoring in the setting of shock. The use of heart rate, electrocardiography. and atrial pressure monitoring is advantageous in specific clinical scenarios (postoperative cardiac surgery); however, the evidence for this is based on numerous case series only.

Critical Care Medicine reported on "Comparison of SpO2 to PaO2 based markers of lung disease severity for children with acute lung injury." [Crit Care Med. 2012 Jan 5. Khemani R.G., et al.] The authors wrote: Given that pulse oximetry is increasingly substituting for arterial blood gas monitoring, noninvasive surrogate markers for lung disease severity are needed to stratify pediatric risk. We sought to validate prospectively the comparability of SpO2/Fio2 to PaO2/Fio2 and oxygen saturation index to oxygenation index in children. We also sought to derive a noninvasive lung injury score. The authors designed a prospective, multicentered observational study in six pediatric intensive care units. Patients comprised 137 mechanically ventilated children with SpO2 80% to 97% and an indwelling arterial catheter. Simultaneous blood gas, pulse oximetry, and ventilator settings were collected. Derivation and validation data sets were generated, and linear mixed modeling was used to derive predictive equations. Model performance and fit were evaluated using the validation data set. One thousand one hundred ninety blood gas, SpO2, and ventilator settings from 137 patients were included. Oxygen saturation index had a strong linear association with oxygenation index in both derivation and validation data sets, given by the equation oxygen saturation index = 2.76 + 0.547 oxygenation index (derivation). 1/SpO2/Fio2 had a strong linear association with 1/PaO2/Fio2 in both derivation and validation data sets given by the equation 1/SpO2/Fio2 = 0.00232 + 0.443/ PaO2/Fio2 (derivation). SpO2/Fio2 criteria for acute respiratory distress syndrome and acute lung injury were 221 (95% confidence interval [CI], 215-226) and 264 (95% CI, 259-269). Multivariate models demonstrated that oxygenation index, serum pH, and Paco2 were associated with oxygen saturation index ($p < .05$); and 1/PaO2/Fio2, mean airway pressure, serum pH, and Paco2 were associated with 1/SpO2/Fio2 ($p < .05$). There was strong concordance between the derived noninvasive lung injury score and the original pediatric modification of lung injury score with a mean difference of -0.0361 ± 0.264 sd. The authors concluded that lung severity markers, which use SpO2, are adequate surrogate markers for those that use PaO2 in children with respiratory failure for SpO2 between 80% and 97%. They should be used in clinical practice to characterize risk, to increase enrollment in clinical trials, and to determine disease prevalence.

The Canadian Respiratory Journal reported: "Oxygen desaturation during a 6 min walk test is a sign of nocturnal hypoxemia. [Can Respir J 2011Nov;18(6):333-7. Scott A.S., et al.] The authors noted that patients with chronic obstructive pulmonary disease (COPD) may experience sleep disordered breathing with nocturnal desaturation. An exploratory study was performed to determine whether any commonly measured clinical parameters were useful in predicting nocturnal desaturation in patients with COPD. A validation study was subsequently performed to confirm the utility of the parameter identified in the exploratory study as most useful in this regard. A total of 103 (exploratory cohort) and 200 (validation cohort) consecutive patients with COPD admitted for pulmonary rehabilitation were evaluated. Standard outcome measures including nocturnal oximetry and the 6 min walk test (6MWT) on room air with continuous pulse oximetry were assessed. Patients with sleep apnea or those undergoing long-term oxygen therapy were excluded. In the exploratory study, the mean (± SD) patient age was 70±9.9 years, with forced expiratory volume in 1 s of 0.76±0.34 L, which was 36±16% of predicted. Body mass index, arterial oxygen tension, oxygen saturation by pulse oximetry at rest and during the 6MWT all demonstrated significant correlations with percentage of time spent with a saturation <90%. When the lowest pulse oximetry during the 6MWT was ≤88%, 10 of 21 patients demonstrated a saturation <90% for at least 30% of sleep time. This measure yielded a positive likelihood ratio of 3.77 (95% CI 1.87 to 7.62) compared with those who did not reach this threshold value. The validation study confirmed similar detection characteristics. The authors concluded: Results from the present study suggest that monitoring oxygen saturation changes during a 6MWT is useful in helping to identify COPD patients who may experience significant nocturnal desaturation.

The journal Physiological Measurement reported on "Determination of blood volume by CO-oximetry. [Lalande S., et al, 2012 Jan;33(1):19-27.] The objective of this study was to determine whether changes in carboxyhemoglobin (COHb) saturation following carbon monoxide (CO) rebreathing can be accurately detected by pulse CO-oximetry in order to determine blood volume. Noninvasive measurements of carboxyhemoglobin saturation (SpCO) were continuously monitored by pulse CO-oximetry before, during and following 2 min of CO rebreathing. Reproducibility and accuracy of noninvasive blood volume measurements were determined in 16 healthy non-smoking individuals (15 males, age: 28 ± 2 years, body mass index: 25.4 ± 0.6 kg m(-2)) through comparison with blood volume measurements calculated from invasive measurements of COHb saturation. The coefficient of variation for noninvasive blood volume measurements performed on separate days was 15.1% which decreases to 9.1% when measurements were performed on the same day. Changes in COHb saturation and SpCO following CO rebreathing were strongly correlated ($r = 0.90$, $p < 0.01$), resulting in a significant correlation between invasive and noninvasive blood volume measurements ($r = 0.83$, $p = 0.02$). Changes in SpCO following CO rebreathing can be accurately detected by pulse CO-oximetry, which could potentially provide a simplified, convenient and reproducible method to rapidly determine blood volume in healthy individuals.

Predictors of Health Status Do Not Change Over Three-year Periods and Exacerbation Makes a Difference in COPD

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Abstract

Background: The association between disease markers and health status (HS) over time is unclear. The aim of this study was to verify the predictors of HS at baseline and after three years in Chronic Obstructive Pulmonary Disease (COPD) patients.

Methods: Ninety-five consecutive COPD patients (66% male, age = 67 ± 9 y, FEV1 = 58 ± 23%) underwent the following evaluations at baseline and after three years: body composition, pulse oximetry (SpO2), six-minute walk distance (6MWD), Modified Medical Research Council dyspnea scale (MMRC) and Saint George's Respiratory Questionnaire (SGRQ). The Charlson comorbidity index and BODE index were calculated. COPD exacerbations during the follow-up were evaluated. At baseline, age, gender, smoking, SpO2, BODE index or its components (BMI, MMRC, FEV1 and 6MWD), and Charlson index were included in a multiple linear regression analysis with the baseline SGRQ total score as the dependent variable. After three years, we included the final values of the variables plus the number of exacerbations and the final SGRQ total score as the dependent variable.

Results: SGRQ total score (42 ± 19% vs 44 ± 19%; p = 0.041) and activity domain (52 ± 21% vs 60 ± 22%; p <0.001) deteriorated during follow-up. At baseline, BODE index was selected as a predictor of SGRQ total score (R2 =0.46; p < 0.001); after three years, BODE index and age were the predictors (R2 = 0.49; p < 0.001). When the BODE index was replaced by its variables, MMRC was selected as the only variable associated with the SGRQ total score (R2 = 0.58; p < 0.001). After three years, MMRC, FEV1 and number of exacerbations were selected as predictors of SGRQ total score (R2 = 0.63; p < 0.001).

Conclusion: HS deteriorated significantly over the three-year period and the predictors of HS do not change over time. BODE index and dyspnea were predictors at baseline and after three years. Exacerbation was also a predictor of HS after three years.

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Introduction

Chronic obstructive pulmonary disease (COPD) has significant extrapulmonary consequences that lead to

comorbidity conditions and effects on patients' quality of life (QoL). Jones empathizes that it is important to make a distinction between QoL and and health status (HS) measurement, since QoL has become a central feature of studies in COPD and its impairment reflects the impact of disease in the patient. While HS measurement is a standardized quantification of the impact of the disease. The purpose of these measurements is to address a wide range of effects of the disease, thus provide emotional and psychological aspects of the illness as well as the physical; however the most of their items usually concern practical aspects of disturbance to daily life.

Health status is an important measurable outcome in patients with COPD, since it is identified as a predictor of mortality and often worsens significantly with disease progression. Dyspnea perception, nutritional depletion, exercise tolerance impairment, exacerbation frequency, and the BODE index have been identified as predictors of HS. However, in the best equations, these predictors explain 25% to 46% of the HS differences between patients with COPD. In addition, only two studies verified associations between modifications of disease markers and HS and both did not include exacerbation rate as a predictor over time. Exacerbations of COPD indicate progression of the disease and are associated with reduced health status. Therefore, we hypothesized that the rate of exacerbation may be influential in the health status over time. Identification of predictors of HS overtime may open a window of opportunity to direct resources in disease management. Thus, the aim of this study was to verify the predictors of health status at baseline and after three years in COPD patients.

Methods

Patients: In a prospective study were recruited one hundred and thirty three consecutive COPD patients with mild to very severe COPD from the outpatient clinic of a single institution. Major inclusion criteria were clinical diagnosis of COPD according to criteria set out in GOLD 2009 and the Brazilian Thoracic Society (BTS), age ≥ 40 years, smoking history ≥ 10 pack-years, and a post-bronchodilator FEV1/FVC ratio < 70%. Disease severity was categorized according of BTS and GOLD stages taking in consideration the values of FEV1 (% predicted) and arterial blood gases (GOLD I: FEV1 ≥ 80%; GOLD II: 50 ≤ FEV1 < 80%; GOLD III: 30 ≤ FEV1 < 50%; GOLD IV: FEV1 < 30% or < 50% plus

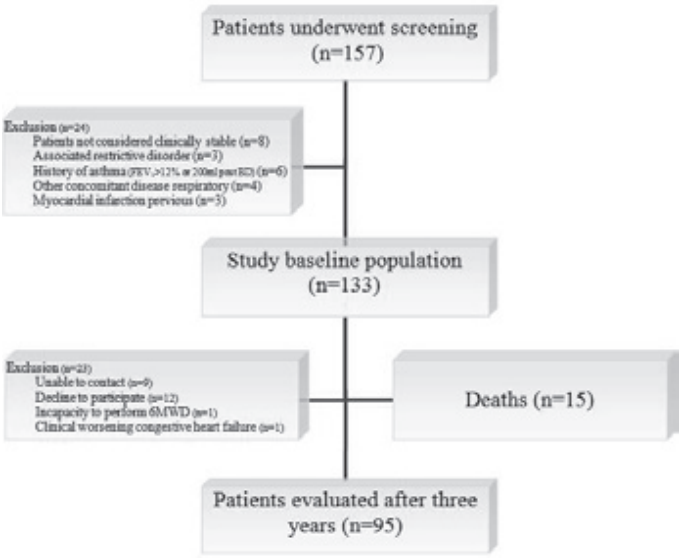

Figure 1. Diagram of patient follow up in three-year period

chronic respiratory failure). The following factors were considered grounds for exclusion: a history of asthma and/or FEV1 increased > 12% or 200 mL post-bronchodilator test, associated restrictive disorder (tuberculosis sequelae, interstitial fibrosis); other clinically significant concomitant respiratory diseases (sleep apnea/hypopnea syndrome, lung cancer); noncompliance with COPD treatment; myocardial infarction within the preceding four months; and unstable angina or congestive heart failure (New York Heart Association class III or IV). Patients not considered clinically stable (ie, with changes in medication dose or frequency, disease exacerbation, or hospital admissions in the preceding 6 weeks) were also excluded. All patients were optimized in terms of standard medical therapy according to GOLD and BTS guidelines. Active smoking patients received practical advice to quit smoking and were referred to smoking cessation program. Patients with chronic hypoxemia received a stable dose of oxygen therapy over the 6 months before study enrollment.

Measurements: Spirometry was performed, using the KOKO Spirometer, before and 15 minutes after the inhalation of 400 mcg salbutamol (Ferrari KOKO Louisville, CO), according to criteria set by the American Thoracic Society. FEV1 values are expressed in liters, percentages of FVC, and percentages of reference values. Pulse oximetry (SpO2) was assessed using a Onyx oxymeter (Model 9500 Oximeter; Nonin Medical Inc, Minneapolis, MN) while patients were breathing room air. Body weight and height were measured. Body mass index [BMI = weight in kg/(height in m)2] was calculated. Smoking history was obtained by patient interview using standardized instruments at baseline and smoking cessation by self report during patients' contacts. A translated version of the Saint George's Respiratory Questionnaire (SGRQ), validated for use in Brazil, was utilized to evaluate patient HS. Minimum clinically important difference (MCID) was defined as a decrease of ≥ 4% in the SGRQ domains. Dyspnea was assessed using a translated version of the Modified Medical Research Council (MMRC) scale. The six-minute walk distance (6MWD) was performed according to American Thoracic Society guidelines. BMI/airflow obstruction/dyspnea/exercise capacity (BODE) index was calculated using the model described by Celli et al. BODE scores were categorized as class 1 (score: 0 to 2), class 2 (score: 3 to 4); class 3 (score: 5 to 6); and class 4 (score: 7 to 10). Comorbid disease data were collected from patient medical records and quantified according to the Charlson index. Patients or family, in the case of death, were contacted by telephone every 3 months to determine the occurrence of exacerbations or hospital admissions. During the telephone interview a structured questionnaire was used to identify data associated with exacerbation and/or hospitalizations. Data were confirmed during clinic visits and by reviewing medical records. An exacerbation was defined as an increase in dyspnea, sputum purulence, and increased sputum volume and classified as moderate (requiring a visit to a doctor or the emergency department and treatment with antibiotics or systemic steroids or both) or severe type II (requiring hospital admission). Mild exacerbations not requiring intervention were not included in the study.

Statistical analysis: All data were analyzed using SigmaStat 3.2 (Inc, Chicago, IL, USA) and STATA 10.0 (Stata Corp, TX). Mean ± SD or median interquartile range (25-75%) was used depending on distribution. Paired t-test or Wilcoxon test was performed to compare characteristics at baseline to those presenting after three years. At baseline, age, gender, smoking status, SpO2, BODE index or its components (BMI, MMRC, FEV1 and 6MWD), and Charlson index were included in a multiple linear regression analysis with the baseline SGRQ total score as the dependent variable. This analysis was done separately for all patients evaluated at baseline and for those followed during three years. After three years, we included the final values of the same

Table 1 Characteristics of COPD patients followed-up over a three-year period

Variables	Initial Assessment (n = 95)	Final Assessment (n = 95)	p-value
FEV_1 (%)	59.3 ± 23.2	58.5 ± 22.7	0.228
FEV_1 (L)	1.4 ± 0.6	1.3 ± 0.5	**< 0.001**
FVC (%)	90.8 ± 23.8	88.9 ± 24.7	0.167
FVC (L)	2.7 ± 0.8	2.5 ± 0.8	**0.004**
FEV_1/FVC	52.2 ± 11.7	51.3 ± 10.4	0.123
BMI (kg/m^2)	25.9 ± 5.8	25.8 ± 5.6	0.382
SpO_2 (%)	93.6 ± 3.1	92.0 ± 4.8	**< 0.001**
MMRC (score)	1.5 ± 1.0	1.9 ± 1.1	**0.002**
6MWD (m)	437.7 ± 85.6	412. 4 ± 100.0	**0.001**
Charlson index (score)	3.5 ± 1.5	3.9 ± 1.4	**0.009**
BODE index (score)	2.2 ± 1.8	2.6 ± 2.3	**0.008**

Paired t-test or Wilcoxon. Values are presented as mean ± SD or as median (25-75% interquartile range). FEV_1: forced expiratory volume in the first second (% of predicted); FVC: forced vital capacity (% of predicted); BMI: body mass index; SpO_2: pulse oximetry; MMRC: Modified Medical Research Council; 6MWD: six-minute walking distance; $p < 0.05$.

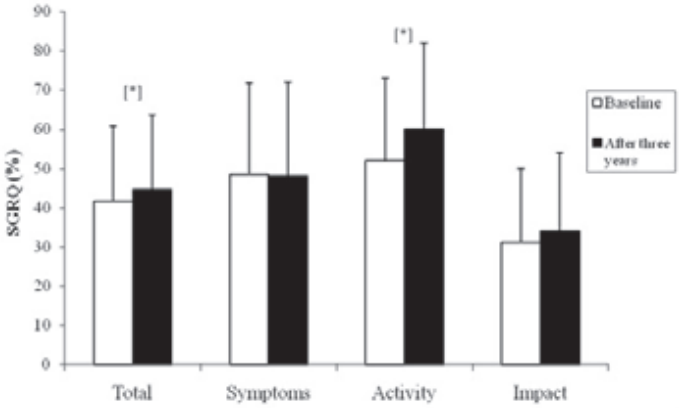

Figure 2. Mean SGRQ domains at baseline and after three years. SGRQ: Saint George's Respiratory Questionnaire; *p < 0.05.

variables with the final SGRQ total score as the dependent variable. In another model, we evaluated the influence of the number of exacerbations in the previous model. This variable was included only in the final moment because reliable information on exacerbations was not available at baseline and was collected during the follow-up period. The variables included were those known to be associated with HS in the literature and the potential confounders. Age and gender at baseline and the difference between baseline and after 3 years measurements (Δ) for pulse oximetry (Δ SpO2), Δ Bode index, Δ Charlson index and number of exacerbation were included in a multiple logistic regression to evaluate the influence of these variables on clinically significant stability/improvement or worsening, defined as a change ≥ 4%, of the SGRQ domains. We repeated the previous analyses replacing the BODE index by its components. A $p < 0.05$ was defined as statistically significant.

Results

The baseline characteristics of the 133 patients (69% men) were mean age of 65 ± 9 years and smoking exposure of 53 ± 28 pack-years; 45 patients (34%) were active smokers. Seventy-two patients were using long-term bronchodilators and 49 patients were regularly using inhaled corticosteroid, 25 had been on stable oxygen flow therapy for the last six months. No patients were medicated with theophylline or leukotriene modifiers. A total of 3 (2%) patients presented congestive heart failure class I or II, 6 (4%) patients presented dyslipidemia, 9 (6%) patients presented diabetes mellitus and 42 (31%) patients presented arterial hypertension at baseline.

Of the 133 patients initially evaluated, 38 were excluded from the final analyses; 15 patients died and 23 dropped out. Thus, 95 patients were monitored for three years (Figure 1). Comparisons of the excluded patients versus those completing the study did not show significant differences at baseline.

At baseline, the mean age of the 95 studied patients (66% men) was 64 ± 9 years and smoking exposure was 54 ± 28 pack-years; 32 patients (33%) were active smokers, and 8 of them stopped smoking during follow-up. The comparison of patient characteristics between baseline and after three years is shown in Table 1 and has been presented in a previous publication.

At baseline, 18% of patients were in GOLD stage I, 39% were in stage II, 19% were in stage III, and 24% were in stage IV COPD. There was no difference in the proportion of patients within each disease severity between baseline and after three years ($p = 0.865$). According to BODE index, at baseline, 57 were in class 1, 21 in class 2 and 17 were in class 3. After three years, there was significant different between the classes, since 51 were in class 1, 23 in class 2, 14 in class 3 and 7 patients in class 4 ($p < 0.05$).

Health status showed significant worsening in the activity domain score (52 ± 21 vs. 60 ± 22%, $p < 0.001$) and SGRQ total score (42 ± 19 vs. 44 ± 19%, $p = 0.041$) (Figure 2). The SGRQ total scores were significantly higher for patients in stage IV than for patients in stages I and II, and also for patients in stage III than for patients in stage I and for patients in stage II than patients in stage I. We did not identify differences between stages II and III and stages III and IV after three years. In the BODE classification, we found that HS change between the classes 1 and 2, classes 1 and 3 and classes 1 and 4 after three years.

Seventy-two patients (75.8%) had at least one exacerbation during the study period and in these patients the baseline SGRQ total score was significantly higher [44 (30-61)%] in those without exacerbation [27 (14-39)%, $p < 0.001$].

In the multiple linear regression analysis, the BODE index was selected as predictor of SGRQ total score at baseline ($R2 = 0.46$; $p < 0.001$). After three years, the BODE index and the patient age were the predictors in the model without exacerbation ($R2 = 0.49$; $p < 0.001$) (Table 2). When exacerbation was included, the variables selected did not change ($R2 = 0.51$; $p < 0.001$) (data not shown). When BODE index was replaced by its variables (BMI, MMRC, FEV1 and 6MWD), MMRC was the predictor of SGRQ total score at baseline ($R2 = 0.58$; $p < 0.001$) and MMRC and FEV1 after three years ($R2 = 0.61$; $p < 0.001$) (Table 3). When number of exacerbations was included in the model, the predictors of HS were MMRC, FEV1 and exacerbation ($R2 = 0.63$; $p < 0.001$) (Table 4). At baseline, predictors of HS for 133 patients were the same shown for 95 patients followed during three years, BODE index and the patient age.

Fifty-one percent of the patients presented with clinical worsening (≥ 4%) on SGRQ total score, and 59% of them were in severe to very severe stages of the disease. A total of 28% reported clinical improvement and 21% had no clinical change on

Table 2 Multiple linear regression model to evaluate predictors for baseline total SGRQ and after three years follow-up (n = 95)

Variables	Baseline total SGRQ Coefficient (95% CI)	p-value	Final total SGRQ Coefficient (95% CI)	p-value
Male	-3.41 (-11.09, 4.27)	0.380	-0.42 (-7.59, 6.73)	0.905
Age (years)	-0.52 (-1.08, 0.03)	0.063	-0.62 (-1.13, -0.10)	**0, 019**
Smoking status	1.68 (-5.83, 9.20)	0.658	-2.70 (-10.21, 4.75)	0.470
SpO_2 (%)	-0.60 (-1.72, 0.52)	0.291	-0.35 (-1.06, 0.35)	0.326
Bode index (score)	5.59 (3.73, 7.45)	**< 0.001**	4.90 (3.41, 6.40)	**< 0.001**
Charlson index (score)	-1.54 (-4.46, 1.36)	0.294	0.29 (-2.60, 3.20)	0.840

SGRQ: SpO_2: pulse oximetry; Baseline ($R^2 = 0.46$; $p < 0.05$); After three years ($R^2 = 0.49$; $p < 0.05$)

Table 3 Multiple linear regression model to evaluate predictors for baseline total SGRQ and after three years follow-up (n = 95)

Variables	Baseline total SGRQ Coefficient (95% CI)	p-value	Final total SGRQ Coefficient (95% CI)	p-value
Male	1.11 (-6.32, 8.56)	0.766	-1.02 (-7.67, 5.62)	0.760
Age (y)	-0.51 (-1.05, 0.01)	0.059	-0.14 (-0.67, 0.37)	0.570
Smoking	5.68 (-1.55, 12.93)	0.122	1.96 (-5.46, 9.40)	0.600
SpO_2 (%)	-0.22 (-1.29, 0.84)	0.675	-0.27 (-0.91, 0.36)	0.395
FEV_1 (%)	-0.11 (-0.25, 0.25)	0.105	-0.18 (-0.32, -0.05)	**0.007**
6MWD (m)	-0.01 (-0.05, 0.03)	0.731	0.01 (-0.02, 0.56)	0.426
BMI (kg/m^2)	-0.24 (-0.75, 0.23)	0.349	0.18 (-0.34, 0.72)	0.489
MMRC (score)	11.72 (8.17, 15.26)	**< 0.001**	10.44 (7.08, 13.80)	**< 0.001**
Charlson index	-1.16 (-3.82, 1.48)	0.384	-0.39 (-3.10, 2.30)	0.770

SpO_2: pulse oximetry; FEV_1: forced expiratory volume in the first second (% of predicted); 6MWD: six-minute walking distance; BMI: body mass index; MMRC: Modified Medical Research Council; Baseline ($R^2 = 0.58$; $p < 0.05$); After three years ($R^2 = 0.61$; $p < 0.05$).

SGRQ total score. In the multiple logistic regression analysis, modification in the BODE index was the predictor of clinically significant worsening on SGRQ total score [OR 1.48 (95% CI 1.04-2.09); p = 0.027] (Figure 3) and on SGRQ activity domain [OR 1.45 (95% IC 1.04-2.03); p = 0.029]. In a second model, when BODE index was replaced by its variables (BMI, MMRC, FEV1 and 6MWD), Δ MMRC was the predictor of clinically significant worsening on SGRQ total score [OR 2.73 (95% IC 1.47-5.07); p = 0.001] (Figure 4) and on activity domain [OR 1.67 (95% IC 1.04-2.03); p = 0.031]. Predictor variables of clinically significant stability/improvement or worsening on SGRQ symptom and impact domains were not identified.

Discussion

Results of this study showed that the BODE index was a predictor of HS at baseline and after three years. The components of BODE index associated with HS were dyspnea sensation and FEV1. The rate of exacerbations also influenced the HS over time. Clinically significant deterioration of HS was associated with increase in dyspnea perception during the follow-up. These findings reinforce the importance of therapeutic measures to control the dyspnea, prevent progression of airflow obstruction and exacerbations as tools to maintain or improve the health status of COPD patients.

We observed a significant worsening in the activity domain and SGRQ total score during the follow-up.

Our results are consistent with those of Oga et al, who showed a deterioration of health status as indicated by increased activity and impact domains and SGRQ total scores after a five-year period. Besides the statistically significant deterioration of HS overtime, our results showed that 51% of the patients presented clinically significant worsening (≥ 4%) on SGRQ total score; 59% of these patients presented severe to very severe disease. Oga et al showed that the mean annual change in the health status scores was 1.87 units/year from the SGRQ total score and took 2.14 years to deteriorate by a clinically significant worsening of 4 units.

We observed that the SGRQ total scores tended to be higher in patients with more advanced disease according to GOLD staging system; however, we did not find differences when patients with moderate and severe disease were compared or between patients with severe and very severe disease. Hajiro et al also demonstrated that patients in the worst disease stage had the worst scores on SGRQ total score; in addition, GOLD staging of COPD was shown to be associated with important differences in health status between severe and moderate disease, but not between other disease stages. Cross-sectional studies showed that BODE index is better correlated to health status as assessed by a diseasespecific index for COPD than the GOLD staging criteria based largely on the FEV1. Ong et al evaluated 100 patients with stable COPD and found that important differences in health status between the highest classes (classes 3 and 4) of the BODE classification system were observed but not between lower grade consecutive classes. In our study, we found that HS did not change between the classes 2, 3 and 4. Despite the small number of patients in class 4, this finding shows that the health status cannot be inferred from the BODE index and should be systematically assessed in the individual patient. Therefore, these studies show that there is not linearity of differences between SGRQ values in different stages of severity.

Table 4 Multiple linear regression model to evaluate predictors for total SGRQ after three years follow-up (n = 95)

Final total SGRQ (%)	Dependent variables	Coefficient (95% CI)	p-value
	Male	-0.14 (-6.69, 6.40)	0.965
	Age (y)	-0.16 (-0.67, 0.34)	0.525
	Smoking	3.05 (-4.28, 10.39)	0.410
	SpO_2 (%)	-0.27 (-0.89, 0.35)	0.389
	FEV_1 (%)	-0.14 (-0.28, -0.01)	**0.043**
	6MWD (m)	0.01 (-0.02, 0.05)	0.433
	BMI (kg/m^2)	0.27 (-0.26, 0.79)	0.315
	MMRC (score)	9.99 (6.68, 13.30)	**< 0.001**
	Charlson index (score)	-0.19 (-2.84, 2.45)	0.883
	Number of exacerbations	1.29 (0.11, 2.47)	**0.031**

SpO_2: pulse oximetry; FEV_1: forced expiratory volume in the first second (% of predicted); 6MWD: six-minute walking distance; BMI: body mass index; MRC: Modified Medical Research Council; $R^2 = 0.63$; $p < 0.05$.

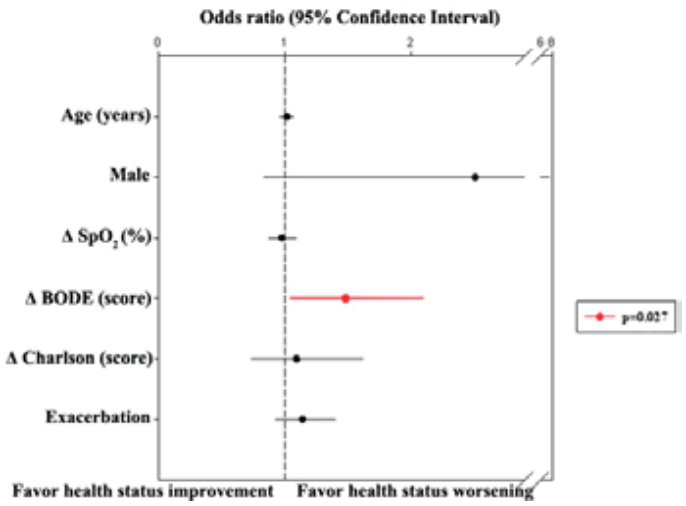

Figure 3. Multiple logistic regression analysis to evaluate the predictors for stability/improvement or worsening (≥ 4%) on SGRQ total score (n=95). Δ: final assessment values-initial assessment values; SpO2: pulse oximetry; Exacerbation: number of exacerbations for patient in the three-year period.

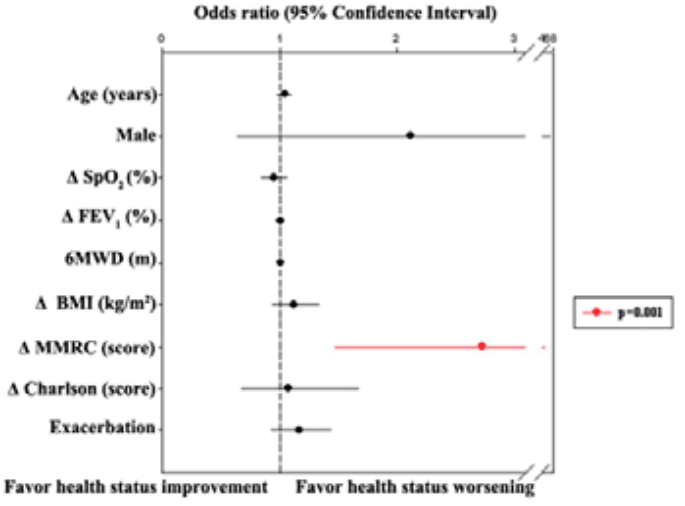

Figure 4. Multiple logistic regression analysis to evaluate the predictors for stability/improvement or worsening (≥ 4%) on SGRQ total score (n=95). Δ: final assessment values-initial assessment values; SpO2: pulse oximetry; FEV1: forced expiratory volume in the first second (% of predicted); 6MWD: six-minute walking distance; BMI: body mass index; MMRC: Modified Medical Research Council; Exacerbation: number of exacerbations for patient in the three-year period.

Our results showed that FEV1 was a predictor of HS after a three-year period. Lin et al showed that with the decrease of airflow limitation, SGRQ total and SGRQ subscales were increased correspondingly at baseline and the end of 1 year. However, in Oga et al, the changes in health status assessed by the SGRQ total scores were weakly correlated with the changes in FEV1%.

In our study, dyspnea was strongly associated with HS at all times. The Transition Dyspnea Index (TDI) measures changes in dyspnea sensation from baseline over time; however, the patient has to recall their baseline (Baseline Dyspnea Index) in order to answer questions regarding the TDI. Therefore, we used the MMRC scale which is a traditional instrument included in the BODE index. In multiple logistic regression, when the BODE index was replaced by its variables, worsening of one unit in MMRC doubled the risk of worsening of the SGRQ total score. The association between dyspnea and HS is known from results of previous cross-sectional and longitudinal studies. In a five year follow-up study, annual changes of the SGRQ total score showed correlation with changes in the dyspnea intensity, assessed by MMRC. In the same study, the authors verified correlation of annual changes of SGRQ total score with anxiety, depression scores and peak oxygen uptake. However, the authors did not evaluate the influence of the BODE index and the number of exacerbation in the changes of health status.

Our results showed that exacerbation rate was associated with impairment of HS during follow-up. This finding reinforces the impact of exacerbation in clinical outcomes; exacerbations of COPD indicate clinical instability and progression of the disease and are associated with increased morbidity, deterioration of comorbidities, and reduced health status. In our study, patients who had at least one exacerbation during follow-up presented with higher SGRQ scores at baseline when compared to patients without exacerbations. Spencer et al showed that baseline SGRQ scores were significantly higher in patients who experienced an exacerbation as compared to those without exacerbations during the three-year follow up. Miravitlles et al found that among patients with moderate COPD, those with frequent exacerbations had a greater change in SGRQ total score (2 units per year) than those with infrequent exacerbations, after controlling for baseline characteristics at 2 year follow-up. However, the number of exacerbation variables may have limitations, since Seemungal et al have shown that about 50% of exacerbations are untreated, or at least not reported to physicians.

In the multiple linear regression analysis, we verified that the BODE index was a predictor of health status overtime. In addition, worsening of one unit of the BODE index has a 50% increased risk of worsening in the SGRQ total score and activity domain. Our findings are in accord with Lin et al., who found by multiple linear regression that the BODE index was associated with SGRQ at baseline at the end of 1 year follow up after adjustment for age, gender, and smoking status. COPD is a complex multidimensional disease and the BODE index, a multidimensional grading system, has been shown to be a superior predictor of the risk of death. BODE index is also predictor of acute exacerbations, hospitalization and health status. However, it does not incorporate the exacerbation of COPD, which is an important outcome marker.

As shown in our study, HS impairment was associated with more than one outcome measure and may reflect the lung and systemic effects of COPD. Therefore, predictors of HS assessments will enable clinicians to evaluate the overall efficacy of the management of disease. Health-status as a concept of high complexity is assessed indirectly and requires the application of specially designed questionnaires. The SGRQ has been widely used in clinical trials as an endpoint to assess the effects of treatment and management interventions on health status in COPD, although their use in clinical practice is hampered since this instrument is relatively time and resource consuming. Self-rated health (SRH) data may be an alternative because of their simplicity of collection and strong association with outcome; such it has been shown that SRH predicted exacerbations and hospitalizations in patients with COPD. In additional, SHR was associated with similar HS determinants as in present study. However, nowadays the formal questionnaires can be completed in computers, in several places, and the scores

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Weight and Metabolic Effects of CPAP in Obstructive Sleep Apnea Patients with Obesity

Jose M. Garcia, Hossein Sharafkhaneh, Max Hirshkowitz, Rania Elkhatib, Amir Sharafkhaneh.

Abstract

Background: Obstructive sleep apnea (OSA) is associated with obesity, insulin resistance (IR) and diabetes. Continuous positive airway pressure (CPAP) rapidly mitigates OSA in obese subjects but its metabolic effects are not well-characterized. We postulated that CPAP will decrease IR, ghrelin and resistin and increase adiponectin levels in this setting.

Methods: In a pre- and post-treatment, within-subject design, insulin and appetite-regulating hormones were assayed in 20 obese subjects with OSA before and after 6 months of CPAP use. Primary outcome measures included glucose, insulin, and IR levels. Other measures included ghrelin, leptin, adiponectin and resistin levels. Body weight change were recorded and used to examine the relationship between glucose regulation and appetite-regulating hormones.

Results: CPAP effectively improved hypoxia. However, subjects had increased insulin and IR. Fasting ghrelin decreased significantly while leptin, adiponectin and resistin remained unchanged. Forty percent of patients gained weight significantly. Changes in body weight directly correlated with changes in insulin and IR. Ghrelin changes inversely correlated with changes in IR but did not change as a function of weight.

Conclusions: Weight change rather than elimination of hypoxia modulated alterations in IR in obese patients with OSA during the first six months of CPAP therapy.

Background

Obstructive sleep apnea (OSA) is characterized by sleep-related airway obstructions that produce apnea. These events provoke arousals and cause oxygen desaturations and heightened sympathetic activity during sleep and waking hours[1] that may play a role in the development of insulin resistance.[2] Obesity is a strong risk factor for OSA[3] and both obesity and OSA are associated with increased insulin resistance and diabetes.[4]

Hormones involved in the regulation of body weight and glucose metabolism include ghrelin, leptin, adiponectin and resistin. Ghrelin is an orexigenic hormone and it has been proposed as a cause of increased appetite and obesity.[5] Administration of ghrelin increases adiposity, food intake and body weight.[6] It also regulates glucose homeostasis increasing glucose levels and decreasing insulin secretion.[7] Leptin is a hormone secreted by adipocytes in proportion to fat mass. It is elevated in obesity and its administration suppresses appetite and induces weight loss.[8] Resistin and adiponectin are also adipocyte-derived hormones linked to obesity, insulin resistance, and diabetes. Adiponectin levels inversely correlate with BMI and are lower in individuals with diabetes whereas resistin directly correlates with obesity and insulin resistance.

Whether treatment of OSA can reverse insulin resistance and prevent body weight gain is controversial. Because hypoxemia-induced sympathetic activation is thought to be the source of the endocrine abnormalities often seen in patients with OSA, and continuous positive airway pressure (CPAP) effectively reverses hypoxemia in patients with OSA, we hypothesized that CPAP will decrease insulin resistance, ghrelin and resistin levels and increase adiponectin levels in a group of obese individuals with OSA.

Methods

The protocol was approved by the Baylor College of Medicine Institutional Review Board, and the Research and Development Committee of the Michael E. DeBakey Veterans Affairs Medical Center in Houston. This study was conducted between April 2004 and March 2006. All clinical investigation was conducted in accordance with the guidelines in The Declaration of Helsinki and all subjects provided written informed consent.

Adult subjects with no prior history of diabetes were recruited from patients referred to the hospital's Sleep Center for evaluation of OSA. OSA was confirmed by laboratory polysomnography (PSG). Twenty-three patients with an apnea+hypopnea index (AHI) ≥15 obstructive and/or mixed events/hour as criteria participated in the project. We did not enroll subjects with AHI <15 because CPAP compliance in these patients may not be optimal. For PSG, we scheduled bedtimes and morning awakening times to resemble each participant's usual habit. We made PSG recordings using Grass Heritage computerized polysomnographic systems. Briefly, standard

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Table 1 Baseline Subjects Characteristics (n = 20)

Age (yrs)	59.7 ± 2
Body weight (Kg)	108 ± 5.3
BMI (Kg/m^2)	36.5 ± 1.8
Race (W, AA, H)	14, 4, 2
Male/Female	17/3
Leptin (ng/dL)	22.7 ± 6
Active ghrelin (pg/mL)	131 ± 48
Insulin (mU/mL)	22 ± 3
Adiponectin (ng/mL)	8.3 ± 1.2
Resistin (ng/mL)	3.1 ± 0.4
Glucose (mg/dL)	105 ± 4
QUICKI	0.31 ± 0.008
ISI	2.6 ± 0.55
HOMA-IR	5.9 ± 1
ESS	14.6 ± 1
AHI (episodes/hr)	50 ± 6
Lowest O2 sat. (%)	77 ± 3
Mean O2 sat. (%)	91.9 ± 0.9

Data shown are mean +/- SEM. BMI: Body mass index, W: White, AA: African American, H: Hispanic, QUICKI: quantitative insulin sensitivity check index, ISI: Insulin sensitivity index, HOMA-IR: homeostasis model assessment, ESS: Epworth Sleepiness Scale, AHI: Apnea/Hypopnea Index.

surface electrodes were used to record electroencephalographic, electrooculographic, electromyographic (submentalis and anterior tibialis), and electrocardiographic activities. Nasal-oral thermocouples monitored airflow, while thoracic and abdominal movements indicated respiratory effort. The respiratory tracings were scored for the presence of apneas (10-second, or longer, cessation in nasal-oral airflow) or hypopneas (a 10-second, or longer, reduction of nasal-oral airflow of 30% or more with O_2 desaturation more than 4% or arousal). Blood oxygen saturation was monitored with pulse oximetry. Recording and scoring technique followed the current American Academy of Sleep Medicine standards for human subjects. AHI was calculated to indicate the number of sleep-disordered breathing events/hour of sleep. Subjects qualifying for study underwent an oral glucose tolerance test (OGTT) and completed an Epworth Sleepiness Scale (ESS). After this baseline evaluation, the subjects underwent an attended CPAP titration with polysomnography. The best pressure was the one associated with the lowest AHI while the patient slept 20 minutes, or more. After titration, subjects received a CPAP machine and related accessories (Respironics, REMStar Pro) with card reader to monitor the compliance of CPAP and were followed for 6 months. Subjects were seen 2-3 times during the study and CPAP compliance was checked during the visits by using the EncorPro SmartCard (Respironics). CPAP efficacy was rechecked with overnight pulse oximetry at the end of the study. To mimic their real-life situation, subjects were given no specific instructions regarding diet or physical activity.

Table 2 Sleep and metabolic parameters before and after CPAP use

	Baseline	Post-CPAP	p value
CPAP pressure (cm H2O)		10 ± 3.2	
CPAP use (days)		165 ± 17	
CPAP use (Hrs/day)		5.3 ± 0.35	
ESS	14.6 ± 1	9.5 ± 1	**0.002**
Lowest O2 sat. (%)	77 ± 3	89.3 ± 3	**0.005**
Mean O2 sat. (%)	93.2 ± 0.7	93.8 ± 0.62	**0.5**
Systolic blood pressure (mmHg)	124 ± 3	129 ± 4	0.07
Diastolic blood pressure (mmHg)	76 ± 2	76 ± 2	0.99
Heart rate (bpm)	77 ± 3	72 ± 3	0.27
Body weight (Kg)	108 ± 5.3	109.6 ± 5.4	**0.04**
BMI (Kg/m^2)	36.5 ± 1.8	37.1 ± 1.8	0.06
Leptin (ng/dL)	22.7 ± 6	21.6 ± 4	0.61
Adiponectin (ng/mL)	8.3 ± 1.2	8.2 ± 1.2	0.94
Resistin (ng/mL)	3.1 ± 0.4	3.2 ± 0.4	0.79
HOMA-IR	5.9 ± 1	7.5 ± 1.2	**0.04**
ISI	2.6 ± 0.55	2.1 ± 0.33	0.09
QUICKI	0.31 ± 0.008	0.3 ± 0.006	**0.02**

Significant differences compared to baseline ($p \leq 0.05$) appear in bold. ESS: Epworth Sleepiness Scale, QUICKI: quantitative insulin sensitivity check index, ISI: Insulin sensitivity index, HOMA-IR: homeostasis model assessment.

Blood was collected in the morning between 7 and 8 AM in EDTA-containing tubes and kept at 4°C during processing. Aprotinin (100 µL containing 0.6 TIU per mL of blood) was added to one of the tubes and the samples were then centrifuged at 3000 rpm for 30 minutes. Active ghrelin levels were measured by a radioimmunoassay (RIA) kit (LINCO Research, St Charles, MO) in plasma treated with HCL and phenylmethylsulfonyl-fluoride. Insulin and leptin levels were measured by a radioimmunoassay kit (Linco Research, St. Charles, MO) as we have previously described.[9] Glucose levels were measured in the same plasma samples by the MEDVAMC's laboratory. Adiponectin levels were measured by RIA with a kit from LINCO Research (St. Charles, MO) in diluted plasma samples (1:450). Resistin was measured in plasma samples by ELISA (Biovendor, Candler, NC).

The subjects underwent an early morning 75 g. OGTT at baseline and after six months of CPAP therapy. Blood samples were taken at -5, 30, 60, 90, and 120 min. for the measurement of plasma active ghrelin, glucose and insulin concentrations. Fasting insulin sensitivity was assessed using the homeostasis model assessment (HOMA) and the quantitative insulin sensitivity check index (QUICKI). Both HOMA [HOMA-IR = fasting glucose (mmol/L) × fasting insulin (microU/ml)/22.5] and QUICKI (1/[log fasting insulin + log fasting glucose]) were calculated as previously described. Estimates of insulin resistance from both indices correlate well with estimates from the "gold standard" hyperinsulinemic euglycemic clamp method.[10,11] In addition, from the OGTT we calculated a previously validated index of whole-body insulin sensitivity (ISI) (10,000/square root of [fasting glucose × fasting insulin] × [mean glucose × mean insulin during OGTT]), which is highly correlated ($r = 0.73$, $p < 0.0001$) with the rate of whole-body glucose disposal during the euglycemic insulin clamp.[12]

SPSS version 12.00 software for Windows (SPSS Inc Chicago, IL) was used for statistical analysis. Parametric variables are expressed as mean ± S.E. unless otherwise stated. Categorical parameters are expressed as percentages. The areas under the curve ($AUC_{0\text{-}120}$) for active ghrelin, insulin and glucose levels were calculated using the trapezoidal rule. For normally distributed data, statistical comparisons were performed using the Fisher's exact test or Chi-square test for categorical data and t-test for parametric data. Pearson's correlations were obtained between continuous variables. When data were not normally distributed, Wilcoxon rank test or Mann-Whitney tests were used

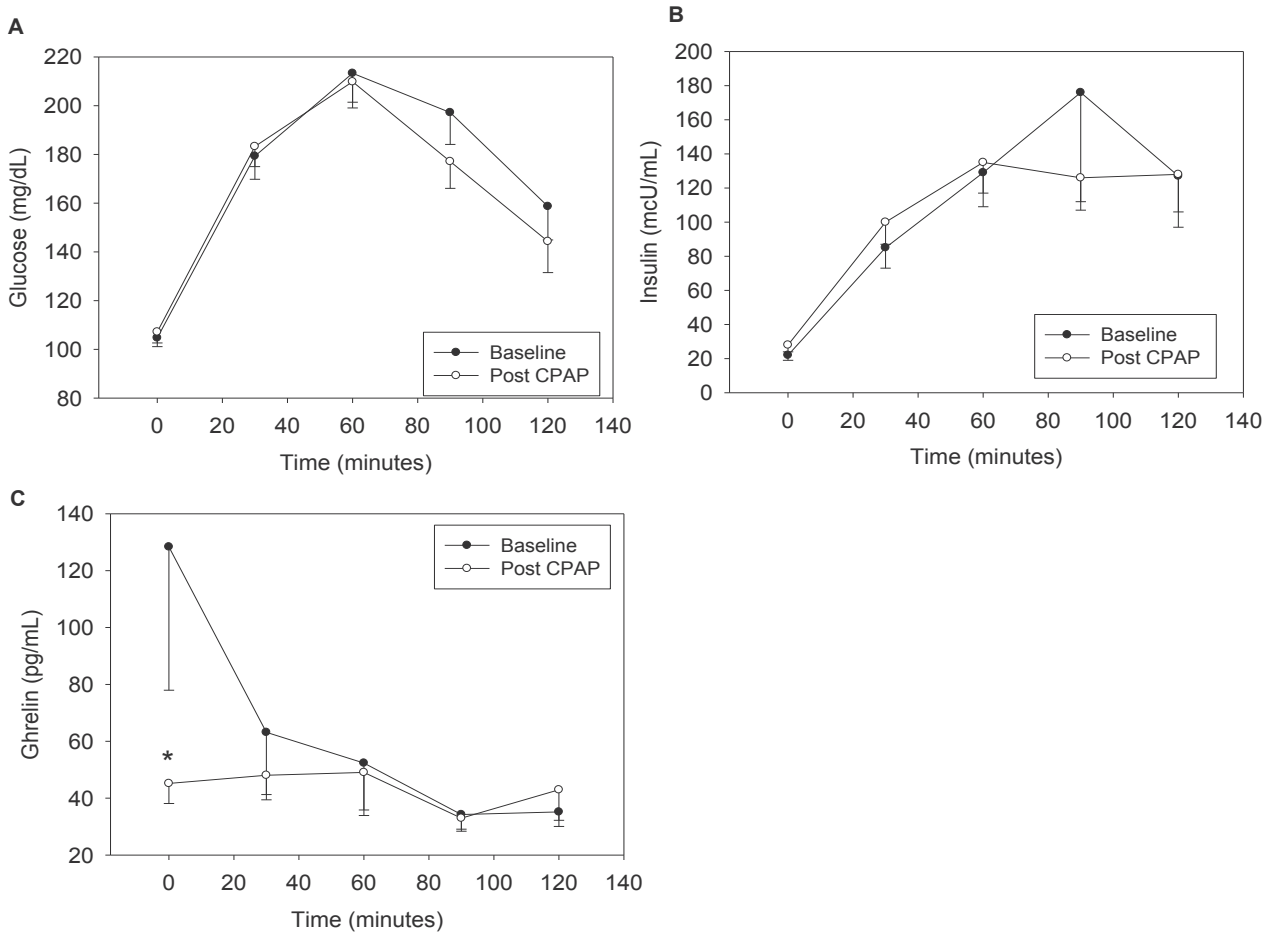

Figure 1 Glucose (A), insulin (B) and active ghrelin levels (C) during OGTT before and after CPAP. *p < 0.05 for baseline values. p values for fasting and $AUC_{0\text{-}120}$ glucose were 0.88 and 0.24 respectively. p value for insulin $AUC_{0\text{-}120}$ was 0.7; p value for ghrelin $AUC_{0\text{-}120}$ was 0.4.

and Spearman's correlation was obtained to measure associations between continuous variables. Linear regression tested the predictive value of changes in BMI and nadir SpO_2 entered individually on the following outcomes: changes in insulin, insulin resistance as measured by HOMA-IR, leptin, ghrelin, adiponectin and resistin. Inclusion was set at probability $F<0.05$, and exclusion was set at $F>0.10$. Collinearity diagnostics used to test for multicollinearity included tolerance, variance inflation factor and condition index. Inferential analysis was conducted using an alpha error level of ≤0.05 to determine significance. Power calculations were done using paired t-test, two-sided methodology based on previously published insulin sensitivity and ghrelin mean changes from baseline where insulin sensitivity improved after 3 months of CPAP by 1.37 mcmol/Kg × min[13] and ghrelin decreased by 38.2 pg/mL after two days of CPAP[14] in OSA patients. Assuming a SD of 1.7 mcmol/Kg × min and 45 pg/mL respectively, we estimated that a sample size of 23 subjects would be sufficient to detect statistically significant differences ($p \leq 0.05$) in the outcomes measured with a power of 90% and taking into account an attrition rate of 15% (20 completers).

Results

Twenty-three subjects enrolled and 20 subjects completed the study. One subject died unexpectedly at home, from unknown cause. Two subjects were lost to follow up. We did not enroll any subjects with a diagnosis of diabetes. Table 1 shows demographic, PSG and metabolic parameters for these subjects. CPAP effectively reversed hypoxia in all subjects (nadir O_2 saturation 77 ± 3% at baseline and 89.3 ± 3 post CPAP, $p = 0.005$) although mean O_2 saturation did not change significantly (Table 2). Subjects used CPAP for 165 ± 17 days and 5.3 ± 0.35 hrs/night. As shown in Table 2, ESS decreased with CPAP therapy. However, subjects as a group experienced weight gain after CPAP treatment compared to baseline with a mean difference of 1.6 Kg ($p < 0.05$) or 0.6 Kg/m^2 ($p = 0.06$). Systolic blood pressure, diastolic blood pressure and heart rate remained unchanged throughout the study period.

Fasting and postprandial glucose levels were unchanged after CPAP use compared to baseline (Figure 1A). Fasting insulin levels increased significantly after CPAP use (Figure 1B). However postprandial and $AUC_{0\text{-}120}$ insulin remained unchanged compared to baseline (baseline insulin $AUC_{0\text{-}120}$ 549 ± 129 µU*h/mL, post-CPAP insulin $AUC_{0\text{-}120}$ 491 ± 56 µU*h/mL; $p = 0.7$). Insulin resistance increased as measured by HOMA-IR, QUICKI and ISI, although it only reached significance for the first two indices (Table 2).

Fasting active ghrelin levels decreased significantly after CPAP use. However, postprandial active ghrelin levels and active ghrelin $AUC_{0\text{-}120}$ remained unchanged compared to baseline (Figure 1C). Circulating leptin, adiponectin and resistin levels remained unchanged after CPAP use (Table 2).

Changes in BMI were directly correlated with changes in

Table 3 Correlation analysis for changes in weight, hormone levels and sleep parameters [r(pvalue)]

	HOMA-IR	Ghrelin	Leptin	Insulin	Adiponectin nectin	Resistin	ESS	CPAP use
BMI	**0.56 (0.01)**	0.04 (0.87)	0.32 (0.17)	**0.58 (0.008)**	-0.24 (0.29)	-0.35 (0.13)	-0.02 (0.95)	0.02 (0.94)
HOMA-IR		**-0.51 (0.026)**	0.13 (0.59)	**0.95 (0.001)**	-0.04 (0.9)	-0.32 (0.18)	-0.01 (0.98)	0.22 (0.35)
Ghrelin			0.18 (0.46)	-0.43 (0.066)	-0.27 (0.26)	0.11 (0.68)	0.09 (0.7)	-0.19 (0.43)
Leptin				0.22 (0.34)	0.21 (0.38)	0.11 (0.65)	0.15 (0.53)	-0.27 (0.26)
Insulin					-0.17 (0.48)	0.4 (0.08)	-0.07 (0.8)	0.21 (0.37)
Adiponectin						0.24 (0.33)	0.13 (0.59)	-0.11 (0.65)
Resistin							0.04 (0.87)	-0.26 (0.28)

Significant correlations ($p \leq 0.05$) appear in bold. ISI: Insulin sensitivity index, HOMA-IR: homeostasis model assessment. Changes in all variables including ESS were use for analysis.

insulin levels and in insulin resistance as measured by HOMA-IR. Changes in ghrelin levels were inversely correlated with changes in insulin resistance, although there was no correlation between changes in ghrelin and changes in BMI or any of the other parameters measured (Table 3). On regression analyses, changes in BMI predicted changes in insulin (B = 4.9 ± 2, p = 0.03), insulin resistance (B = 1.75 ± 0.65, p = 0.02) and leptin (B = 2.2 ± 1, p = 0.046) but not on ghrelin (B = 38 ± 72, p = 0.61), adiponectin (B = -0.02 ± 1, p = 0.98) or resistin (B = -0.09 ± 0.25, p = 0.74). Nadir SpO2 did not predict any of the outcome variables (B = 0.8 ± 0.78, p = 0.78 for insulin; B = 0.15 ± 0.25, p = 0.6 for HOMA-IR; B = 0.46 ± 0.39, p = 0.26 for leptin; B = -0.36 ± 24, p = 0.17 for ghrelin; B = 0.34 ± 0.42, p = 0.44 for adiponectin and B = -0.09 ± 0.095, p = 0.37 for resistin). Baseline AHI correlated with changes in ESS (r -0.57, p 0.009) but was not correlated with CPAP use, changes in nadir or mean O_2 or any of the other metabolic parameters. Baseline ESS did not correlate with baseline HOMA-IR.

To determine the effect of weight changes in the other parameters measured, we analyzed separately the data from those subjects who gained a significant amount of weight (defined as an increase ≥2% of their initial body weight, n = 8) and those whose body weight remained stable (n = 12). There were no significant differences at baseline between the two groups and none of the groups experienced significant changes in blood pressure or heart rate (data not shown). Leptin, resistin and adiponectin levels after CPAP remained stable in both groups compared to baseline (Figure 2A).

Fasting insulin levels were significantly increased in subjects who experienced weight gain but remained stable in those subjects with stable body weight. Fasting glucose levels remained unchanged in weight stable individuals and tended to increase in subjects experiencing weight gain but it did not reach statistical significance (Figure 2B). Postprandial and $AUC_{0\text{-}120}$ insulin and glucose levels remained unchanged in both groups after CPAP use (Figure 2C). Fasting ghrelin levels decreased in both groups; although it did not reach statistical significance. Insulin resistance as measured by HOMA-IR, ISI and QUICKI remained unchanged in subjects with stable body weight. However, it was significantly increased in the weight gain group (Figure 2D).

Discussion

Our study suggests that glucose metabolism is disturbed in obese patients with OSA and that weight change rather than hypoxia is the major long-term modulating factor in insulin resistance after CPAP treatment in this population. These findings also suggest that CPAP alone may not reduce body weight, and that in the face of weight gain CPAP treatment may not reduce insulin resistance and leptin or increase adiponectin in obese subjects. The results of our regression analyses where the predictive value of BMI and nadir SpO_2 was explored support this hypothesis given that changes in BMI but not changes in nadir SpO_2 predicted changes in insulin, insulin resistance and leptin.

We did not observe any changes in blood pressure, or heart rate after CPAP treatment in contrast to what most[15-17] but not all studies[18-20] have reported. Possible explanations for this discrepancy include: 1) A higher body weight in our cohort compared to others or the fact that body weight remained stable or increased in our cohort. This could have negated the beneficial effects of CPAP on these outcomes as suggested by a previous report that showed that the course of hypertension in OSA is more closely linked to weight loss than to elimination of sleep apnea by CPAP;[16] 2) Different duration of CPAP treatment (6 months in our study vs 1-2 months in other reports); 3) Time of the day at which BP was assessed given that CPAP effects on BP are reportedly more pronounced during sleep and we monitored our patients in the morning; 4) Methods of BP measurement since this factor has been shown to influence results;[17] and 5) We did not power the study to detect differences in these outcomes so a negative result should be interpreted with caution.

Several reports have demonstrated an association between OSA and insulin resistance.[2,21-24] However, the effect of CPAP therapy on insulin resistance remains controversial (recently reviewed[25]). Some reports failed to detect an improvement in insulin sensitivity,[26] others showed an improvement in glucose levels only during sleep[27,28] and others showed an almost immediate improvement, especially in non-obese patients.[13] In our study, we found increased insulin resistance after 6 months of CPAP use. This insulin resistance was associated with weight gain indicating that body weight plays a major role in determining insulin resistance in obese CPAP-treated patients with OSA.

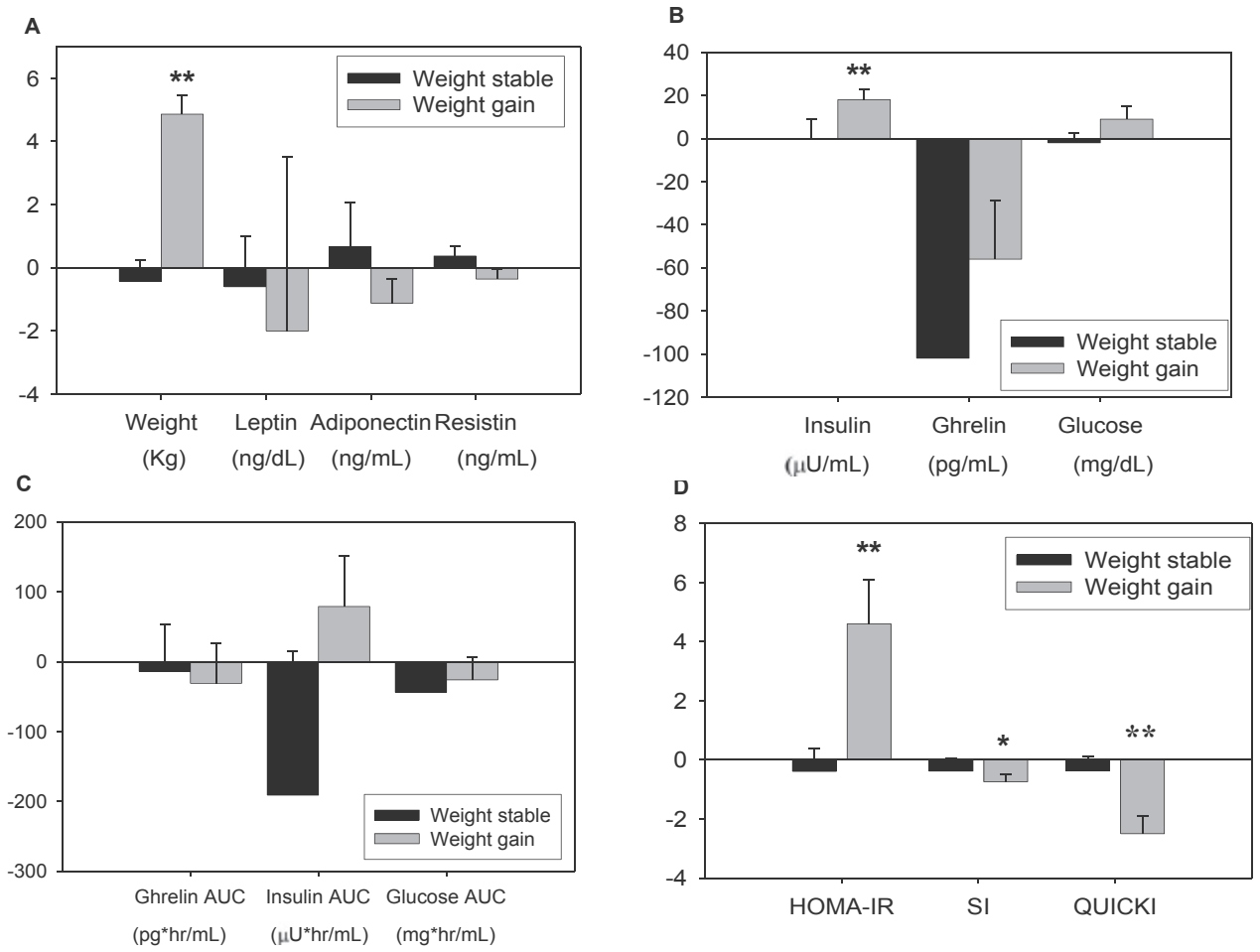

Figure 2 Body weight, adipokines (A), glucose, insulin (B-C) and insulin resistance changes (D) after CPAP according to changes in body weight. Weight gain was defined as an increase ≥2% of their initial body weight (n = 8). Weight stable was defined as a weight fluctuation ≥2% (n = 12). *p < 0.05, **p < 0.01 compared to other group.

These results are in agreement with those reported by Ip and others.[21] The apparently divergent findings between our results and those previously reporting an improvement in insulin sensitivity also may relate to differences in sample timing. Our assessment was done 6 months after starting treatment whereas most reports have been done between 48 hours and 3 months after starting CPAP. It is possible that CPAP use has only a transient effect on insulin sensitivity and that changes in body weight are a much more important factor in the long-term regulation of insulin sensitivity.

Ghrelin is an appetite-increasing hormone postulated as a contributor to OSA-associated obesity as ghrelin levels were elevated in one report.[14] In the same study, fasting total (the sum of active and inactive) ghrelin levels decreased after 2 days of CPAP. Another study reported equivalent fasting total ghrelin levels in obese subjects with OSA and BMI matched controls without OSA.[29] In our study, we measured active ghrelin instead of total ghrelin because 75% of the circulating peptide is biologically inactive and the ratio between inactive and active ghrelin changes in different clinical scenarios.[9] Since ghrelin is suppressed by food intake, ghrelin levels were measured while fasting and during the OGTT. Our results show that 6 months of CPAP treatment significantly decreased fasting active ghrelin levels but that postprandial levels of this hormone remained unchanged. This is in agreement with a recent report of fasting active ghrelin levels being decreased by CPAP after one month of treatment.[30] Although ghrelin inversely correlates with body weight in the setting of obesity, we did not found any association between changes in ghrelin levels and changes in BMI, CPAP use or changes in the ESS in this setting. Ghrelin correlated with changes in insulin resistance, suggesting that other factors besides body weight may play a role in its regulation including changes in insulin sensitivity. Insulin administration has been shown to suppress circulating ghrelin levels in some[31] but not all studies.[32] Plasma insulin levels and insulin resistance correlate inversely with ghrelin. This association was BMI-independent in some studies.[33] However in a study using euglycemic hyperinsulinemic clamp method, insulin sensitivity did not correlate with ghrelin concentrations.[34] Independent of metabolic factors, ghrelin may also act as a sleep-inducing hormone. Ghrelin levels increase after sleep deprivation[35] and slow wave sleep is enhanced after ghrelin administration.[36] Based on these data, we postulate that the fasting ghrelin level increase seen in patients with OSA is a compensatory response to poor-quality sleep and could explain why fasting ghrelin levels decreased after CPAP use.

Leptin is secreted by adipocytes in proportion to body fat, being elevated in obese individuals and decreasing with weight loss. Leptin-deficient animals exhibit respiratory depression and CO_2 retention. Leptin administration to these animals

increases minute ventilation and improves lung mechanics.[37] These animal experiments suggest that an increase in leptin levels in patients with OSA may represent a compensatory response to hypoxia. Consistent with this hypothesis, elevated leptin has been described in OSA patients compared to BMI-matched controls. This elevation in leptin was reversed by CPAP treatment,[14,38] although this was associated with a decrease in fat accumulation in some studies[39] that may have accounted at least partially for the changes in leptin. Others have reported that leptin levels are similar in obese OSA patients when compared to non-OSA controls and that these levels do not change significantly after 1 month or 1 year of CPAP.[30,40] In agreement with the latter study, our data showed that leptin levels remained stable after CPAP use. Taken together, these data suggest that if CPAP has an effect on leptin levels, it is short-lasting.

The role of resistin in diabetes remains a matter of debate. Circulating resistin levels directly correlate with BMI and have been shown to decrease with weight loss.[41] Resistin also directly correlates with insulin resistance in some studies, but not in others.[42,43] In our study, resistin levels did not change after 6 months of CPAP and its levels did not correlate with changes in body weight, insulin and other adipokines or sleep parameters. In agreement with our data, resistin levels were stable after 2 days and 2 months of CPAP use in a group of subjects with OSA, suggesting that resistin is unlikely to play an important role in the insulin resistance or obesity seen in OSA.[13]

Adiponectin is decreased in obese individuals and in those with type 2 diabetes. It is thought to play a role in many of the metabolic complications suffered by these patients including metabolic syndrome and cardiovascular disease. However, its role in patients with OSA remains controversial. Elevated adiponectin was found in subjects with OSA when compared with non-OSA controls in one report and diminished in another.[44,45] In agreement with prior reports of adiponectin levels after CPAP use,[46] we report here that adiponectin levels remained unchanged after 6 months of CPAP treatment. Harsch et al. had previously reported a decrease in adiponectin levels after 48 hrs of CPAP use but levels returned to baseline at 3 months. The data suggest that chronic CPAP treatment does not play a role in the regulation of adiponectin levels.

Although the study was powered a priori using published data,[13,14] the small sample size is a limitation of this study. Other limitations include the lack of data on changes in dietary habits; physical activity and body composition that could help us better understand the effects of CPAP on hormonal regulation. Also, it would have been useful to compare changes in body weight and other parameters with a non-interventional group of controls. However, such a group was not included in our design because these subjects have a clinical indication for CPAP use and delaying its use would have been unethical. Our study was powered to detect significant differences in insulin resistance and ghrelin levels. Consequently, we cannot conclude that the lack of changes in leptin, adiponectin and resistin levels in this relatively small sample would not be seen in a larger sample. Significant associations detected during simple correlation analysis should be interpreted with caution given the number of variables compared which increase the chance for a type I error. Future studies should include a larger number of patients along with an assessment of dietary habits; physical activity, energy expenditure, anthropometrics (ie waist-to-hip ratio) and body composition in order to better understand the effects of CPAP in this setting.

Conclusions

In summary, six months of CPAP treatment did not improve insulin resistance in obese subjects. In fact, in subjects who gained weight during the study, insulin resistance increased suggesting that changes in insulin sensitivity induced by CPAP in this setting are mainly determined by changes in body weight. CPAP treatment induced a decrease in fasting ghrelin levels, although body weight increased in most subjects. Adipokines such as leptin, adiponectin and resistin also appear to be influenced much more by adiposity rather than hypoxia. The fact that these adipokines remain unchanged after 6 months of CPAP treatment suggests that they are unlikely to play an important role in the development of the metabolic complications seen in the setting of OSA. When obese patients with OSA are treated with CPAP, other measurements targeting obesity should also be pursued.

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can be easily obtained. We believe that both forms are necessary to be available to attend outpatients units with different resources.

There are some limitations in our study. We did not include depression and anxiety evaluations. In fact, psychological factors were shown to have an important impact in health status of COPD patients. The lack of these evaluations in our study may have influenced the results and therefore, psychological or socio-cultural aspects should also be verified in further studies designed to evaluate the HS over time. In addition, patients came from the outpatient clinic of a university hospital and therefore may not represent the COPD population at large.

Conclusions

In summary, HS deteriorated significantly over the three-year period and the predictors of HS do not change over time. BODE index and dyspnea were predictors at baseline and after three years. Exacerbation was also a predictor of HS after three years. These results suggest that health status scores should be included as part of a comprehensive assessment to evaluate disease progression.

Severe Bronchopulmonary Dysplasia Improved by Noninvasive Positive Pressure Ventilation

Christian Mann, Walter Bär

This is the first report to describe the feasibility and effectiveness of noninvasive positive pressure ventilation in the secondary treatment of bronchopulmonary dysplasia.

A former male preterm of Caucasian ethnicity delivered at 29 weeks gestation developed severe bronchopulmonary dysplasia. At the age of six months he was in permanent tachypnea and dyspnea and in need of 100% oxygen with a flow of 2.0 L/minute via a nasal cannula. Intermittent nocturnal noninvasive positive pressure ventilation was then administered for seven hours daily. The ventilator was set at a positive end-expiratory pressure of 6cmH2O with pressure support of 4cm H2O, trigger at 1.4 mL/second, and a maximum inspiratory time of 0.7 second. Over the course of seven weeks, his maximum daytime fraction of inspired oxygen via nasal cannula decreased from 1.0 to 0.75, his respiratory rate from 64 breaths/minute to 50 breaths/minute and carbon dioxide from 58mmHg to 44mmHg.

Conclusion: Noninvasive positive pressure ventilation may be a novel therapeutic option for established severe bronchopulmonary dysplasia. In the case presented, noninvasive positive pressure ventilation achieved sustained improvement in ventilation and thus prepared our patient for safe home oxygen therapy.

Introduction

Although there is some evidence that nasal noninvasive ventilation has the potential to reduce bronchopulmonary dysplasia (BPD) in preterm newborns, there have been no studies of nasal noninvasive positive pressure ventilation (NIPPV) in former preterm infants with an established diagnosis of BPD requiring high oxygen concentrations.

The main pathophysiological finding in BPD is a low functional residual capacity accompanied by inefficient gas mixing. Respiratory rate is increased. Small airway function may worsen during the first year. Significant gas trapping is found in some BPD infants. We report the response to intermittent nocturnal therapy with nasal NIPPV in an infant with severe BPD.

Case presentation

Our patient was a male preterm of Caucasian ethnicity, born at 29 weeks and one day gestation by Caesarean section from a spontaneous dichorionic diamniotic twin pregnancy complicated by preterm premature rupture of the membranes with near- total loss of fluid nine days before delivery. His birth weight was 940g. A chest X-ray showed pulmonary hypoplasia and grade 3 hyaline membrane disease. Surfactant (beractant 100mg/kg) was given one hour after birth and repeated 24 hours later.

Our patient was started on high frequency oscillatory ventilation, with highest mean airway pressure 22cmH2O on day one, and then switched to pressure-controlled synchronized intermittent mandatory ventilation on day 20 (highest peak inspiratory pressure 24cmH2O). Inhaled nitric oxide was delivered for five days in decreasing amounts (starting on day one with 26ppm).

A left pneumothorax was drained on day four. The clinical course was complicated by ventilator-associated pneumonia on day 15. Tracheal aspirates grew coagulase- negative Staphylococci and Enterobacter cloacae. Treatment consisted of piperacillin and tazobactam with fusidic acid for two weeks. Extubation was successful on day 26 after a two-day course of dexamethasone. Ventilatory support was continued with nasal continuous positive airway pressure (nCPAP; 8cm H2O). BPD was diagnosed at postmenstrual age 36 weeks. Shortly thereafter, nasal swab cultures from copious upper airway secretions proved colonization with Stenotrophomonas maltophilia, Escherichia coli as well as Staphylococcus aureus which was treated with a two-week course of oral sulfamethoxazole and rifampin.

After 10 weeks nCPAP was switched to nasal cannula flow of 2L/minute with a fraction of inspired oxygen (FiO2) of 0.5. Pulse oximetry target was set at arterial blood oxygen

Table 1. Ventilator settings for NIPPV

Pressure support	4 cm H_2O
Positive end-expiratory pressure	6 cm H_2O
Trigger	1.4 mL/second
Ramp	25 ms
Expiratory trigger sensitivity	10%
Backup respiratory rate	8/minute
Maximum inspiratory time	0.7 second

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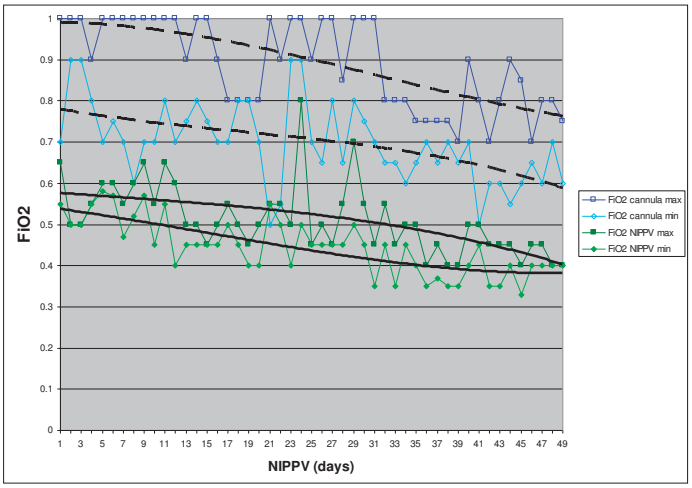

Figure 1. Decrease in FiO_2 requirement over seven weeks of nocturnal NIPPV. Open rectangles and blue lines: oxygen concentrations (maximum and minimum for each day) delivered via nasal cannula during daytime; full rectangles and green lines: oxygen concentrations for nocturnal NIPPV. Oxygen saturation target was set at ≥90%.

saturation (SaO2) ≥90%. During subsequent weeks the oxygen concentration had to be increased to a FiO2 of 1.0 due to progressive deterioration of gas exchange. At the age of six months our patient was in constant dyspnea and tachypnea. Spontaneous inspiratory time was markedly shortened. Streaky densities and cystic areas on a chest X-ray confirmed the diagnosis of severe BPD. Echocardiography revealed concomitant pulmonary hypertension with a tricuspid regurgitation pressure gradient up to 30mmHg. The FiO2 1.0 requirement created a high risk of urgent reintubation in the event of sudden desaturation. The boy's increasing drive to move around ruled out reintroducing nCPAP.

A ventilator set to NIPPV was installed providing nocturnal ventilatory support for an average of seven hours every night. Ventilator settings are presented in Table 1. For the first 18 days, sedation was provided with chloral hydrate in decreasing amounts from 52mg/kg to 7mg/kg per evening dose.

The features of the NIPPV device included a limited dead space, highly sensitive automated circuit leak compensation, and high trigger sensitivity. NIPPV was administered via a nasal mask in a semirecumbent position to enhance air entry into West zones 1 and 2 and to diminish expansion of the radiologically over-distended lung bases.

In the course of seven weeks of intermittent nocturnal NIPPV, the spontaneous respiratory rate decreased from 64 breaths/minute to 50 breaths/minute, morning (post-NIPPV) carbon dioxide dropped from 58mmHg to 44mmHg, and—most importantly—nasal cannula maximum FiO_2 decreased from 1.0 to 0.75 and the minimum FiO2 from 0.8 to 0.6 (Figure 1). At this point, NIPPV was stopped and the baby was discharged on home oxygen (flow rate 0.25L/minute) at the postnatal age of eight months. His weight increased by 200g per week during NIPPV therapy and reached 7490g at discharge.

Two intercurrent lower respiratory tract infections were managed on an outpatient basis. Our patient was completely weaned off oxygen nine months after discharge at the age of 17 months.

Neurological examination at the age of one year showed less delay in the mental scale than in the psychomotor scale (Bayley II) with scores of 76 and 56, respectively. Free walking was achieved at 22 months of age.

Conclusion

The clinical course of this ex-preterm boy suggests that secondary NIPPV therapy has the potential to improve severe BPD. A course of nocturnal intermittent NIPPV in a timely manner (seven weeks) improved ventilation and reduced oxygen need to a degree which provided sufficient safety for subsequent home oxygen therapy. Its positive effect was essential for our patient's discharge after eight months of hospital stay. In terms of practicability, NIPPV was superior to nCPAP in that it reliably avoided hypoventilation when the child initially needed sedation to tolerate a nasal mask.

According to the literature, a bundle of different mechanisms may have contributed to the improvement observed. Synchronized NIPPV is known to increase functional residual capacity, enhance ventilation uniformity, improve respiratory drive, lead to greater lung recruitment and decrease inspiratory effort and respiratory work in comparison to continuous flow nCPAP. The duration of ventilatory support is shorter with primary use of NIPPV than with nCPAP .

We think this observation provides useful information on NIPPV in established BPD before larger randomized studies are performed on this topic. Further studies incorporating lung function tests should identify the level of respiratory support at which the repetitive stimulus of nocturnal NIPPV exerts most of its positive influence. It would be interesting to find out how NIPPV propagates lung remodeling or if it even has the potential to accelerate lung maturation in severe BPD.

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