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Editorial

RRT Clinician-Scientists in the 21st Century... an Emergent Solution

Faced with declining revenues, hospitals across the country are searching for ways to increase the quality of patient care, boost clinical productivity and reduce unnecessary costs. Increasingly, medical institutions are turning to clinicians who can accomplish these economic objectives through expanded use of clinical practice protocols that are based on the best available scientific evidence. Originally described by Nielsen-Tietsort in 1981, evidence-based protocols are commonplace in top-tier clinical departments of respiratory care because of their ability to facilitate high-quality respiratory care while reducing resource utilization. Advances in cardiopulmonary science are transforming the clinical landscape at an unprecedented rate. The transformations should be seen as opportunities for respiratory therapists who can recommend modifications to established clinical protocols or perhaps design brand new protocols. Given this milieu, the American Association for Respiratory Care has recommended that respiratory therapists should prepare to embrace evidence-based protocol-guided clinical practice by 2015 and beyond.

As the acknowledged experts in respiratory care, tomorrow's RRTs will be expected to formulate compelling recommendations regarding changes in clinical practice and will need to reference solid scientific evidence in support of those recommendations. This higher-order functioning in a clinical environment is the purview of the RRT clinician-scientist. In order for RRT clinician-scientists to improve patient care using evidence-based protocols, they will need to be conversant with scientific methodology to enable them to design and implement clinical protocols. RRT clinician-scientists will need to carefully measure clinical outcomes after implementing protocols to determine whether patient care has improved. They will need to know how clinical research findings, from appropriately powered studies, inform clinical practice and the extent to which such findings may be generalized to specific patient cohorts. RRT clinician-scientists will need to understand how to design and implement bedside protocols that translate scientific evidence into excellent bedside care and will need to masterfully communicate their findings with hospital administrators, insurance representatives and a host of other stakeholders.

RRT clinician-scientists with these important competencies will be highly valued by hospital administrators, who will view them as indispensable partners capable of nimbly adapting to rapidly changing clinical conditions by designing and implementing protocols that improve quality of care and reduce healthcare costs. While many clinical departments are already designing and implementing sophisticated respiratory care protocols that maintain a clinically and economically competitive advantage, many others will need time to familiarize themselves with the task, internalize the content and slowly scale upward. Partnerships between clinical departments and colleges or universities will need to be actively facilitated. Training will likely include hospital-based structured opportunities that enable therapists to immediately apply what they have learned. Training will also need to be problem-focused so that RRTs can learn how to research real-world clinical problems. Training will also need to be inquiry-centered with an emphasis on performing actual research, not just discussing what scientific research involves.

Transitioning to the role of RRT clinician-scientist will take dedication, hard work, systematic mitigation of clinical cultures that promote the status quo and multiple, interdisciplinary champions in clinical as well as academic environments. Gradually, as practicing RRTs become accustomed to designing, implementing and modifying protocols, increasing numbers of RRT clinician-scientists will emerge with expertise in performing clinical research. These will become the mentors who will guide all RT students completing a clinical research practicum as part of their academic preparation prior to graduation in 2025 and beyond.

Charles J. Gutierrez, PhD, RRT, FAARC
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Continued on page 17...

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* Mireles-Cabodevila, E., Hatipoğlu, U., & Chatburn, R. L. (2013). A rational framework for selecting modes of ventilation. *Respiratory Care*, 58(2), 348-366.

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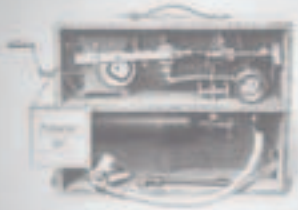
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A black and white photograph of a nurse in a hospital room. The nurse is wearing a headscarf and is looking down at a handheld device (likely the epoc PDA) while standing by a patient's bedside. The patient is lying in a hospital bed, and medical equipment is visible in the background.

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PATIENTS READY FOR BED

ImThera Medical announced that the final patient has been implanted in its Targeted Hypoglossal Neurostimulation #2 (THN2) study looking for a “viable” treatment option for people with moderate to severe obstructive sleep apnea (OSA). ImThera Medical, a global medical device company, said the goal of its international, prospective multi-center study is to evaluate the safety and efficacy of its aura6000 Sleep Therapy System for people suffering from OSA. The study enrolled 57 subjects at 9 medical centers in 5 countries, including the US, with subjects implanted through simple surgeries that take under 60 minutes. The aura6000 Sleep Therapy System is seen by the company as an alternative for people diagnosed with OSA who are unable to comply with the “rigors” of CPAP. ImThera puts the percentage of people diagnosed with OSA, but unable to use CPAP as between 20% to 80%. The aura6000 System is based on ImThera's THN Sleep Therapy technology, which delivers neurostimulation to the hypoglossal nerve and thereby increases the muscle tone of key tongue muscles, preventing the tongue from collapsing into the upper airway during sleep. This technology is designed to address nighttime upper airway blockage, permitting normal and restful sleep for OSA patients. The system consists of two implantable components, a rechargeable pulse generator placed under the skin near the collarbone, and a multi-electrode lead placed in the upper neck. The electrodes deliver mild pulses to the hypoglossal nerve, stimulating various muscles and thereby improving upper airway muscle tone. OSA is characterized by repetitive episodes of respiratory arrest despite continuing breathing efforts. More than 800,000 people in the US are diagnosed with OSA annually.

HIV TESTING

Alere Inc. announced that it had received US Food and Drug Administration (FDA) approval to market its testing method that the company says is more effective than other tests at identifying individuals with HIV. Alere said the FDA approval means it can market its Alere Determine HIV 1/2 Ag/Ab Combo in the United States for the detection of HIV-1 p24 antigen and antibodies to HIV-1/HIV-2. The FDA approval allows Alere to market it as a Clinical Laboratory Improvement Amendments (CLIA) moderately complex medical device. The next step, according to Alere, is to complete the CLIA waiver trials with the intention to submit the data in late 2013 or early 2014. Alere Determine HIV-1/2 Ag/Ab Combo is the only FDA-approved rapid point-of-care test that detects both HIV-1/2 antibodies and the HIV-1 p24 antigen, which can appear days after infection and prior to HIV-1/2 antibodies. Alere said its Alere Determine Combo can

help to identify additional cases that would not be detected using second and third generation antibody-only tests. According to the Centers of Disease Control and Prevention, there are 1.4 million Americans living with HIV, and approximately 207,000 (18%) whose infections have not been diagnosed. In 2010, the CDC estimated that there were 47,500 newly infected people with the virus in the United States, indicating that HIV remains a serious health problem.

CPAP ALTERNATIVE UNMASKED

With many sleep apnea sufferers struggling to wear the CPAP mask at night, new research has found many patients had success with an alternative method - oral appliance therapy. In a two-year follow up to a clinical trial, the Netherlands' University of Groningen compared treatment outcomes for Obstructive Sleep Apnea patients using CPAP and oral appliance therapy, contending that the oral appliance therapy - using a retainer or a mouth guard - was an effective alternative for treating sleep apnea. The study tracked the progress of 103 OSA patients, with “successful” treatment defined as a reduction in the apnea-hypopnea index (AHI) of less than five interrupted breathing episodes per hour, or a reduction of at least 50% from subjects' initial AHI readings. Their analysis found that for people with OSA ranging from mild to severe, there were similar levels of success in both CPAP and oral appliance therapy, with significant improvements to the quality of sleep and their levels of daytime sleepiness. Both treatments also showed similar reductions in the type of depression and anxiety that are often reported by sleep apnea patients. Both treatments were effective in reducing frequency of interrupted breathing episodes, although CPAP was found more effective than oral appliance therapy at lowering AHI. CPAP also demonstrated greater effectiveness in raising blood oxygen levels than oral appliance therapy. Researchers concluded that oral appliance therapy was a viable treatment option for patients with mild to moderate sleep apnea. For severe cases of OSA, researchers recommend CPAP as the best treatment option. Information is from an article written by sleep specialist Dr Michael J. Breus.

PROPELLER APPS TAKE FLIGHT

Mobile health technology company Asthmapolis announced it was changing its name to Propeller Health and expanding its services for people with chronic respiratory disease. The Propeller platform is designed to help patients and their physicians better understand and control respiratory disease to reduce preventable emergency room visits, hospitalizations and unnecessary suffering. The company said the change means expanded mobile apps for asthma, COPD and other respiratory disease, as well as new sensors for additional inhaled medications pending regulatory clearance. Propeller uses a combination of snap-on sensors, mobile apps, analytics and personal services designed to improve people's self-management of their respiratory disease, while reducing the burden of chronic disease management. Remote monitoring is used to track when and how often patients use their inhaled medications. This real-time information is used to help improve the understanding of symptoms and triggers, and reveal insights about both medication adherence and rescue medication frequency. Propeller aims to stimulate more productive conversations between users and their care teams by coupling analytics with personalized feedback and individual support, including access to health educators and community managers. Propeller for COPD is available now, and the company is filing applications for international regulatory clearance for additional sensors.

TIME TO BUTT OUT

Chronic bronchitis is linked with worse clinical outcomes in asthma, especially among smokers, according to researchers from the University of Glasgow. Their study found 20% of 59 people with asthma who had never smoked reported chronic bronchitis, or chronic mucus hypersecretion, compared to 56% of 61 smokers with asthma. Poorer asthma control was observed among smokers with chronic bronchitis, while never smokers with chronic bronchitis were more likely to have required emergency oral corticosteroids in the previous year. Asthma control was particularly poor among smokers with severe asthma and chronic bronchitis — with a mean Asthma Control Questionnaire score of 2.9 versus 1.9 in never smokers with severe asthma and chronic bronchitis. They also found that smokers with severe asthma and chronic bronchitis had reduced airway lumen area on computed tomography compared with never smokers with severe asthma and similar symptoms, which the team says may be related to mucus accumulation and bronchodilator use. Information is from an article on medwireNews, written by Kirsty Oswald. Copyright medwireNews.

SWIFT AND SURE

ResMed, which develops products for the treatment of sleep-disordered breathing and respiratory conditions, has announced a new nasal mask for use with positive airway pressure (PAP) therapy. It's called the Swift FX Nano, and it combines the headgear design of a nasal pillows mask with the seal of a nasal mask. The goal was to keep the mask small and unobtrusive without the need for rigid frames or forehead support. ResMed said the new mask would include whisper-quiet venting, an easy

fit with only two points of adjustment and an ultra-smooth ball joint. The mask will also have a “for her” option with headgear and cushion sizes designed for women.

HELP FOR RDS

Specialty biotechnology company Discovery Laboratories, Inc. announced the US Food and Drug Administration (FDA) has agreed to the company's updated product specifications for Surfaxin Intratracheal Suspension. Surfaxin was approved for the prevention of respiratory distress syndrome (RDS) in premature infants at high risk for RDS. With this approval in place, the company has now started the process of manufacturing Surfaxin for its planned commercial introduction in the fourth quarter of 2013. Surfaxin is the first FDA-approved synthetic, peptide-containing surfactant available for the prevention of RDS in premature infants and the only approved alternative to animal-derived surfactants currently used today. Discovery said infants receiving Surfaxin should receive frequent clinical assessments so that oxygen and ventilatory support can be modified to respond to changes in respiratory status. More details at surfaxin.com.

DOSING EXPANDED

CSL Behring announced that the US Food and Drug Administration (FDA) has expanded the dosing options for Hizentra so people with Primary Immunodeficiency can self-administer their treatment less frequently. Hizentra was approved in 2010 as a once-weekly immunoglobulin G (IgG) replacement therapy. The latest FDA approval means dosing for people with PI can be reduced to once every two weeks. PI is a group of serious diseases of the immune system that afflicts

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approximately 250,000 in the US alone. PI prevents infections from improving, meaning repeated rounds of antibiotics or hospitalization for treatment and increased chances of organ damage. Self-administered weekly or biweekly, Hizentra aims to deliver consistent levels of IgG to help protect those with PI against infections.

LIGHTWEIGHT OPTION

Philips Respironics introduced the SimplyFlo Stationary Oxygen Concentrator, a lightweight option to free up the lives of patients. At just 8.5 pounds, the SimplyFlo unit is for patients who may refuse therapy due to lifestyle disruptions associated with the size and weight of traditional stationary concentrators. Philips said it integrated the insights and feedback from homecare providers and patients to design a small, lightweight, stationary oxygen concentrator. The company said that for many patients new to therapy who only require nocturnal treatment, the intimidating size, weight, and sound of a traditional oxygen concentrator can be factors in their rejection of therapy.

SAFETY FIRST

Masimo announced its Patient SafetyNet respiratory monitoring system has been installed in Rochester General Hospital. Patient SafetyNet is a remote monitoring and clinician notification system that Masimo said has been shown to dramatically reduce rapid response activations, transfers to intensive care units, and deaths related to opioid-induced respiratory depression. The installation at RGH took place after an evaluation process resulting in the organization's standardization to Masimo SET Measure-Through Motion and Low Perfusion pulse oximetry. Patient SafetyNet combines this with ventilation monitoring

and wireless clinician notification. When changes occur in the measured values, which may indicate deterioration in the patient's condition, the system automatically sends wireless alerts directly to clinicians — prompting a potentially life-saving response to the patient's bedside.

BEYOND THE MASK

Help is coming for people struggling with sleep apnea through the use of alternative devices that are light years away from the Darth Vader-esque CPAP mask. Continuous positive airway pressure has helped many, but studies show that despite design changes that have improved operation, anywhere from 30% to more than half of patients can't or won't use CPAP as directed by their doctors. The main complaint is the machines are noisy and the masks are uncomfortable. The new treatments include nasal attachments and surgical implants that stimulate a nerve near the base of the tongue. Winx, which was approved by the Food and Drug Administration in March 2012, uses negative pressure to pull the soft palate and tongue forward, which opens the airway. Patients wear a mouthpiece attached to a slim piece of tubing and a bedside console. ImThera Medical and Inspire Medical Systems are testing implantable devices that keep the airway open during sleep by stimulating the hypoglossal nerve, which runs just beneath the base of the tongue. The device is surgically implanted under the skin of the chest. One lead extends to the middle of the chest and another extends up to the neck and encircles the hypoglossal nerve. This type of device is more invasive and is still being tested. One CPAP alternative is much easier to put on. It's called Provent and it sticks onto the nostrils so you'll need a new pair each night. Provent, which requires a prescription, has tiny valves that open when patients breathe in and close when they breathe out, creating pressure that props the airway open. However, it doesn't work for people who breathe through their mouth. All of these new devices are designed to offer alternatives to CPAP in the quest to help the estimated 18 million Americans who suffer with sleep apnea. Information from an article by Andrea Petersen in the Wall Street Journal, copyright Wall Street Journal.

SPOTLIGHT ON BLOOD GAS

BLOOD GAS RESULTS GO PAPERLESS

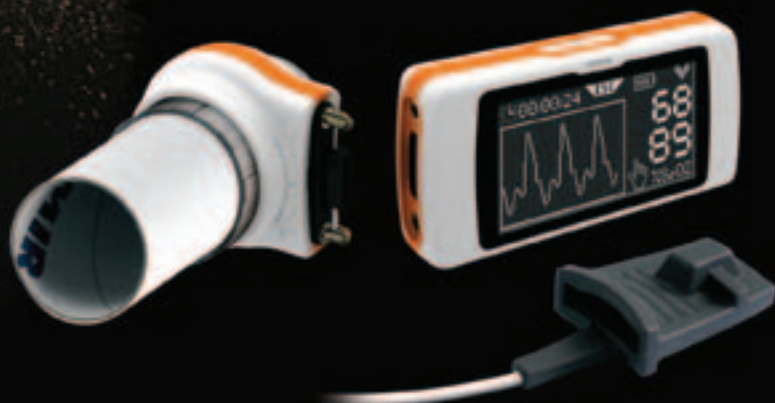
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The advertisement features a purple and white color scheme. At the top right, it lists the address: 21 Goldenland Court, #100, Sacramento, CA 95834, with phone numbers (916) 434-6034 and (916) 648-6711. The Vortran logo is on the left, with the text 'VORTRAN® MEDICAL TECHNOLOGY I, INC.' below it. The main headline reads 'One of the Only Percussive Treatments that can be Performed at Home and the Hospital!'. A central image shows a man using the PercussiveNEB nebulizer. To the right of the image, it says 'PercussiveNEB® A High Frequency Intrapulmonary Percussive Nebulizer'. At the bottom left, there are four bullet points: '• New improved modulator operates more consistently', '• Pressure dial adjustable between SOFT to HARD setting', '• Single patient, multiple use', and '• Home or hospital use'. At the bottom right, there is a QR code and the website 'www.vortran.com'.

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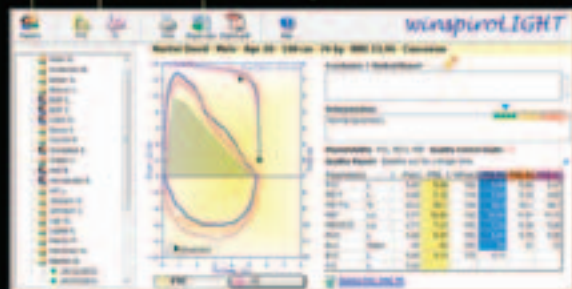


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RAPIDComm Data Management System: The RAPIDComm Data Management System allows centralized management of multiple RAPIDSystems blood gas testing instruments, as well as Siemens CLINITEK Status Connect urinalysis system and DCA Vantage analyzers for HbA1c testing. The seamless connectivity provided by the RAPIDComm Data Management System enables operators to standardize procedures, facilitate compliance and improve risk management. For example, by using the RAPIDComm Data Management System, clinicians are able to limit access to trained and authorized users, and remotely lock out users when necessary. Also, manual data handling is eliminated as the system electronically transmits

patient and QC data, and test protocol standardization and QC testing can be driven remotely. With specific regard to blood gas testing, the RAPIDComm Data Management System can ensure regulatory compliance with monitoring of event logs and audit trail reports. Also, the RAPIDComm Data Management System enables clinicians to experience real-time remote viewing and management of connected RAPIDLab 1200, RAPIDPoint 500 and RAPIDPoint 400/405 blood gas analyzers from the comfort of their offices. For more information visit: <http://usa.healthcare.siemens.com/point-of-care/information-technology>.

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nnd Medical Technologies is committed to setting new standards in pulmonary function testing by offering innovative, easy-to-use products and excellent customer support. Our newest product, The EasyOne Pro LAB offers all the benefits of the EasyOne Pro — Single Breath CO Diffusion in one square foot — with Multiple-Breath Nitrogen Washout for the measurement of FRC and LCI. The EasyOne Plus series of spirometers are based on the best technology, packed with features and easy-to-use; while the Easy on-PC offers real-time curves and pediatric incentives. For more information visit us at www.nddmed.com or call us toll free at (877) 904-0090.

EXTENSIVE RANGE

Vitalograph is a global leader in pulmonary diagnostic device manufacturing and clinical trial professional services. Our extensive respiratory range includes a variety of world-class spirometers, asthma monitors, COPD screeners, peak flow meters, e-diaries and inhaler trainers. As we celebrate our 50th anniversary we are proud to introduce the latest version of Spirotrac PC-based Spirometry Software offering advanced spirometry, pulse oximetry, ambulatory blood pressure, ECG and more. All the spirometers in the Vitalograph product line meet the 2005 ATS/ERS guidelines for both accuracy, precision and test performance. Pneumotrac model 6800 with Spirotrac V software — our flagship research-grade Fleisch pneumotach is coupled with the latest spirometry software, featuring all spirometry tests including seamless, wizard-based mannitol, exercise and methacholine challenge protocols. The software is capable of supporting add-in Bluetooth EGC, automated blood pressure, pulse oximetry and Bluetooth weight scale. The

In2itive model 2120 is a hand-held spirometer with all the power of a research-based system in a very portable package. With a memory capacity of 10,000 tests and utilizing a brilliant color touchscreen, it can dock to a charging/communications cradle, connecting it to computers for reports or to the Spirotrac V enterprise software suite. It can also print directly to an external standard office printer. The Alpha desktop spirometer comes in two varieties, the standard Alpha and the Alpha Touch, both with integrated internal printing. The Alpha Touch adds a color touchscreen, external option printing, colorful incentive displays and 10,000 patient storage. For quick screening spirometry, the simple Vitalograph micro offers a low-cost alternative with the ability to print a report with an expiratory graph on a connected computer. Vitalograph offers a range of home spirometric devices such as the asma-1 and the COPD-6 for the monitoring of asthma and COPD, and the tracking of personal lung indices. These products come in varieties from simpler, non-connected devices to models with either USB or Bluetooth wireless connectivity. For routine asthma monitoring, there is also a line of mechanical peak flow meters including the Asthma Plan+ and the new myPEF, supported by a patient opt-in asthma web portal. With headquarters in Lenexa, Kansas, Buckingham, England, Ennis, Ireland, Hamburg, Germany and Hong Kong, Vitalograph truly offers global coverage for all your spirometry needs.

CENTRALIZED BENEFITS

ERT is the industry leader in centralized spirometry for use in the clinical development of new medical products, providing products and services that ensure the most accurate data and efficient trial management. Our standardized approach to spirometry ensures that clinical investigative sites receive the same equipment with the same protocol-specific software, eliminating protocol violations during data collection. Our offerings include: Forced/slow Spirometry, Dynamic IC Measurements, Home Spirometry, Integrated Peak Flow and eDiary, Body Box (Body Plethsmography), Exhaled Nitric Oxide (eNO), Energy Expenditure and Activity Monitoring, 6 Minute Walk Test (6MWT), DLCO Diffusion Test, Bronchial Provocation Tests, Impulse Oscillometry (IOS).

By reducing variability inherent to effort-dependent pulmonary tests, ERT's centralized spirometry benefits the development of new compounds for the treatment of asthma, chronic obstructive pulmonary disease (COPD), cystic fibrosis, and many others. Since proper training of technicians and therapists administering these tests is critical, our respiratory experts educate and monitor study personnel to help clinical trial sponsors achieve increased data quality and ultimately improve the accuracy of reporting. Powered by our EXPERT platform, ERT collects data from respiratory equipment across all sites and transfers it into a single database, where spirometry OverRead is performed and consistent feedback is delivered to the sites. In this way, clinical trial sponsors gain insight into when and why data is poor, ways to improve data quality and a grade card summary of trial data as a whole — enabling clinical trial sponsors to conduct a successful data collection process that's repeatable. ERT's centralized approach to spirometry enables clinical trial sponsors to see treatment effects as small as a <55ml deviation for FEV1 — approximately 200ml less than the standard deviation. And, we institute quality control measures in each step of the respiratory clinical trial process so each study has the advantage of cleaner data. With experience providing equipment for more than 25,000 sites, collecting data from more

than 300,000 patients and processing more than 10 million flow-volume loops, ERT can be trusted to deliver reliable, efficient centralized respiratory services. For more information, visit www.ert.com.

SLEEP ROUNDTABLE

Philips Respironics

Tell us about the sleep products your company offers.

As a global leader in the Obstructive Sleep Apnea (OSA) marketplace, Philips Respironics has, for more than three decades, pioneered standards across the sleep care cycle. We focus on sleep-disordered breathing diagnosis, therapy and compliance. Our sleep products are designed to provide more natural therapy options to enhance patients' comfort and compliance.

What are the range of applications for your products (that is, home, sleep lab, hospital)?

Working as an ally throughout the entire care cycle, from awareness and diagnosis to long-term success, Philips Respironics' innovations are designed to enable greater patient compliance and care team success. We are a total solution provider, offering a range of sleep diagnostics, therapy devices, masks, and software to meet the needs of our customers and the patients they serve.

In today's evolving home healthcare environment, there's certainly no shortage of questions. And Philips Respironics is proud to be able to offer a much-needed answer: a comprehensive portfolio of masks, services and support options that are just the right solution.

Diagnostics

Philips Respironics offers a range of diagnostic solutions. From in-lab and portable sleep testing systems that can be used in the home, to a full line of quality sensors, our diagnostic options handle basic to advanced studies.

Therapy devices and masks

Our PAP portfolio is positioned to support the movement to home sleep testing and drive for improved outcomes. We have a full range of devices to meet many patient needs, from basic CPAP treatment through complicated sleep-disordered breathing. Each includes full capabilities of Encore detailed reports and SleepMapper support.

Additions to our mask portfolio promote quick acceptance and long-term use by patients. Nuance is the latest in a groundbreaking series of new masks designed to outperform traditional masks and improve patient satisfaction. It started with Amara, the lightest-weight mask in the traditional full face category, and Wisp, the first hybrid minimal contact mask, pairing the best features of nasal masks and pillows masks. That innovation streak continues with Nuance and a new Amara Gel option.

Nuance delivers better performance, with a superior seal and less nasal irritation than the leading pillows mask. With its sleek design, Nuance has been patient-rated easier to assemble and use than the leading pillows mask.

Patient Management

SleepMapper is a mobile and web-based system designed to help OSA patients enhance their sleep therapy experience through feedback, education and troubleshooting. The system is designed to drive improved patient outcomes and is unique in that it incorporates motivation enhancement therapy techniques to encourage adherence to sleep therapy. The RT can direct the patient to SleepMapper as a resource for learning more about living with OSA and the importance of sleep therapy, and for learning helpful details and tips about their Philips Respironics therapy device and mask.

Services

We offer tools like EncoreAnywhere and medSage that provide access to patient information to promote compliance and help boost resupply efforts.

Discuss the training and support you offer to the users of your product.

Caregivers worldwide count on Philips Respironics for an unsurpassed level of service and support. Complementing our portfolio of products are programs and educational resources to helping providers deliver practical, ongoing care. Our technical/patient support line, which fields thousands of calls each day, offers best-in-class support.

How do users pay for your product; that is, is it reimbursable?

Most of our products that are distributed by homecare providers (HMEs) are reimbursed through Medicare, Medicaid, and commercial plans. The HME generally submits a claim for the patient to be reimbursed for the item they supplied to the patient. The patient usually has a co-pay, which is typically 20% of the amount the payer allows.

Will you be offering any new products in the near future?

We approach innovation with an intimate understanding of the needs of those who use our devices. In the sleep market, we're continuing to innovate our mask portfolio to provide solutions that streamline inventory for providers and promote quick acceptance and long-term use by patients.

Sleepnet Corporation

Tell us about the sleep products your company offers.

Sleepnet Corporation is a US-based designer and manufacturer of AIRgel masks for the sleep-disordered breathing (SDB) and acute care product industry across more than 40 countries worldwide. Sleepnet offers high-quality masks for adult and pediatric SDB patients, as well as respiratory support for acute and critical care environments. Only Sleepnet offers AIRgel masks. Our AIRgel is softer than ever — creating a luxurious cushion that reduces pressure while maintaining an effective seal. We also provide the only custom-fit masks. Our Aura, Mojo, iQ Blue, MiniMe, MiniMe 2 and Phantom masks feature Custom Fit Technology — moldable shells you can shape to precisely fit your face for a truly custom fit.

What are the range of applications for your products (ie sleep lab, home, etc.)?

Sleepnet offers both vented and non-vented versions of most of our masks so that they can be used with a variety of positive

pressure devices in sleep centers, at home, or in the hospital. We offer adult and pediatric masks for both home and hospital care use. We also have a full line of disposable full face masks appropriate for CPAP, single or dual limb circuits. Each mask is color coded for easy identification.

What training and education do you offer in the use of your product for healthcare providers or for patients?

We pride ourselves on designing easy-to-use sleep care products. Our masks come with illustrated step-by-step instructions. We also provide how-to videos and other educational material on our website (www.sleepnetmasks.com).

Will you be offering any new products in the near future?

Our team has talked extensively with patients and healthcare professionals about their preferences to aid our quest to create the interfaces of the future. We are thrilled to show off the results of this effort. We are releasing four new masks.

The Aura — our new custom fit nasal mask — was released in the fall of 2013. Enjoy comfort and a great seal with the world's first nasal mask featuring both Custom Fit Technology and an Active Headgear Connector. With three sizes and a Flexible Spacebar, the Aura will give you the rest you deserve.

The Veraseal 2 disposable mask brings AIRgel technology to the acute care environment for a giant step forward in patient comfort. Three color-coded elbow designs make choosing the right mask for single or dual limb circuit NIV systems simple. The Veraseal 2 fits quickly and easily while enhancing patient comfort.

We will be introducing our first replaceable cushion masks in early 2014. The Zojo i Nasal and Zojo i2 Full Face Mask will feature an easy-to-use replaceable AIRgel cushion, an Active Headgear Connector, and a Flexible Spacebar.

SOMNOmedics America Inc

Tell us about the sleep products your company offers.

SOMNOmedics supplies powerful and innovative solutions for sleep diagnostics and related fields, using latest medical discoveries and technological developments. At the same time, SOMNOmedics devices are easy to apply, reliable in their results and durable during the daily routine.

The SOMNOscreen plus is currently the smallest full telemetric Polysomnography system available. Thanks to its miniaturization the SOMNOscreen offers unlimited mobility for the patient as well as the physicians. All SOMNOmedics devices are patient worn.

All SOMNOmedics devices are made in Germany and fully manufactured in the SOMNOmedics headquarters. This ensures the highest quality and a long life cycle.

What are the ranges of applications for your products (that is, home, sleep lab, hospital)?

The SOMNOscreen is the only complete PSG system that allows performing all levels of sleep testing in any environment. SOMNOmedics devices can be used for home sleep testing as well as sleep studies in medical offices, sleep labs or hospitals.

Thanks to its mobility, the studies can be performed wherever it is most suitable for the physician and patient. The possibilities of application range from basic cardio respiratory screenings to full PSG recordings with or without video, 24-hour EEG recordings or stationary EEG recording.

Discuss the training and support you offer to the users of your product.

Along with an individual training of the handling of the device itself and the sophisticated analysis software DOMINO that comes with every system you purchase, SOMNOmedics also offers a toll-free 24/7 service hotline that helps to solve all issues that may occur during your daily routine. We can directly assist you using VPN and Team Viewer. Additionally, WebEx Trainings are regularly offered to cover the updates of the latest software version or new features that the devices offer.

How do users pay for your product; that is, is it reimbursable?

Sleep studies are reimbursed by the majority of insurance companies.

Will you be offering any new products in the near future?

We are currently in the process of receiving FDA certificate of our latest product SOMNOtouch, which we have already launched successfully into the European market. The credit card-sized SOMNOtouch is currently the smallest cardio-respiratory screener available and therefore offers highest comfort for the patient during recordings. It comes with a high-resolution touch screen, which not only simplifies the handling of the product with the intuitive operation but also allows signal checks directly on the screen. The feature Intelligent Connect automatically detects which sensors have been connected to it and therefore prevents incorrectly connected sensors. Physicians do not have to worry about pre-selecting montages anymore; patients cannot confuse sensors when they attach the device by themselves.

Editorial...continued from page 4

Evolution vs Extinction: Is the rapid growth of surfactant use and NIPPV leading to the extinction of neonatal mechanical ventilation skills sets?

As surfactant use became more mainstream and a first-line intervention, non-invasive ventilation quickly evolved in its delivery systems and interfaces. These two changes created a tipping point in neonatal ventilation. Instead of a prolonged intubation and ventilated state, the neonate is intubated, given surfactant and rapidly extubated to NIPPV. The duration of NIPPV is actually reduced as the effects of the surfactant administered improves compliance. This is repeated right across neonatal ICUs across north America.

At the Ottawa Hospital's Civic Campus Rich Little Special Care Nursery (an enhanced level 2 NICU), in the last two years, there has been a 60% reduction of mechanical ventilation and the average time on NIPPV is down to 36-48 hours with a large number <12 hours. The ability to maintain intubation skills and mechanical ventilation skills is in doubt. The effects are being repeated across North America and being noticed by leaders in the neonatal world and efforts to ensure these skills are maintained are mixed. Therapists are expressing concerns as they see their skills erode over time and their ability to safely deliver the mandated patient care is not seen as sustainable. The government ministry (Ontario Ministry of Health and Long Term Care) responsible for healthcare has closely monitored the situation and is considering implementation of mandatory transfer guidelines to ensure that intubated neonates, after 48 hours and not being actively weaned, are transferred to level 3 centers to ensure that the skills sets required are maintained and level of care provided appropriate to the needs of the patient.

Such rapid evolution in patient care has rarely been seen in the Respiratory Therapy profession and many have not noticed or acknowledged the rapid changes occurring. As technologic advances improve the delivery of NIPPV, the interfaces available reduce risks of damage and patient response capabilities improve, the utilization of mechanical ventilation will drastically drop further. Evolution or Extinction, either way the changes are accelerating and show no sign of slowing. Our understanding of the role of NIPPV in the neonates needs to keep pace with this evolution. We must embrace the changes or be left behind as other clinicians rise to meet the needs.

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Barlow Respiratory Hospital

In this feature, Respiratory Therapy interviews clinicians and healthcare providers about the actual application of specific products and therapies. Participating in the interview from Barlow Respiratory Hospital was: Glenn Payne, MPA, BSA, RCP, Director of Respiratory Care; Hao Chen, RRT, Clinical Supervisor; Douglas Vela, RCP, Respiratory Care Manager; and Rachel dela Rosa, MS, CCC-SLP.

Specializing in ventilator weaning, pulmonary rehabilitation and care of medically complex patients, Barlow Respiratory Hospital in Los Angeles delivers on its mission to help patients breathe easier. As a long-term acute care (LTAC) hospital, Barlow is widely trusted for the specialized care offered to chronically critically ill patients in the post-ICU setting.

Respiratory Therapy: Tell us about the protocol for Passy-Muir Valve (PMV) use and why Barlow made Passy-Muir Valves a standard of care for weaning patients from mechanical ventilation.

Barlow Team: At Barlow Respiratory Hospital, Passy-Muir Valve trials are completed within 72 hours of admission for all patients with tracheostomy tubes as long as the patient is medically stable. The respiratory therapist (RT) and speech-language pathologist (SLP) work together to initially place the valve. This team approach increases the likelihood of successful application. The RT makes any necessary ventilator changes, monitors vital signs, and checks for airway patency. The SLP focuses on breathing and speaking coordination issues and also monitors the patient's response and airway patency issues. Following the assessment, the SLP and RT recommend the patient to wear the valve either with direct supervision or unsupervised. Direct supervision indicates that a trained individual must be in the room with the patient during valve use. Unsupervised indicates that the valve can be worn independently by the patient with external monitoring in place.

Barlow made the PMV a standard of care because the PMV helps facilitate the weaning process of this patient population. This is done through the help of positive pressure in the upper airway created by the PMV, which helps the patient manage his or her own secretions. This process tends to lessen the risk of aspiration and promotes coughing to help the patient expectorate.

RT: Initially, clinicians were not familiar with the practice of placing the Passy-Muir Valve in-line with mechanical ventilation. What were the initial reactions of staff for trying this new approach?

BT: Initially, therapists were hesitant to place the valve in-line with mechanical ventilation. The therapists felt that not enough time was allocated to properly monitor the patients. The therapists were concerned that the patients were 'too sick' and that the PMV would place the patients in an unstable situation or



Barlow Respiratory Hospital staff, from left to right: Hao Chen, RRT; Glen Payne, MPA, BSA, RCP; Rachel dela Rosa, MS CCC-SLP; Scott Sasse, MD; Douglas Vela, RCP.

that the valve would make breathing more difficult. They soon realized that most patients were actually able to tolerate the valve the first time it was placed, and many patients felt more comfortable with their breathing. Teamwork and education were keys to increasing use of the valve and clinicians' comfort level with the process.

RT: Were there any other barriers to using the valve at your facility and how did you address these?

BT: The main barrier was related to the timing for initiation of PMV trials. Therapists initially felt that the most appropriate time for placement of the PMV was during spontaneous breathing trials (SBT). This thought was resolved by educating therapists on the importance of placement of the PMV while the patient was still on the ventilator to allow for rehabilitation of the pharyngeal, laryngeal and expiratory muscles to prevent further muscle atrophy.

Another barrier was that some therapists believed that deflating the cuff and placing the valve increased the risk for aspiration. Through evidenced-based research, RTs learned that the PMV helps to reduce aspiration risk by restoring subglottic air pressure and improving cough strength. This allowed for earlier and safer oral intake.

Some therapists did not understand the ventilator changes for a more successful application or would not place the valve because there was not a protocol. Education of simple ventilator

adjustments ensured competency for using the valve in-line. For the Puritan Bennett 840, this included use of non-invasive mode of ventilation and possibly increasing the tidal volume to compensate for air leaks. The RTs and SLP worked together to create a protocol. Barlow's full protocol can be found at www.passy-muir.com/policiesandprocedures.

RT: What educational opportunities did Barlow utilize to learn safe and appropriate ventilator application of the valve?

BT: First, staff participated in a live webinar on the basics of PMV in-line application. The educational approach also involved onsite in-servicing of the staff by the PMV Clinical Specialist. The specialist came to Barlow to demonstrate valve placement and adjustments specifically for the Puritan Bennett 840. Therapists learned safe alarm practices. With cuff deflation and PMV placement, air is not exhaled via the ventilator circuit and back to the machine, therefore the ventilator will not read any exhaled volumes. In non-invasive mode, volume alarms are automatically turned off. Inspiratory pressure alarms are adjusted by RTs to ensure sensitive fatigue and disconnect low-pressure and sensitive high-pressure alarms. In addition, the speech-language pathologist and Clinical Supervisor provided one-on-one training regarding the allowance of air leaks and proper monitoring of the patient. Education involved removal of the valve if vital signs were outside allowable ranges. Per protocol, the PMV is removed if oxygen saturations fall below 90%, HR changes by 20 beats per minute, respiratory rate increases over 35 breaths per minute, or if the patient is in respiratory distress.

RT: What patient and hospital outcomes have you realized after implementation of the valve into your weaning protocol?

BT: Implementation of the valve has really improved the ability of the patients to communicate their needs and issues. For a patient on a ventilator, being able to speak immediately decreases anxiety, improves quality of life, and provides a psychological boost for the patient and family toward weaning success. Many patients have expressed that their breathing improved with use of the valve in-line with mechanical ventilation and only with the valve on was weaning able to progress in some patients. It also restores a closed respiratory system, approaching normal physiology, improving patients' ability to control intra-thoracic positive pressure. With this, the valve allows graded exhalation and improves internal pressure support for postural control resulting in improved: upper extremity force production, bowel and bladder emptying, and swallowing mechanics as well as voicing. Although there are no control studies to verify the process, the staff believes that the PMV is beneficial for weaning mechanically ventilated patients. We are very proud of the fact that Barlow is a Passy-Muir Center of Excellence.

Editor's Note: Input on questions was provided by Nicole Riley, MS CCC-SLP Director of Clinical Education at Passy-Muir. If you would like to participate in this feature, as a company or healthcare provider, please contact Christopher Hiscox or Steve Goldstien at s.gold4@verizon.net.

Comparison of the Efficacy of Two Nebulizers in Treating Acute Exacerbation of COPD in the Emergency Department

James Rish, MD; Isaac Timmons, RRT

Introduction

Over 1.5 million adults are treated annually in the Emergency Department (ED) for acute exacerbation of COPD (AECOPD). A series of aerosolized bronchodilator treatments is the standard of care in treating AECOPD. The type of nebulizer used affects the dose and deposition of the aerosolized drug. Substantial evidence demonstrates that the breath-enhanced and breath-actuated nebulizers are more efficient in medication delivery than the traditional T-piece small volume nebulizer. There are few published clinical trials comparing the outcomes of two high performance nebulizers.

Objective

This study compared the efficacy of two high performance small volume nebulizers used in the initial medication regimen for AECOPD patients admitted to the ED. The outcomes of interest were length of stay (LOS) in the ED, treatment time, and number of treatments.

Methods

A comparison of the performance of two nebulizers was conducted in the ED on patients with acute exacerbation. A total of 36 patients with similar demographics were included in the product evaluation. In the first group, eighteen patients were treated with the breath-actuated nebulizer. The second group of eighteen patients was treated with the breath-enhanced high density nebulizer (HDN) small volume nebulizer. The same flow rate of 8 LPM and the same mouthpiece were used with both nebulizers. The hospital's AECOPD Respiratory Protocol was followed. For the first treatment, patients received either 1.25 mg Xopenex with 500 mcg Ipratropium or 2.5 mg Albuterol/500 mcg Ipratropium depending on their home medication and heart rate. The ED LOS, total number of treatments given per patient and nebulization times were recorded.

Results

Following completion of the evaluation, the median number of treatments was 3.0 and 3.5 for the breath-enhanced HDN group and breath-actuated group, respectively ($p = .0006$). Treatment times (4.0 ± 0.0 vs. 8.0 ± 1.7 min, $p < .0001$) and length of ED stay (2.5 vs. 3.1 hrs, $p < .0001$) significantly favored the breath-enhanced HDN device.

Summary

Our results showed significantly less number of treatments, shorter treatment duration, and shorter ED LOS with breath-enhanced HDN nebulizer. A cost savings from the shorter ED LOS, fewer treatments and less therapist time should be recognized. Further evaluations to assess the efficacy of the breath-enhanced HDN nebulizer in different hospital settings and patient groups may be beneficial.

Table 1. Evaluation data

Data	Breath-Enhanced HDN N=18	Breath-Actuated N=18	p-value
Albuterol w/Ipratropium	14	13	-
Xopenex w/Ipratropium	4	5	-
Median # Treatments	3.0	3.5	0.0006 ¹
Nebulization time/min	4.0 ± 0.0	8.0 ± 0.3	< .0001 ¹
Length of ED stay/min.	150.6 ± 17.0	187.7 ± 25.7	< .0001 ¹

¹ = Statistically significant difference

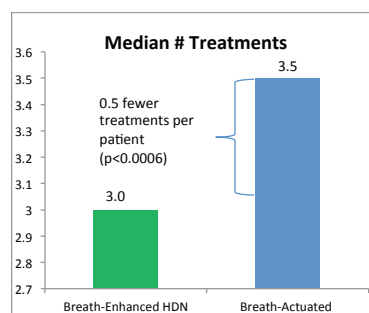


Figure 1: Median number of treatments per patient for each nebulizer.

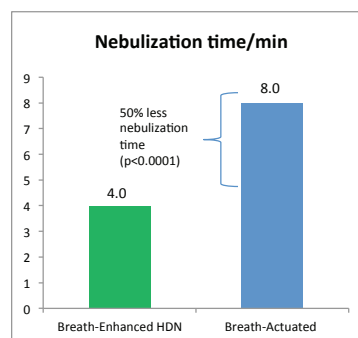


Figure 2: Average medication nebulization time for each nebulizer.

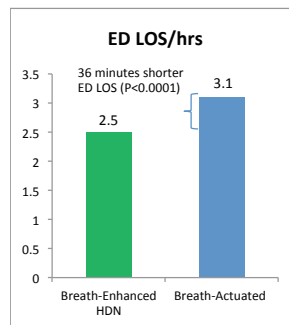


Figure 3: Average length of stay in the Emergency Department for each nebulizer.

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Case Study: Respiratory Collaborative Group Savings Initiative

Kathy Ehlers, BA, RRT; James Rish, MD

Introduction

Respiratory Care managers have always explored ways to reduce operational costs without compromising patient safety or quality of the respiratory services provided. The Patient Protection and Affordable Care Act of 2010 (ACA) added additional challenges for department managers to become more creative and find solutions for managing our respiratory patients, especially those with COPD, asthma and pneumonia. To maintain a high quality of patient care, while managing the budget and keeping staff positively engaged can be a juggling act. Managers are on the lookout for anything that improves the patient experience, decreases Emergency Department (ED) length-of-stay, and reduces total costs for the entire system.

Two years ago, the North Mississippi Medical Health Systems, consisting of 6 facilities, implemented a Respiratory Advance Program (RAP). The RAP provides a mechanism for respiratory therapists to receive recognition for their performance and contributions, participate in community programs and identify areas for improvement. One RAP participant requested to conduct an evaluation comparing two high performance small volume nebulizers, a breath-actuated versus breath-enhanced high density nebulizer (HDN), in COPD patients admitted to the ED for acute exacerbation. Breath actuated nebulizers are designed to generate aerosol only during the inhalation phase of the breath; maximizing the drug delivery and preventing loss of medication during exhalation. The breath-enhanced HDN nebulizers utilize one-way valves. During exhalation the aerosolized medication is captured in a reservoir tower, therefore reducing waste on exhalation. When the patient inhales, a high density bolus of medication is delivered during the first part of the breath.

At first I was hesitant about the nebulizer evaluation. In 2008, our respiratory department had a very successful transition to the breath-actuated nebulizer using concentrated medication. To optimize performance, the manufacturer sited the use of a concentrated medication with the breath-actuated nebulizer. I was not expecting to see a significant difference in patient outcomes or ED length of stay between the two nebulizers.

Product Evaluation

Isaac Timmons, RAP participant, conducted a product evaluation on COPD patients admitted to the Emergency Department (ED)

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with acute exacerbations. Eighteen patients received treatments using the breath-actuated nebulizer and eighteen patients received treatments using breath-enhanced HDN nebulizer. Objective data collected included length of ED stay from the time seen by a respiratory therapist to the time of discharge from ED, the number of nebulizer treatments given and percent change in FEV1 measured by spirometry. Due to the improved efficiency in medication delivery, patients treated with the breath-enhanced HDN required fewer nebulizer treatments, recognized a reduction in total treatment time, and had a shorter ED length of stay (Table 1).

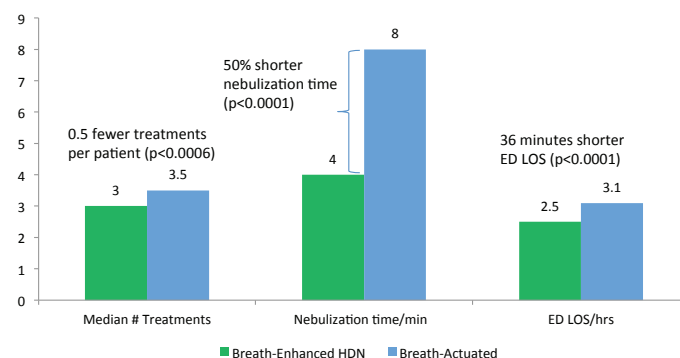


Table 1. Outcomes from nebulizer evaluation.

Cost Improvement

The biggest source of savings is on medication. In order to speed up treatment time with the breath-actuated nebulizer, our pharmacy unit orders a special concentrated form of the respiratory drugs. Per our AECOPD protocol, the first nebulizer treatment is given with the patient's home medication and Ipratropium. The concentrated unit dose for 2.5 mg albuterol with 0.5 mg Ipratropium is \$2.59. With the breath-enhanced HDN nebulizer; a generic albuterol solution can be used without impacting treatment times. The medication cost is reduced to \$0.24 per unit dose. A representative from Pharmacy and the Supply Chain Director met with the Respiratory Collaborative group and discussed the potential cost savings associated with standardizing supplies. Based on the previous year's usage of 136,000 nebulizer treatments, the main unit pharmacy would yield a savings of \$168,875/year. In addition, the respiratory department would realize a cost savings of \$20,000/year in nebulizer disposables. This does not include the potential savings the other 5 facilities will recognize.

Table 2. Cost of nebulizer treatments including therapist's time.

	First Treatment (includes nebulizer)		Subsequent Treatments	
	Breath-Actuated	High Density, Breath-Enhanced	Breath-Actuated	High Density, Breath-Enhanced
Medication used	2.5mg albuterol 0.5mg ipratropium	2.5mg albuterol 0.5 mg ipratropium	2.5mg albuterol	2.5mg albuterol
Treatment Time	15 min	11 min	15 min	11 min
Therapist Wage	\$11.10	\$7.06	\$6.47	\$4.41
Medication Cost	\$2.59	\$0.24	\$1.10	\$0.32
Total Cost	\$13.69	\$7.30	\$7.57	\$4.63
High-Density, Breath-Enhanced Savings per treatment	\$6.39		\$2.94	

In our hospital group, the average Respiratory Therapist's salary is \$25.91/hour. Using the breath-enhanced HDN nebulizer; we shaved 4 minutes from each nebulizer treatment. Based on the number of procedures performed last year that equates to 9,000 hours/year or in theory, \$200,000 of labor costs. To actually capture the labor savings is unlikely; however, a portion of the time may shift to other revenue-generating therapies. The recognized cost improvement from the ED evaluation, including therapist's time, nebulizer and medication cost, was \$273.78.

Hospital-Wide Adoption

Based on the combination of shorter treatment times and ED LOS, equivalent-to-better clinical outcomes, and substantial cost savings, we made the decision to implement the high density, breath-enhanced nebulizer throughout our hospital. Working closely with the Pharmacy Department, and the supply chain director we proposed a new regimen for our nebulizer protocol. The other facilities in our health system conducted an evaluation and plan to adopt the new nebulizer protocol. The Ambulance Services department is reviewing the protocol for use of the breath-enhanced HDN nebulizer in the pre-hospital setting for asthma and COPD patients.

Conclusion

To adapt to the new ACA guidelines, utilizing a multidisciplinary team approach is essential. Any contribution made that reduces the cost of inpatient care and prevents re-admissions of respiratory patients is a valuable asset. Often there is a tradeoff between efficiency and clinical outcomes. However, in our evaluation we found that the breath-enhanced HDN nebulizer improved both speed and clinical outcomes compared to a breath-actuated nebulizer. It shows that there are real performance differences between various high-performance nebulizers. The leadership and participation from the pharmacy, supply chain and our medical director was vital for the successful implementation of the new respiratory protocol. Additional evaluations are needed to capture North Mississippi Medical Health System's true cost savings over the next 6 to 12 months.

A Culturally Sensitive Asthma Self-Management Program

Linda G. Galloway PhD RRT; Shelley C. Mishoe PhD, RRT, FAARC

Introduction

Childhood asthma is a costly chronic disease; costly in personal and financial resources, as well as the lives changed. There have been 8 million children under age 18 who have suffered from asthma attack episodes (American Lung Association, February 2010). Pediatric asthma is reaching epidemic proportions and affecting African-American children at unprecedented rates (Gern, 2010; Office of Minority Health 2011). An estimated \$15.6 billion a year is spent on asthma direct healthcare with another \$5.1 billion spent in indirect healthcare costs (Office of Minority Health, 2013). Hospitalization and medications are found to be the most important cost driver of direct costs in asthma care. Work and school loss has accounted for the greatest percentage of indirect costs. In the United States, asthma has accounted for about 15% of non-surgical admissions to the hospital (Cloutier, 2008).

In 2011, 23.3 million Americans had asthma and over seven million were children. (American Lung Association, February 2010; Office of Minority Health, 2011). Update to current year asthma also accounted for 14.2 million lost school days for children. Asthma is one of the leading causes of missed school days and a considerable cause of an amount of morbidity and mortality of all ages. One study entitled "Health Expenditures Statistics and Numerical Data" (Bahadon et al., 2009) said "the cost of asthma correlated with morbidities, age, and disease severity." Additionally, the study found that even though effective preventive therapy such as asthma education programs exist, costs associated with asthma are increasing. The morbidity and mortality rate of asthma are increasing. In 2000, asthma was responsible for 4,487 deaths, approximately 465,000 hospitalizations, an estimated 1.8 million emergency department visits, and approximately 10.4 million physician office visits among people of all ages in the United States (Cloutier, 2008). Every year asthma is responsible for about 5,000 deaths and 2.5 million hospitalizations or emergency room visits (Koinis-Mitchell et al., 2010; Cloutier, 2008).

Dr Linda Galloway volunteers in the community on several initiatives to address asthma morbidity and mortality, including education of children and their families on asthma management. She also works on special projects in the Dean's Office of the College of Health Sciences at Old Dominion University. Dr Shelley Mishoe is Dean of the College of Health Sciences and Professor of Community and Environmental Health at Old Dominion University. She is a past president of the Committee on Accreditation for Respiratory Care (2007-2009) and has been recently elected to the Board of Directors for the Association of Schools of Allied Health Professions (ASAHP) for a three-year term.

Asthma Health Care Disparities

Asthma is the most chronic childhood disease and is clearly overrepresented in ethnic minority urban children (Cloutier et al., 2009; Celano et al., 2010; Office of Minority Health, 2011). Asthma is more prevalent in children from African-American and Puerto Rican backgrounds. This is in comparison to non-Latino White children, and the rates remain high even when controlling for socioeconomic factors (George et al., 2006). The disparity is attributed to unequal access to preventive care. African-American children and Puerto Rican asthmatic children statistics reveal under-usage of routine care and over-usage of emergency room visits. Asthma in African-American children and Puerto Rican children is consistent with reports of poor adherence to asthma care, poor adherence to medicine, and common healthcare barriers such as no insurance or no money for medication, not enough trained healthcare personnel and the lack of incorporation of the healthcare beliefs of the family's culture. In some cultures, families have misconceptions about asthma and believe things such as: the medicine can become addictive, it can be treated by prayer alone, and even that asthma is contagious. One research study went as far as to say the asthma care program had been provided but there were no resources provide to treated the asthmatic (Celano et al., 2010).

The severity and prevalence of asthma has increased in the inner city area (CDC, 2007; Office of Minority Health, 2011). There are certain limits on controlling asthma in the inner city area: socioeconomic burdens, other factors such as environmental allergens, pollutants, infections, and stress add to the significantly disease burden found in these children (Josie, Neff-Greenley & Drotar, 2007).

The greatest increases in the incidence, morbidity, and mortality rates have been among African-American youth and youth living in the inner city. The last several years have indicated African-American youths have higher death rates from asthma and mortality over time. African-American hospitalization rates are higher with increased healthcare utilization. African-American youth between the ages of 5-17 years of age in 2003 had a prevalence rate of 1.62 times and an attack prevalence rate of 1.50 times the rate of Caucasian youth (Yinusa-Nyahkoon et al., 2010).

Some explanations for the increase are air pollutants, aeroallergens, diet, infections, and tobacco smoke due to congested and crowded urban areas, with garbage pollution and smoky smells. Additionally, there is a smell that accompanies

unclean and crowded areas. Research information suggests that psychosocial stress is likely to be a factor contributing to the development of asthma. Not knowing where your next meal is coming from or how to pay for the medicine that is so badly needed are psychosocial stressors (Byori, 2010). Research suggests stress is related to asthma and some investigators have related psychosocial distress to mortality (Mishoe et al., 1998; Razvodovsky, 2010; Williams, Portnoy & Meyerson, 2010).

Statistics, hospital records, asthma educational programs, Centers for Disease Control, and school records have revealed even with the asthma education programs the prevalence of asthma is increasing in the low-income communities (Patel et al., 2007). Low-income African-American children with asthma in New York, Connecticut, Washington D.C., Chicago and several other cities have used the asthma education programs, but the prevalence of asthma is still on the increase (CDC, 2007; Farber, 2009; Office of Minority Health, 2011).

The studies, however, reveal the programs have reduced the use of the emergency room visits and children who have maintained asthma action plans control their asthma somewhat better. But, what if the stress from worry of where your next meal is coming from or the frequent smells that accompanies the inner city areas aggravates an asthma attack? Programs specifically for the inner city pediatric asthma population should be designed. Programs such as Open Airways program, Easy Breathing and The C.A.R.E., designed for the pediatric asthma population, have revealed enhanced control of asthma in the inner city, yet asthma in the inner city area remains on the increase (Cloutier, et al., 2006; Horner, 1998). The inner city areas offer a challenging environment with limited resources for the management of asthma (Koinis-Mitchell et al., 2010; Patel, 2007; Farber, 2009; Razvodovsky, 2010).

Disparities exist in the inner city area among African-Americans and Puerto Rican children (Cloutier, 2008). Asthma is more prevalent in the inner-city ethnic minority population (Josie, Neff-Greenley & Drotar, 2007). According to the Office of Minority Health (2011) almost 4,500,000 non-Hispanic Blacks were reported to have asthma. Additionally, African-Americans were 30 per cent more likely to have asthma than non-Hispanic Whites. In 2011, the Office of Minority Health found African-Americans were 3 times more likely to die from a related cause of asthma than the White population. African-Americans had emergency room asthma related visits 4.5 times more often than Whites in 2004. Black children were 3.6 times more likely to visit the emergency department for asthma than compared to non-Hispanic White children.

Children in poor families are more likely to ever have been diagnosed with asthma according to the Office of Minority Health. The exact causes of asthma have not been diagnosed yet children exposed to second-hand and third-hand smoke are at increased risk for acute lower respiratory tract infections, such as asthma, and children living below or near the poverty level are more likely to have higher blood cotinine levels, a breakdown product of nicotine, than children living in higher income levels.

Measures have been taken to contain the prevalence of asthma as education programs and training of healthcare staff has been developed. There should also be regular follow up of the asthma education program and the costs associated with the program. The problem as stated “appears to be not the therapeutic

treatment potential of the disease, but inadequate effective medical care delivery” (Weinberger, 2006).

Because this is a disease that requires the support of the family and community, it is important to determine if the treatment strategies are family centered and culturally focused. This discussion will explore the current methods used in self-management of asthma with children. In addition, the current programs will be reviewed to determine the utilization of culturally focused methods and strategies.

Asthma Management Programs

There are numerous asthma management programs for the pediatric asthma population. Yet, there seems to be conflicting approaches to the actual management of asthma. Asthma management especially in the inner city area where it is most prevalent has helped parents and children to better manage their asthma, but the prevalence is still increasing. Statistics have revealed African-American and Puerto Rican children in the inner city areas suffer the most from asthma (Koinis-Mitchell et al., 2010). Conflicting programs from multiple sources seem to result in confusion and lack clear, concise, and culturally defined guidelines. Guidelines are needed that can be adhered to in the inner city, poverty-stricken areas. Asthma management programs aimed at the culture of the target population could be more effective. Information about asthma and how to manage it must be framed within the cultural context of the patient and the family to be understood and implemented.

Here is an overview of the most common Asthma Management Programs:

The Open Airways Program

The Open Airways program educates the parents and the child on asthma triggers, asthma management, the peak flow meter and the importance of adhering to the asthma attack and self-efficacy. The Open Airways program has been validated by Dr Evans, Dr Clark and their research team with the American Lung Association (CDC, 2009). This program was first used in 1985 but was extended to include current guidelines in 2009. When the program was first used, it had to be altered due to lack of parental participation. The parents had a low attendance rate so parental packages were made and sent home with the child (Clarke et al., 1985). The program includes an instructor guide with theoretical information, step-by-step instructions on how to conduct the program, and a sample letter to parents explaining the benefit of the program. A bilingual (English and Spanish) curriculum book details the six sessions including a flip chart, a handout and a list of American Lung Association (ALA) offices (CDC, 2009).

- Lesson 1. Information about feelings and about asthma. Children are given an opportunity to talk openly about their asthma attacks and how they manage the attacks.
- Lesson 2. Recognizing and Managing Asthma Symptoms. Children talk about warning signs and how to detect if an asthma attack is about to occur.
- Lesson 3. Solving Problems with Medicines/Deciding How Bad Symptoms Are. Children are told when to use certain medications and practice decision methods.
- Lesson 4. Finding Triggers and Controlling Asthma. Environmental triggers are identified and ways to avoid them are discussed.
- Lesson 5. Keeping Your Battery Charged-How to Get Enough Exercise. Six ways to stay physically active are identified.

Children also learn about managing conflict with parents and others concerning physical activity.

- Lesson 6. Doing Well At School. Children learn to manage when and when not to go to school due to asthma and how to make up school work (CDC, 2009).

Different teaching approaches are used as real, active, and participatory. The real approach uses child experiences as the basis of learning. Lesson 2 asks the child how they manage their asthma. Here, children brainstorm as a group and use personal experiences to solve problems. Active interaction uses hands-on activities to practice exercise techniques used in the package. Some of these activities include musical chairs, the straw breathing game, bingo, belly breathing, and red light/green light, which are participatory interactions in decision making. The kit also has homework and a package for parents to work with the child on managing their asthma (CDC, 2009).

Easy Breathing Program

This program was developed from the 1997 National Asthma Education and Prevention Program (NAEPP) guidelines. This program was originally designed to assist clinicians in recognizing asthma, classifying asthma severity, and creating a written asthma plan. This program was expanded in 2001 and became Easy Breathing II. The program is two pages and has allowed other healthcare personnel to incorporate their own programs into it. Easy Breathing is not a program in its entirety but focuses on four main areas (Cloutier, 2008). These areas are from the NAEPP guidelines. They are: (1) asthma diagnosis, (2) determination of asthma severity, (3) use of ICS (inhaled corticosteroid) with other appropriate medications, and (4) development of a written asthma plan. The program includes a survey provider assessment and a written asthma plan. The clinicians are responsible for including other needed aspects of the asthma program, such as patient education, allergy skin testing, patient adherence techniques, and use of the peak flow meter.

The C.A.R.E. Program

This is a mobile care program established in Chicago that provides free, ongoing medical care, health education, medications, and supplies for asthma to children in Chicago's underserved communities. Researchers have documented the lack of medical resources and other resources that accompany poverty and inner city living (Wilson, 1990; Moynihan, 1985). The C.A.R.E. Program is one that addresses poverty's impact on asthma management by providing the actual resources needed in addition to patient education. The children are evaluated by a physician according to the National Asthma Education and Prevention Program (NAEPP) guidelines (Office of Minority Health, 2011). From the beginning of the program, children are examined by the physicians for the severity of their disease. The clinicians then give the appropriate medications with a full supply of the medications. This is one program that supplies the actual medications to the patient.

A Culturally Sensitive Asthma Management Program

We have used and propose a culturally sensitive asthma management program to achieve understanding and create changed behaviors. Different authors (Wilson, 1990; Diller, 2004) have supported how the low educational ability of minority children impact asthma management. Socioeconomic studies have revealed the low educational ability of parents in the low income areas. One aspect of child development that researchers

support is children of color perform academically at a lower level than their white counterparts in the public school system (Diller, 2004). Programs offer advice on how to manage asthma but do not provide adequate resources or adaptations to inner city living (Farber, 2009).

The widely used asthma management programs consist of providing the same basic information to the many, many different groups of asthmatic children, without sufficient incorporation of cultural and contextual variables. The educational programs allow perhaps 5-10 minutes to disengage current beliefs of the culture but insufficient time to incorporate the beliefs of the inner city, minority populations. We propose that in order to be effective in addressing morbidity and mortality of asthma in African-American and other minority children living in the inner city, more time must be taken to understand and adapt asthma management programs. For example, one study reviewed the relationship between prayer, relaxation exercise and control of asthma (George, et al., 2006). The results indicated prayer and relaxation exercise were used by patients to control their asthma and these beliefs should be incorporated into a culturally sensitive asthma management program. Yet, another research study examined the relationship between English proficiency and language barriers involving inner city asthmatics (Wisnivesky, et al., 2009). The results of this study revealed a low English proficiency to be associated with low medication adherence, more worry, higher rates of resource utilization, and poor control of asthma. Clearly, the beliefs and practices of the minority, inner city culture must be incorporated for asthma education and management to be effective.

A common belief among inner city, minority children and their families is that you should treat asthma when you get a wheezing attack. Therefore, urban children with asthma treat their asthma when an attack occurs and not on a regular basis. There is lack of understanding that asthma is a chronic disease, not an acute illness that responds to episodic inhaler use. It is, therefore, not surprising that there is low medication adherence in common. Many children with asthma do not have an asthma management plan or an understanding of their chronic disease. Additionally, caregivers often do not understand asthma treatments and protocols. Adherence to medication is not taken seriously by the caregiver or the asthmatic child. In many African-American communities the belief that medication and adherence to a management program can actually help to control asthma is very vague (Galloway, 2000). For instance, some believe the medication was addictive and causes additional health problems. The basic understanding that asthma is a chronic disease that will not go away, but can be managed, is never fully relayed to the parent or the child with asthma in a way they comprehend. This very basic information is not given enough attention to change the expectations of the asthmatic child and the family because there is lack of appreciation for the cultural beliefs. Based on experience, initiating three asthma programs, we propose that cultural considerations using change theory should be incorporated in pediatric asthma programs, especially for families living in the inner city (Galloway, 2000).

We propose that educational materials for control of asthma in children for this critical target population of African American families living in the inner city incorporate Kurt Lewin's change theory with the concepts of Freezing and Unfreezing (Kurt Lewin's Change Theory) including sessions on cultural mores and beliefs. This theory teaches change and how to successfully

implement change. Using this theory, we propose that a specific program be adapted for each target population as the same program does not work for all ethnicities.

Time and education with the caregivers or parents is essential before even starting the asthma management program for the child (Houle, 2010; Kaul, 2011). For instance, the theory of freezing and refreezing should be taught in addition to the asthma management program. Old ideas such as prolonged use of asthma medication will only lead to dependence on the medicine rather than help the disease of asthma in the long run must be dealt with. We refer to this as the “unfreezing” stage whereby the asthma educator first understands the commonly held belief and then attempts to have the person release these unfounded beliefs. These untrue beliefs and folklores that have been in the African-American community for many years must be appreciated and unfrozen before any meaningful explanation or education can occur. Failure to address commonly held misconceptions and cultural beliefs will result in poor understanding, minimal change in behavior and poor adherence to asthma management plans, regardless of what program is adopted. Knowing and incorporating commonly held cultural beliefs about asthma can lead to better understanding of asthma and its management and ultimately better control of asthma.

Even when culturally bound misconceptions are “unfrozen” and new knowledge and beliefs are adopted or “frozen” there will still be limitations for successful asthma control in the inner city. The additional limitations are socioeconomic burdens, environmental allergens, environmental pollutants, infections, and stress that add to the significant disease burden found in these children. However, implementing a culturally specific program using Kurt Lewin’s change theory may achieve better adherence and improvement in long-term management in spite of these limitations.

Kurt Lewin’s Theory of Change and the Health Belief Model

We propose a new model for asthma management that incorporates Kurt Lewin’s theory of change and the Health Belief Model (see fig. 1). Kurt Lewin’s theory of change is very simple but it constitutes the requirements necessary for effective change to take place. The current asthma management programs provide a short period of time to discuss some health beliefs of asthma management. The literature has not revealed a more consistent, organized, and carefully replicated plan. For instance, Lewin’s theory has been used successfully to implement change in various healthcare organizations. Additionally, the theory has been used in organizational change with nurses and college administrative healthcare personnel (Ting & Ting Lee, 2010; Shriner, 2006).

The culturally sensitive asthma management program consists of an introduction and a thorough discussion of the culture’s health beliefs concerning asthma. This should include the culture of the targeted audience, i.e. African-American, Hispanic, or Caucasian. In other words, the discussion should focus around the audience being taught with ample time for interaction and dialogue about what beliefs the group has about asthma. For these discussions, the instructor should incorporate a consistent approach. We recommend using the Health Belief Model.

The Health Belief Model is used here also to support the concept of Lewin’s change theory being used in a healthcare

environment. The Health Belief Model was developed in the 1950s and updated in 1980. The Health Belief Model constructs are:

1. Perceived Susceptibility
2. Perceived Severity
3. Perceived Benefits
4. Perceived Barriers
5. Cues to Action
6. Self Efficacy.

This model is a psychological model that seeks to explain how to predict healthcare behavior. The concept of self efficacy was introduced to this model in 1988 since a person’s confidence in oneself has to be there for the action to be successful.

Additionally, the model indicates that if a person has an understanding of the perceived severity of the health concern they would act to receive the benefits and overcome the perceived barriers. The inclusion of this model with Lewin’s theory is necessary for the asthma educator and the caregivers and children to thoroughly understand the effects of the changed behavior.

The Unfreezing, Change and Refreezing

Step 1. Identify the culture and discuss current health beliefs of the Asthma Management program to an African-American audience. It has been documented (Celano, 2010) within this culture that asthma medications are considered habit forming. Additional false beliefs that are widely held based on the groups we work with include: “The medicine can make you sicker,” “Prayer will help an asthma attack,” “The medicine Advair is very harmful to African-Americans” and “Death has occurred from using Advair.” These beliefs are held in the community, though they are not true. Therefore, it is critical to discuss these and any other commonly held misconceptions as the first part of the program. After confidence and trust is achieved, false beliefs should be discussed thoroughly with alternative suggestions given. This first session alone may take an hour or more depending on the size, participation and viewpoints of the group. This step can be repeated and should continue until it appears there is adequate unfreezing of the misbeliefs. The end of the first session will include a review of untrue mores of the culture concerning asthma. The instructor will further reiterate these beliefs are not true. This session can conclude with trying to achieve belief of one common truth: “Asthma management will not cure asthma but will help to control it and definitely reduce attacks, if the medicine is used according to the directions.”

Step 2. Change Process. This step involves teaching the new Culture Sensitive Asthma Management program. This step introduced a better way to control the patient’s asthma. For instance, the group should learn that the new asthma management program will help you to decrease the frequency of emergency room visits. It is important to explain that if they and their children follow the instructions, they will have less asthma attacks and coughing episodes. Encouragement with confirmation through participation is essential to this step, such as repeated reminders that if they and their children remember to follow the asthma management program, they will feel better and have fewer asthma attacks. Additional reinforcement, with small prizes to those who answer correctly, can build engagement, confidence and understanding to achieve changed behaviors. Repeatedly encourage that if they do the program exactly as you explain, they will feel better and so

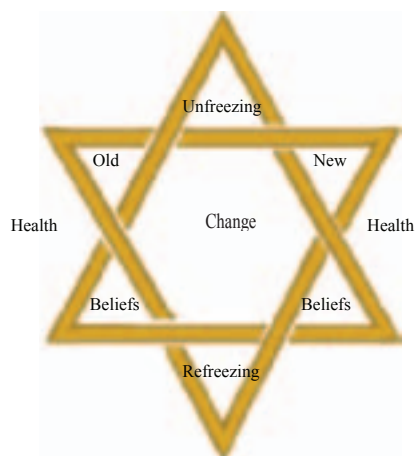


Figure 1. Model for a Culturally Significant Asthma Management Program

will their child. The most common belief to change is that nothing is needed if the person is not wheezing or having an attack. Repeated explanation, with interaction and positive reinforcement, can achieve change that even if the patient is not having an asthma attack or any symptoms, the management program must still be used.

Step 3. Refreezing of the New Asthma Management Program. This stage reiterates the asthma management program and the old beliefs that should be substituted with new beliefs. The goal is that misconception and false beliefs no longer exist. Once that occurs through Steps 1 and 2, it is possible to refreeze the new beliefs and knowledge. The new beliefs are thoroughly discussed, having them give clear examples to show their understanding of the program.

As previously mentioned with Lewin's Theory of Unfreezing, change and refreezing is the theoretical premise of this program with the Health Belief Model. Additionally, the instructor of this program must be trained in multiculturalism of the target audience. The whole family of the asthmatic should be present for this class. This includes any person who provides care for the asthmatic child such as the grandmother or any family member. At the completion of the class, the asthma management program will be reviewed, and the instructor will ascertain whether or not the new health beliefs and the change process had enhanced the behavior of the asthmatic. A follow-up program of telephone calls from the instructor will be put in place for six months.

The class will consist of questions such as has the asthmatic had any emergency room visits or asthma attacks. Additionally, the use of the asthmatic's inhaler will be discussed to include questions such as, is the individual still using a spacer with his/her inhaler, how many times a day is the inhaler being used and which inhalers are being used currently.

In conclusion, African-Americans like any other nationality have different cultural mores and beliefs. We believe a more culturally targeted asthma management program will enhance the process of understanding asthma management, thereby producing a more effective behavioral response to the management of childhood asthma. Numerous asthma management programs have been instituted yet the prevalence of asthma continues. A change process implemented into the asthma management program will provide a better understanding to the healthcare workers and the asthmatics concerning their disease. Cultural

mores and traditions are built into a culture by years of doing things the same way. The ideas become imbedded in the culture over time. These mores are passed on through many generations. Therefore, a total change process must occur not only to enhance the new beliefs but to dispel the old beliefs. This process cannot take place in ten or fifteen minutes but must be taught, replicated and understood by the culture thoroughly. This will allow for a better understanding of the asthma management process.

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Clinical Experience with the Ram Cannula and other Novel Interfaces with Neonatal NIV

Dave Lockwood, RRT

Historically, non-invasive ventilation of the neonate has mostly been defined as nasal CPAP in some form, such as bubble CPAP where the exhalation limb is placed in a water column to create higher than atmospheric pressure during the expiratory phase or with commercially available flow generators and fluidic valve breathing circuits. It has only been within the last 8 years or so that there have been ventilators offering any form of positive inspiratory pressure to allow the use of biphasic non-invasive ventilation of infants. Depending on the brand of ventilator or flow generator one either had a pretty good bi-phasic capability but poor interface or vice versa. A good interface that could be used with almost any apparatus had not yet been developed.

At Renown Regional Medical Center, Reno, NV, where I was a clinical practitioner up until January 31 of this year, we started NICU units to use the Ram cannula (NeoTech, Valencia, CA) immediately after its debut in November 2011. Prior to the introduction of the Ram cannula, we had been using a commercial system that, while it had a pretty good interface circuit using fluidic a fluidic valve, the flow generator itself was poorly thought out. Peak inspiratory pressure was limited to 11cmH₂O and only non-synchronized machine breaths were pressure supported. Any spontaneous breathes by the infant were merely CPAP supported. While I did like the fluidic breathing circuit, it could not be incorporated into a ventilator.

The Ram cannula was used with a new NIV mode on our Hamilton G5 ventilators called nCPAP-PS. (Hamilton Medical, Inc., Reno, NV) Prior to the Ram cannula we had considered other commercial nasal prong interfaces but those required that the infant stay relatively supine which our neonatal group (M.D.s, RCP's, RN's) did not care for. Using the Ram cannula allowed us to perform our usual rotation of the infant and with good leak minimization and leak compensation on the G5, we were able to progress in our desire to minimize intubation of the infant. Another of our Neonatal Respiratory Practitioners came up with the brilliant idea of taking the tracheal tube adapter from a 6.0mm adult tracheal tube and placing it on the end of a Fisher & Payakel (Fisher & Paykel, New Zealand) neonatal Optiflow cannula which turned it into a Ram cannula equivalent. For reasons that I won't go into in this article, within a year of its debut NeoTech Products pulled all reference of the use of the Ram cannula as a NIV interface off of its website. But the "cat was out of the bag". The Ram cannula was effective for NIV and so was the modified F & P Optiflow cannula. At the 2012 AARC

Congress in New Orleans there were Open Forum abstracts displayed from 3 different facilities documenting and comparing the Ram and modified Optiflow for NIV use.

My use of both systems is limited to use with the Hamilton G5 ventilator. When the Ram cannula debuted the company stated in a handout that for proper use the cannula should create a 60% - 80% occlusion of the nares. Somehow that fact was misconstrued and many practitioners believed that the Ram was supposed to be able to function with a 60% - 80% leak! Dr Ramanathan also stated that "And one of the other things I really don't like is a tight fit nasal cannula because how is the baby going to exhale" (Teleconference with Dr Ramanathan, Jan 12, 2012) but his statement has not been tested clinically. Our group decided to go with the concept of the largest fitting cannula that did not cause any pressure on the nares or septum. With NIV in pediatric or adult patients, you want a machine with good leak compensation but for the most effective NIV, you also want to minimize the leak as much as possible. We felt it should be the same with infants. We also used a skin barrier to protect the septum. Using this set up with either cannula we were having good success using nCPAP on the G5. When I left Renown we had successfully used nCPAP-PS on infants in the low 600gm range using the premie size Optiflow cannula.

nCPAP-PS on the G5 ventilator allows for pressure supported spontaneous breaths in addition to machine generated mandatory pressurized breathes. A unique feature of nCPAP-PS on the G5 is that with good leak minimization (leak \leq 50%) the infant can usually sync well with the vent and no mandatory machine breaths will be delivered as long as spontaneous breaths are detected. The mandatory breaths are only generated if no spontaneous breath is detected (mouth breathing/leak or large leak around the nasal interface) or the infant is apneic. The key here is to minimize the leak. This is important for effective NIV no matter what brand of patient interface or ventilator. I have heard anecdotally from other practitioners using ventilators that superimpose the mandatory machine breaths in addition to spontaneous breaths that the infants seem to have more gastric bloating. While this could happen with the G5 nCPAP, due to the breath detection feature mentioned above it doesn't seem to happen as much.

The other discussions that NICU practitioners need to have when progressing down the path of NIV is, at what peak inspiratory pressure and or ventilator rate does it make sense
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ASV in Eight Questions

Dave Lockwood, RRT

Many Clinicians and Physicians don't have a clear understanding of how Adaptive Support Ventilation (ASV) works or is regulated. Because ASV takes over a lot of the decision making regarding ventilator settings and modes, some tend to shy away from using it as a mode of ventilation. Below is a short review of how ASV works compared to other modes of ventilation.

1. Explain the concept of ASV?

ASV is a closed loop mode of ventilation. This means that the operator sets certain parameters, in this case; patient sex, height and desired minute ventilation. The ventilator then looks at the patient's spontaneous respiratory rate, tidal volume, resistance and static lung compliance* (these are the feedback from the patient inputted into the ASV algorithm) ASV then determines the best target tidal volume, respiratory rate and inspiratory time to achieve the desired target minute volume setting (called "%MinVol" in the ASV settings).

ASV also has a set of safety rules which limits pressure, volume and autopeep. ASV can provide full support, partial support and transition to a spontaneous breathing trial without the need to manually change to another ventilator mode. ASV can also detect if the patient's lungs are becoming too stiff and automatically adopt an ARDS protocol low tidal volume higher RR strategy. If the patient is apneic or passive, ASV delivers time cycled volume targeted pressure control breaths. If the patient is actively breathing then ASV delivers patient triggered, flow cycled volume targeted pressure support breaths.

2. What logic does the machine use to come up with these parameters?

ASV utilizes the Otis Least Work of Breathing equation. The Least Work of Breathing equation was developed by Dr Otis in the 1950s. He observed that mammals at rest naturally breathe at a RR/Vt combination that imposes the least work of breathing on the respiratory system and results in the least calorie expenditure. So a patient with a stiff lung or restrictive disease (low compliance) and low resistance adopts a higher RR and lower tidal volume as it's less work for them, whereas a patient with obstructive disease naturally adopts a lower RR and higher volume to avoid air trapping.

3. Explain how ASV works as a primary mode.

When using another mode of ventilation, let's say volume control, you would choose the Vt, the RR and the Ti. Then you

obtain an ABG and see that your PaCO₂ is higher than you want. What do you normally do? Generally you would increase the RR, maybe even increase the Vt a little. And if your PaCO₂ is too low you would decrease either RR or Vt. Changing either Vt or RR changes the minute volume (RR x Vt). ASV works by you adjusting the %MinVol knob either up or down thereby changing the target minute volume setting and allowing the ventilator to choose the ideal RR, Vt and Ti based upon the lung compliance and resistance at that moment. So ASV is automatically doing what we do manually but it is always looking at the pulmonary mechanics when making a change. Do we as clinicians always remember to factor in lung mechanics when deciding what vent parameters to change?

4. So does the %MinVol setting tell us if the patient is on high support? And what would be considered a common setting for %MinVol when using ASV during the acute phase of a disease process?

The default 100%MinVol setting means that the patient's minute volume target is the normal predicted minute ventilation for that patient based upon their ideal body weight. Adjusting the %MinVol knob up or down means you are merely increasing or decreasing the predicted minute ventilation by that percentage. During the acute phase of a disease process depending on the pulmonary mechanics, you might have the %MinVol commonly at anywhere from 100% to 200%. For a 70 kg IBW male, 100% MinVol setting would target 7 lpm, 200% would target 14 lpm 12-16 L/min range. If you look at the measured minute volume of a patient in ARDSnet protocol on a manual mode such as volume control this will be in the same range.

5. So if I'm past the acute stage of the disease process, how do I manipulate ASV?

If you were in a manual mode where you had chosen say a rate of 30 and a Vt of 400ml, as your PaCO₂ and static compliance are improving you start to either drop your rate and/or increase your Vt. With ASV you lower the %MinVol setting and ASV determines if Vt, RR or both will be adjusted. When adjusting the %MinVol, until you are comfortable with how it works a good rule of thumb is go up by 20% and down by 10%.

6. Do I continue to wean the %MinVol down until the patient is extubated?

Not necessarily. If you are at, say 100-125% on the %MinVol setting and your patient is spontaneously breathing, their pressure support level is at or below your criteria for extubation
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Using Low Tidal Volume: How Are We Doing?

Jonathan Beene, RRT

It's hard to believe that it's been over a decade, 13 years in fact, since the ARMA¹ study was published in *The New England Journal of Medicine*. Since then, ARDSNet² recommendations have been adopted as "the Bible" of mechanical ventilation management for many institutions. Using low tidal volumes (ARDSNet target is 6cc/kg/PBW, 4-8ml/kg for some circumstances) in combination with higher PEEP is not only common practice these days, but for many institutions, the only way. But the practice of using low tidal volumes has not been adopted universally, as institutions have not been able to overcome barriers, and recent literature brings up a couple of questions — are we using low tidal volumes on all patients, and do we really need to?

An example of one hospital where ARDSNet guidelines are the "bible" yet barriers still exist is the University of Colorado Hospital, which was a part of the ARMA study. Says Jerome Piccoli, RRT, Critical Care Specialist at UCH, "It is hard to argue against the results of the ARMA study... as a result, all of our mechanically ventilated patients are initiated on low tidal volume targeted ARDSnet settings. Of course, this is not beneficial to every sub-group of patients and some of our medical teams choose to opt out of these settings..." In fact, a recent observational study done in part at the University of Colorado found that patients received proper guideline-compliant lung protective ventilation (LPV) strategy only 53% of the time in the first two days after their diagnosis of ARDS.³ In another study of 465 patients, only 41% of the time the observed ventilator settings were compliant with low tidal volume ventilation guidelines for ARDS, and a somewhat surprising 37% of patients were never treated with low tidal volume ventilation.⁴ An educator at a leading hospital in Pennsylvania who chooses to remain anonymous, states "...we have 11 physicians that all do various things... I could not specify exactly what any of them do on any given day!"

Barriers to implementation of lung protective strategy are even demonstrated in the educational system, and the necessity to teach different philosophies. Jami Sahlie, RT, Education Director, Pickens Technical College, Aurora Colorado Public Schools, says that "We teach ARDSNet from the beginning...so that the students know to use a lower VT in clinicals. We teach 8-10 cc for the NBRC exam and 10-12 cc for vent-dependent trach patients in some cases."

Even if low tidal volume strategy is implemented, estimations of patient PBW are often inaccurate. In ARDS, short people and women tend to get higher tidal volumes and visual estimation of patient height and weight is known to be inaccurate.⁵ Other barriers include under recognition of the onset of ARDS, thus lung protective strategy is not used.⁶

And now, literature published by Lellouche and Lipes in *NEJM*⁷ raises the question of whether all patients receiving mechanical ventilation should receive low tidal volumes 6 cc/kg predicted body weight. The authors conclude that "To recommend prophylactic protective ventilation to all intubated patients may not be justified," only recommending a VT of 6-8 ml/kg PBW in patients with risk factors for the development of lung injury, and simply stating "we recommend the use of VTs below 10 ml/kg PBW from the initiation of mechanical ventilation," concluding that a VT of 8cc may be the best place to start, with optimal PEEP titration an important factor in reducing derecruitment and atelectasis. Perhaps institutions will now re-examine the "one size fits all" notion suggested by the ARMA study. Intra- or post-operative patients with no previous pulmonary history and no factors leading to increased risk of the onset ARDS/ALI might be a good place to look, as is suggested by Lipes and Lellouche. Further investigation seems to be called for.

All this evidence suggests two important lessons in using lung protective strategy. The first is that barriers to proper implementation still exist and are persistent, and the second is that even without these barriers, use of low tidal volume strategy in all patients is still debatable. Solutions to these issues might include more intensive education of physicians and RTs on the research completed on lung protective strategy and low tidal volumes, what patient population should be considered, and when to implement. Use of modern, automated ventilator modes that adapt to the patient's lung mechanics and use a varying tidal volume to reduce to effects of positive pressure⁷ may be useful, especially at institutions that have been slow to adopt low tidal volume strategies or have a low compliance by physicians and staff to implement LPV. Just as importantly, practitioners must use good judgment in examining the patient history and condition, and must use accurate bedside determination of patient PBW.

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- 1 Ventilation with lower tidal volumes as compared with traditional tidal volumes for ALI and ARDS. *N Engl J Med*. *Continued on page 44...*

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A Longitudinal Study of CPAP Therapy for Patients with Chronic Cough and Obstructive Sleep Apnea

Krishna M Sundar; Sarah E Daly; Alika M Willis

Abstract

Background: Chronic cough patients are rendered therapies for gastro-esophageal reflux (GERD), upper airway cough syndrome (UACS) and cough-variant asthma (CVA) with varying benefit. Idiopathic or unexplained cough has emerged as an important clinical entity in both primary care and subspecialty clinics. Recent evidence points to a link between chronic cough and untreated obstructive sleep apnea (OSA).

Methods: A prospective observational study was done to evaluate the effect of OSA therapy in patients with chronic cough. Patients enrolled into the study underwent questionnaires to evaluate for GERD, UACS and CVA along with screening questionnaires for OSA and daytime sleepiness. The Leicester cough questionnaire (LCQ) was done at baseline and during serial visits to evaluate cough intensity and was used as the primary outcome measure of the effect of CPAP therapy on chronic cough.

Results: Out of 37 patients enrolled into the study, only 28 patients had follow up LCQ scores available and therefore underwent analysis. 22/28 patients were suspected to have OSA based on abnormal STOP-BANG screening questionnaire scores and overnight oximetry abnormalities. Of these 19/28 patients had overnight attended polysomnography with definitive diagnosis of OSA yielding a 68% prevalence of OSA in our chronic cough population. Chronic cough patients treated for OSA tended to be older with a significantly higher BMI than chronic cough patients without OSA. Significant improvement of LCQ scores occurred with CPAP therapy for OSA in chronic cough patients.

Conclusion: OSA is significantly prevalent in chronic cough patients. Subjects with chronic cough and OSA tend to be older and obese. Treatment of OSA in chronic cough patients yields significant improvement in their health status.

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Background

Chronic cough is an important health-care problem in both primary care and subspecialty clinics.¹ The 2006 ACCP guidelines emphasize the need to aggressively address the etiologies of gastro-esophageal reflux disease (GERD), upper airway cough syndrome (UACS) and cough-variant asthma (CVA) while treating patients with chronic cough.² Despite undertaking prolonged courses of therapies directed at GERD, UACS and CVA, a significant proportion of patients continue to experience persisting cough.³ The percentage of chronic unrelenting cough termed as “unexplained” or “idiopathic cough” has ranged up to 42% in different studies.⁴

Newer approaches at dissecting the etiology of unexplained cough have focused upon the role of ongoing non-acid reflux,⁵ under-recognized vocal cord dysfunction⁶ and untreated obstructive sleep apnea (OSA)⁷ in perpetuating chronic cough. A large retrospective study from our clinic population during the period 2006-2009 revealed that 44% of the 75 patients with chronic cough had underlying OSA.⁸ More importantly, therapy for comorbid OSA with continuous positive airway pressure (CPAP) resulted in improvement or resolution of cough in 93% of the patients.⁸ While the prevalence of OSA in this large retrospective analysis was felt to be quite high, it was still considered to be an underestimate as all patients were not systematically screened for OSA.⁸ Additionally, while a role for treatment of OSA was implicated in the resolution of cough, all patients received concurrent therapy for GERD, UACS or CVA that may have contributed to the resolution of chronic cough in this study.⁸

The aim of the current study was to prospectively investigate the impact of CPAP therapy on predefined-cough measures in patients with OSA associated chronic cough. Patients referred primarily for chronic cough were evaluated for OSA using validated questionnaires and objective testing for OSA; the effect of CPAP on those diagnosed definitively with comorbid OSA was serially assessed. The primary outcome was the effect of CPAP therapy on the total Leicester cough questionnaire score.

Methods

All consecutive patients with chronic cough seen at Intermountain Utah Valley Pulmonary Clinic, Provo, Utah were given the option to enroll into this study between March 2010-February 2012. Inclusion criteria included the following:

- Cough more than 2 months duration
- Normal spirometry and diffusion capacity <70% of predicted

- Normal chest radiographs and/or CT scans of the chest
- Age >18 years

Exclusion criteria included:

- History of lung disease in the form of prior diagnoses of asthma, COPD, interstitial lung disease or sarcoidosis.
- Chronic disease states such as congestive heart failure, chronic kidney disease, cancer, need for immunosuppressive therapy, or any debilitating illness that prevented follow up.
- Any history of smoking or history of being in occupations that resulted in inhalational exposures.
- Pregnancy.
- Use of opiate containing cough suppressants and/or first-generation antihistaminics.

Based on the above inclusion-exclusion criteria, 37 consecutive patients with chronic cough were enrolled over a 2-year period. A total of 46 patients were found eligible for the study but 9 patients either did not consent for the study, were on cough suppressants that made them ineligible, or turned out to have other diagnoses on follow-up (e.g. one patient had mediastinal adenopathy on chest CT). After enrolment, patients undertook the following questionnaires at baseline and on follow up:

1. Assessments for cough severity using the Leicester cough questionnaire (LCQ). LCQ is a validated, well-studied 19-point questionnaire that assesses the impact of cough severity on multiple aspects of daily living.⁹ Amongst available cough questionnaires, LCQ has been shown to correlate the most with objective cough frequency as assessed by cough monitors.¹⁰ In the current study, subjects underwent LCQ assessments at baseline and during each follow up visit.

2. Screening for OSA was done at baseline visit using the STOP-BANG questionnaire. Amongst available screening tools for OSA, the 8-point STOP-BANG questionnaire has emerged as one of the most easy to use.¹¹ While the sensitivity for a STOP-BANG score of 3 or more for detecting OSA (apnea-hypopnea index (AHI)>5/hour) is 83.6-85.1%, using a STOP-BANG score of 3 or more is not entirely reliable for excluding mild OSA.¹² Workup for further diagnosis of OSA was left up to the treating physician. Further evaluation for OSA was based upon a STOP-BANG score of ≥ 3 along with results of Epworth Sleepiness Score (ESS), and the finding of other symptoms relating to sleep-disordered breathing and daytime dysfunction. Many patients underwent screening oximetry before they were subjected to a polysomnography (PSG) for definitive diagnosis of OSA. Based upon the results of PSG, the OSA severity was categorized based upon the apnea-hypopnea index -AHI. Since the workup for OSA was left up to the treating physician, there was a potential for underestimation of the prevalence of OSA in chronic cough patients since all of these patients were not subjected to the gold-standard for diagnosing OSA-attended PSG. Attended PSG was done at an accredited sleep laboratory (Utah Sleep Disorders Center, Provo, Utah) and studies were performed according to American Academy of Sleep Medicine Criteria. The recording montage included EEG leads C4-M1, C3-M2, Cz-Oz, Cz-Fz, bilateral electrooculogram, chin EMG, electrocardiogram, a microphone for recording snoring, monitors of airflow, chest and abdominal effort recordings, oximetry, and if applied, the level of CPAP mask flow and leak. Sleep stage scoring was performed according to AASM criteria. Apnea was defined as a decrease to $\leq 10\%$ of baseline of thermistor airflow signal and a hypopnea was defined as a 30% or greater decrease in airflow signal

accompanied by a 4% oximetric desaturation or an arousal.

3. Patient-reported assessments of symptoms of GERD, UACS and CVA at baseline. This was done using validated questionnaires for each of these commonly-treated chronic cough etiologies using the GERD,¹³ SNOT-20,¹⁴ and asthma life questionnaires.¹⁵ Each of these questionnaires is used for screening and for following the severity of symptoms of GERD, UACS and asthma over time.¹³⁻¹⁵ Usage of these validated questionnaires was felt to be necessary as clinician-driven assessments of GERD, UACS and CVA in chronic cough patients tend to be subjective with insufficient documentation regarding symptomatology of these problems in chronic cough patients. The GERD questionnaire comprised of 4 questions relating to symptoms of GERD (or their control) with grading of intensity of these symptom intensity from 0-3 (score range 0-12).¹³ The SNOT-20 involved responses to 20 questions with a symptom response score of 0-5 (score range 0-100)¹⁴ and the asthma life questionnaire has 20 questions with a yes or no response (score range 0-20).¹⁵

Following baseline assessments, additional workup and management of OSA was left up to the treating pulmonologist. Since patients were often on therapies for UACS, GERD and CVA at the time of initial evaluation, the need for continuation of these therapies was left up to the treating physician. While it was recommended that newer therapies for GERD, UACS or CVA would not be started unless felt absolutely necessary, in order to ensure patient comfort, treating physicians were allowed to start additional treatments for GERD, CVA and UACS if felt absolutely essential. The use of cough-suppressants such as first-generation antihistaminics and opiates was disallowed due to the possibility that these treatments would confound effects on chronic cough from OSA therapy. Therefore patients receiving these therapies were excluded from the study.

Follow up after initial baseline visit was done at the discretion of the treating physician. Patients non-compliant with CPAP therapy or PSG recommendations were continued until the end of the study if they continued to complete their LCQs during follow up visits. The study and approval for publication without disclosure of identifying data was obtained from the Intermountain Institutional Review Board, Intermountain Healthcare, Salt Lake City, Utah.

Results

Out of a total of 37 patients with chronic cough that were initially enrolled into the study between 2010-2012, 19 patients with chronic cough and objectively verified OSA were followed and showed significant improvement in LCQ scores following CPAP intervention. 9/37 patients enrolled were excluded due to non-compliance with follow up. Out of the 28 patients that completed follow-up LCQ questionnaires, 22 patients reported a STOP-BANG score of 3 or more leading to further evaluations for OSA (Figure 1). In these 22 patients, 13 oximetries were carried out all of which were abnormal. Out of these 22 patients, 3 patients were noncompliant with recommendations for further OSA evaluation but continued to follow-up on therapies for GERD (3/3) and UACS (1/3) (Figure 1). 19/28 patients had objective polysomnographic evidence of OSA. Out of these 19 patients, 2 patients had previously known OSA but were noncompliant with therapy and were optimized on CPAP based on prior polysomnographic data; 17 patients underwent PSGs following enrolment into the study. Of the 17 patients that were studied with PSG following

enrolment into study, the mean AHI was 35.3 ± 29.5 with 6/17 patients being in the mild OSA category (AHI 5-15/hr), 4/17 patients in the moderate OSA category (AHI 15-30/hr) and 7/17 patients being in the severe OSA category (AHI >30/hr).

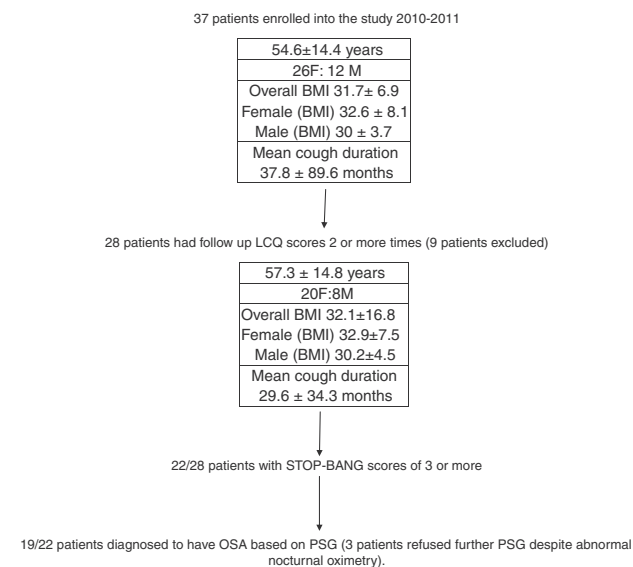


Figure 1. Flowchart detailing enrolment and follow up in the study.

15/19 patients that were treated with CPAP were on proton-pump inhibitors for GERD, 11/19 were on therapy for UACS and 7 were on treatment for CVA (Figure 2a). No ACE-inhibitor use was noted in this population. As reflected in the questionnaires obtained at time of enrolment for this study, mean symptom scores for GERD, UACS and asthma were low for the enrolled chronic cough subjects.

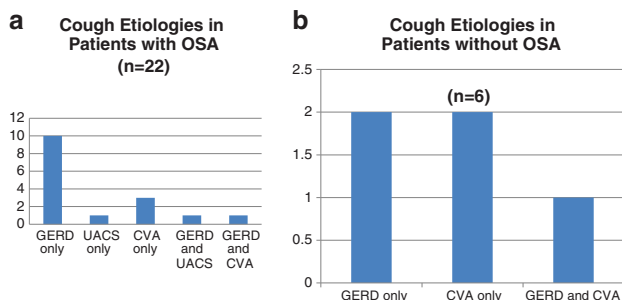


Figure 2. (A & B) Etiologies of cough in patients with OSA and without OSA.

Table 1 details the clinical characteristics of the groups of patients followed in this study. Patients who were treated for OSA with CPAP tended to be older, significantly heavier with higher STOP-BANG OSA screening scores. Although they tended to have longer durations of cough as compared to those diagnosed without OSA, there was no significant difference in durations of cough between patients with and without OSA (Table 1). The six patients that did not undergo further evaluation for OSA based on STOP-BANG scores and clinical evaluation comprised a small comparison group for the group of 19 patients that were treated with CPAP (Table 1). Interestingly, there was no significant difference in the mean scores on the GERD, SNOT-20 and ALQ questionnaires (Table 1) between the OSA and non-OSA groups although there were differences in cough therapies rendered for these two groups (Figure 2b).

Table 2 shows changes in total LCQ scores for the CPAP-treated

group of chronic cough patients with breakdown of LCQ scores into different domains. In patients treated with CPAP, there was a significant improvement in total LCQ scores, and LCQ scores in psychological and social domains (Table 2 & Figure 3).

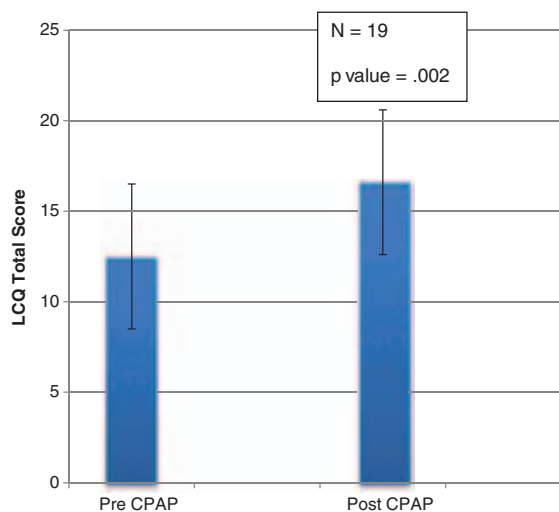


Figure 3. Change in LCQ total score with CPAP therapy.

Discussion

The current emphasis on finding mechanistic bases of cough have led to the recognition that chronic cough is a multi-trigger driven process that is not amenable to a single therapeutic intervention.^{16,17} A disease with a potential to affect a number of processes within the upper and lower airways is OSA.¹⁸ In order to understand the effects from an intervention on chronic cough, studies in the last decade have typically used validated cough questionnaires, cough sensitivity assessments or objective cough monitoring to assess cough serially.¹⁹ Amongst these, serial LCQ measurement of total and individual domain scores in chronic cough subjects is the most-validated and widely utilized instrument to assess effects from an intervention¹⁹ and a change in LCQ score(s) was used to assess the effect of CPAP therapy in chronic cough patients with co-morbid OSA.

Based on the results of the STOP-BANG screening questionnaire and the more definitive gold standard of attended PSG, this study shows a high prevalence of obstructive sleep apnea in chronic cough patients. Reasons for the high prevalence of OSA noted in this study are manifold. OSA is a commonly encountered disorder that has reached epidemic proportions.²⁰ Screening questionnaires while useful in directing the need for further testing, however, are not 100% sensitive for detecting milder forms of disease. Therefore, while these questionnaires are useful for elaborating the need for further evaluation for sleep-disordered breathing, in themselves their results have to be used in conjunction with other diagnostic modalities for OSA.¹² In our study, while we used a cut-off of a score of 3 or more on the STOP-BANG score as a way of directing need for further testing of OSA, not all physicians used this solely for ordering further polysomnographic testing. Increasing STOP-BANG scores are correlated with higher likelihood for OSA and all patients with scores of 5 or more were tested for OSA and all these patients were found to have significant OSA on PSG. 1/19 patients in the OSA group had STOP-BANG scores of less than 3 and 2/6 patients in the non-OSA group had STOP-BANG scores of 3-4. There was also wide variation in the ESS scores in OSA vs. non-OSA groups although OSA patients had a significantly increased ESS than the non-OSA group (Table 1).

Table 1. Results of baseline questionnaires between CPAP-treated and non-treated groups.

	Patients treated with CPAP (n=19)	Patients treated without CPAP (n=6)	P value
Age (years)	58.7±15.1	44.7±13	0.05
Sex ratio	13 F:6 M	5 F:1 M	NA
BMI	34.9±6.7	26.5±4	0.002
Cough duration (months)	33.8±38.1	15.5±12.2	0.08
SNOT-20 score	8.8±4.2	5.5±3.1	0.8
GERD score	1.8±1.3	1±1.3	0.2
Asthma life questionnaire	38.8±20.5	36.3±19.3	0.07
STOP-BANG score	4.3±1.7	1.5±2.7	0.009
0-2	1/19	4/6	
3-5	14/19	2/6	
5-8	4/19	0/6	
Epworth Sleepiness score	11.25±4.2	4±4.8	0.01

Abbreviations: CPAP Continuous positive airway pressure, BMI Body mass index, SNOT Sino-nasal outcome test, GERD Gastroesophageal reflux disease.

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The gold standard for OSA diagnosis remains the attended PSG. In our study 22/28 patients were felt to have a high likelihood of OSA based the combination of abnormal STOP-BANG scores and overnight oximetry yielding an OSA prevalence of 78% in chronic cough patients. Based on definitive PSGs, 19/28 patients had OSA yielding a prevalence of 68% OSA in this chronic cough population. This high prevalence of OSA in our chronic cough population may have been from higher BMIs of the patient population in this study.⁸ This finding of increased BMIs in our population contrasts with the average BMI reported by recent studies on chronic cough from Europe.^{5,21} Aside from a significant difference in BMIs in OSA and non-OSA groups, there was also a trend towards a lower age in chronic cough patients without OSA. Chronic cough patients without OSA tended to be younger with a higher female preponderance. These findings are in congruence with the results of studies that have shown a correlation between OSA prevalence and age,²² OSA and BMI.²³

A number of questionnaires were administered in this study that assessed symptom intensity scores for commonly encountered entities of GERD, UACS and CVA. While the scores from these questionnaires do not accurately assess the severity of the individual disorders of GERD, UACS and CVA, this was undertaken in order to compare the OSA and non-OSA groups in terms of the prevalence for symptoms of these three commonly encountered disorders. While the therapies for GERD, UACS and to some extent even CVA is somewhat empiric in most chronic cough patients, a greater problem lies in the lack of documentation of symptoms pertaining to these three conditions in a consistent manner by physicians. Therefore instead of trying to decipher underlying cough etiologies based upon treatments rendered and clinic records, we decided to use these validated questionnaires to develop scores for GERD, UACS and CVA. This approach to categorize and evaluate these three conditions in diagnostic and testing protocols has been used to direct comprehensive therapy for chronic cough patients^{24,25} although given the high prevalence of these conditions in the general population, their relation to patient's cough is unclear.²⁶ In this

Table 2. Leicester cough questionnaire scores change in CPAP-treated chronic cough patients.

LCQ domains	CPAP treated patients (n=19)		
	Baseline	Final	P value
Physical	4.6±1.2	5.2±1.1	0.086
Psychologic	4.1±1.4	5.3±1.2	0.005
Social	3.8±1.7	5.5±1.6	0.003
LCQ Total	12.5±4	16.6±3.9	0.002
Duration of follow up (days)	157.3±108.5		

Abbreviations: CPAP Continuous positive airway pressure, LCQ Leicester cough questionnaire.

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study as well, there appeared to be a preponderance of therapies rendered for GERD as well as therapies for multiple etiologies for cough as was noted in our retrospective study.⁸ Even though patients with chronic cough and OSA tended to be older and significantly heavier, there was no difference in patient reported scores for UACS, GERD and CVA between OSA and non-OSA subjects.

In the subjects treated with CPAP, there was a significant improvement in LCQ scores in chronic cough subjects with OSA. This occurred in both the total LCQ scores and the individual psychological and social domains. This supports prior observations that CPAP therapy for comorbid OSA improves cough outcomes in this population.⁸ LCQ change is an established method for measuring efficacy of interventions on cough²⁷⁻²⁹ and not all studies have included a placebo arm while assessing efficacy of an intervention on LCQ improvement.³⁰ In these chronic cough studies, the mean LCQ change with intervention have ranged from 2.1-3.5 and with placebo 1.1-2.6.²⁷⁻²⁹ One of the problems with our study was that even though a significant change was not expected in the LCQ score of those patients that were not treated with CPAP for OSA, the three non-compliant patients in the study also showed an increase in LCQ scores. This underscores the need for studying the effect of CPAP on cough intensity in chronic cough patients using a placebo arm.

Recently the observation that CPAP therapy can improve cough in patients with concomitant OSA has been reported by others.^{31,32} In one case report, an improvement in Ryan score (a measure of pharyngeal pH done through a transnasal probe) occurred following CPAP therapy accompanied by improvement in cough intensity and sensitivity.³¹ Further studies need to not only clarify cough populations that improve following CPAP therapy but also the mechanistic bases of cough improvement after CPAP therapy. Studies using a placebo arm (sham CPAP controls) are needed to understand fully the benefit accorded by CPAP therapy on cough intensity and sensitivity in patients with chronic cough.

Conclusion

There is a high prevalence of OSA in patients with chronic cough. Patients with chronic cough and OSA tend to be older and significantly heavier. Significant improvement in health status following CPAP therapy occurs in chronic cough patients with OSA. Further studies trying to demonstrate a role for CPAP therapy should include a placebo arm (or sham CPAP) for conclusively establishing a benefit of CPAP therapy on chronic cough. The mechanisms for cough improvement from CPAP

therapy can multiple and future studies should also attempt to understand the pathways involved in cough improvement with CPAP therapy.

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ASV...continued from page 31

and they meet all of your other criteria for extubation, go ahead and extubate. Decrease the %MinVol knob if the patient appears to "riding the vent". This will challenge them to initiate their own breathing. You might also decrease the knob if the pressure support is still a little too high to meet your extubation criteria.

7. Are there any other parameters I can manipulate to control ASV?

You manually control oxygenation via the FIO2 and PEEP settings and you can limit the maximum pressure limit that ASV can use. Note, outside the US, depending on the country, 'INTELLiVENT-ASV' which provides fully closed loop control of ventilation and oxygenation is available.

8. Are there any disease processes that ASV should not be used on?

ASV is intended for adult and pediatric patients greater than 3kg. There is no "one size fits all" mode of ventilation and that includes ASV. Although ASV can be used on many patients and disease processes it might not be the best choice if there are significant leaks, 'neruogenic'/unstable breathing patterns or in patients with very high inspiratory drives that cannot be controlled with sedation and/or paralytics are not indicated.

General Practice Variation in Spirometry Testing in Obstructive Lung Disease: a Population-Based Study

Mette M Koefoed; Jens Søndergaard; René dePont Christensen; Dorte E Jarbøl

Abstract

Background: Spirometry testing is essential to confirm an obstructive lung disease, but studies have reported that a large proportion of patients diagnosed with COPD or asthma have no history of spirometry testing. Also, it has been shown that many patients are prescribed medication for obstructive lung disease without a relevant diagnosis or spirometry test registered. General practice characteristics have been reported to influence diagnosis and management of several chronic diseases. However, these findings are inconsistent, and it is uncertain whether practice characteristics influence spirometry testing among patients receiving medication for obstructive lung disease. The aim of this study was therefore to examine if practice characteristics are associated with spirometry testing among patients receiving first-time prescriptions for medication targeting obstructive lung disease.

Methods: A national register-based cohort study was performed. All patients over 18 years receiving first-time prescriptions for medication targeting obstructive lung disease in 2008 were identified and detailed patient-specific data on sociodemographic status and spirometry tests were extracted. Information on practice characteristics like number of doctors, number of patients per doctor, training practice status, as well as age and gender of the general practitioners was linked to each medication user.

Results: Partnership practices had a higher odds ratio (OR) of performing spirometry compared with single-handed practices (OR 1.24, CI 1.09-1.40). We found a significant association between increasing general practitioner age and decreasing spirometry testing. This tendency was most pronounced among partnership practices, where doctors over 65 years had the lowest odds of spirometry testing (OR 0.25, CI 0.10-0.61). Training practice status was significantly associated with spirometry testing among single-handed practices (OR 1.40, CI 1.10-1.79).

Conclusion: Some of the variation in spirometry testing among patients receiving first-time prescriptions for medication

targeting obstructive lung disease was associated with practice characteristics. This variation in performance may indicate a potential for quality improvement.

Background

Spirometry is recommended for diagnosis and management of obstructive lung diseases like asthma and chronic obstructive pulmonary disease (COPD).¹⁻³ Spirometry testing is not only essential to confirm a diagnosis of obstructive lung disease, it also enables the general practitioner (GP) to rule out airway obstruction in patients with respiratory symptoms caused by other illnesses, such as heart failure or lung cancer.

Despite international guidelines recommendations, we confirmed that a large proportion of patients prescribed medication targeting obstructive lung diseases do not undergo spirometry testing⁴. Hence, these patients may be medicated without having airway obstruction and exposed to unnecessary economic costs and medication risks.^{5,6} More important, when spirometry is not performed, patients may experience an unnecessary delay in the diagnostic process. In Denmark, the majority of patients with respiratory symptoms are diagnosed and managed in general practice. Spirometry has been shown to be both feasible and reliable in general practice,⁷ but if preferred, GPs can also refer patients to spirometry testing at hospitals or outpatient clinics. Underutilisation of spirometry when diagnosing obstructive lung disease is well known.⁸⁻¹¹ Patient characteristics like age and gender have been shown to influence spirometry testing^{4,11,12} and accuracy of diagnosis.¹³ Also, some doctor and practice characteristics have been shown to influence spirometry testing; unfamiliarity with conducting or interpreting spirometry tests and spirometry being too time-consuming are reported as barriers,¹⁴⁻¹⁷ and practice characteristics like presence of a practice nurse and use of protocols have been reported to enhance spirometry testing.¹⁵ Rural differences in spirometry testing have also been reported.¹⁸

Studies have reported practice characteristics such as practice size, organisation in partnership or single-handed practices and having training practice status to influence diagnosis and management of other illnesses.¹⁹⁻²¹ Doctor characteristics like age and gender have also been associated with different practice patterns.^{22,23} However, we have not found studies assessing these factors association with spirometry testing. Identifying practice characteristics may have important implications for future organisation of primary care services²⁴ and can help target interventions aiming to improve spirometry testing. The aim of

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Table 1. Distribution of practice characteristics within the entire general practice cohort in absolute numbers (N); the mean and standard deviation of the variable “spirometry proportion” is reported for each practice characteristic.

		All general practices		Single-handed practices		Partnership practices		
		N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	
Partnership practice	Yes	773	54.4 (16.8)	-	-	773	54.4 (16.8)	
	No	1207	48.6 (22.7)	1207	48.6 (22.7)	-	-	
Training practice	Yes	566	53.7 (18.0)	239	53.8 (20.2)	327	53.7 (16.1)	
	No	1414	49.7 (21.8)	968	47.3 (23.2)	446	54.8 (17.3)	
No of doctors	1	1207	48.6 (22.8)	1207	48.6 (22.8)	-	-	
	2	388	54.2 (18.7)	-	-	388	54.2 (18.7)	
	3	213	53.4 (15.6)	-	-	213	53.4 (15.6)	
	4	94	57.2 (13.2)	-	-	94	57.2 (13.2)	
	5	52	54.5 (14.2)	-	-	52	54.5 (14.2)	
	>5	23	55.0 (11.3)	-	-	23	55.0 (11.3)	
Age								
(mean for partnership practices)		<45	106	56.0 (19.1)	67	52.2 (18.8)	39	62.5 (18.1)
		45–49	238	55.8 (18.1)	122	54.5 (20.0)	116	57.2 (15.8)
		50–54	516	54.2 (18.8)	228	52.4 (21.4)	288	55.7 (16.3)
		55–59	609	49.7 (20.9)	366	48.3 (23.3)	243	51.7 (16.4)
		60–64	390	46.4 (22.4)	314	45.9 (23.3)	76	50.4 (17.8)
		>65	121	41.2 (23.9)	110	40.7 (24.3)	11	46.6 (-)
Gender	Male	1017	49.4 (22.1)	873	48.7 (22.7)	144	53.4 (17.5)	
	Predominantly male	189	54.4 (15.0)	-	-	189	54.4 (15.0)	
	Equal male/female	283	54.9 (18.6)	-	-	283	54.9 (18.6)	
	Predominantly female	98	54.3 (13.6)	-	-	98	54.3 (13.6)	
Female	393	49.2 (22.3)	334	48.3 (23.0)	59	54.0 (17.1)		
Patients per doctor	<1347	513	49.8 (22.8)	227	43.9 (21.8)	286	54.4 (18.2)	
	1347–1575	489	51.0 (19.8)	277	49.1 (21.8)	212	53.5 (16.4)	
	1576–1756	489	52.3 (20.8)	307	49.9 (23.4)	182	56.5 (14.6)	
	>1756	489	50.3 (19.7)	396	49.9 (20.3)	93	51.9 (17.0)	

*The “spirometry proportion” is defined as the proportion of adult patients within the practice receiving first-time prescriptions for medication targeting obstructive lung disease who had spirometry performed in the 18-month interval.

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this study was therefore to examine if variation in spirometry testing among patients receiving first-time prescriptions for medication targeting obstructive lung disease is associated with specific practice characteristics.

Methods

A register-based cohort study covering the entire population of 5.5 million people and all general practices in Denmark (approx. 2400) was carried out. More than 98% of the population in Denmark is registered with a general practitioner, who provides primary care services, acts as a gatekeeper and refers patients to specialist care when needed. The healthcare system in Denmark is tax funded and patients have free access to all services related to general practice and hospital care, including spirometry.²⁵ All general practices have direct access to spirometry testing; either in their practice where the doctors can conduct these tests themselves or have practice staff conduct spirometry testing or the doctors can refer patients to spirometry testing at hospitals or outpatient clinics. From an earlier study we know that the majority of spirometry tests conducted among new medication users were performed in general practice.⁴

All Danish citizens are registered in the Danish Civil Registration System and assigned a unique personal identification number. Likewise, each general practice is also assigned a unique identification number and these identification numbers are used in all national registers, enabling accurate linkage between patients, healthcare services and general practice.²⁶

This study links several national registers all maintained in Statistics Denmark, where researchers can apply for access.

Study subjects

Patients were identified in the National Prescription Register. We identified all adults who were first-time users of medication targeting obstructive lung disease in 2008. Firstly, all patients who redeemed medication targeting obstructive lung disease, defined as the anatomical therapeutic chemical (ATC) code R03 in 2008, were identified. We then excluded patients who were either under 18 years of age on 1 January 2008 or who had previous records of prescriptions with ATC code R03 in the register (1995-2007). All medication with ATC code R03 requires a prescription and registration is therefore complete. For each patient we identified whether they had redeemed R03

Table 2. Association between practice characteristics and spirometry testing among all practices.

	Model 1	Model 2**
	Crude OR	Adjusted OR
	(95% CI)	(95% CI)
Training practice		
No	1	1
Yes	1.20 (1.06–1.36)*	1.10 (0.97–1.25)
Single-handed practice		
Yes	1	1
No	1.34 (1.16–1.55)*	1.24 (1.09–1.40)*
Mean age of doctors (years)		
≤ 45	1	1
45–49	0.94 (0.74–1.19)	0.87 (0.66–1.14)
50–54	0.88 (0.70–1.09)	0.78 (0.60–1.00)
55–59	0.68 (0.53–0.87)*	0.58 (0.44–0.76)*
60–64	0.58 (0.43–0.79)*	0.52 (0.39–0.70)*
≥65	0.41 (0.27–0.64)*	0.33 (0.22–0.50)*

*P-value < 0.05 **Adjusted for patient factors and practice characteristics.

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medication repeatedly within the first year and how many types of R03 medication they initiated within this first year. These two variables, “redeemed repeatedly” and “number of therapies,” were used as proxies for severity. Additionally, for each patient we retrieved 2008 data on socioeconomic and demographic status such as age, gender, income, highest attained education, labour market affiliation and cohabitation status.

Outcome – spirometry within the first year when initiating medication

All spirometry measurements registered in the time period 2007–2009 were extracted from the National Health Service Register, which covers primary care, and from the National Patient Register, which covers hospitals and outpatient clinics. These registers are administrative databases used for reimbursement and a prerequisite for reimbursement is that all services conducted, including spirometry testing, must be recorded in these registers. For each patient we assessed if spirometry was registered in an 18-month period counting from 6 months before to 12 months after the date of the first redemption of obstructive lung medication. All spirometric procedures were included, irrespective of whether they were performed in general practice, in an outpatient clinic, or in a hospital. The results from the spirometry tests were not available in the register.

General practice

All data on general practice were extracted from the Danish National Health Service Provider Register. We extracted data covering the period July 2007–December 2009, corresponding to the absolute observation time of the cohort. A total of 428 practices were omitted due to missing data at the beginning or end of the time period, indicating that these practices were established or closed in this time period. A further 11 practices were omitted due to a small list size (<500 patients), because these practices are probably atypical and are not representative of general practice. For each general practice we identified the number of established doctors registered at each practice. Doctors not registered in the entire period were defined temporary doctors and were not considered to be in the

Table 3. Association between practice characteristics and spirometry testing in partnership practices.

	Model 1	Model 2**
	Crude OR	Adjusted OR
	(95% CI)	(95% CI)
Training practice		
No	1	1
Yes	0.95 (0.84–1.08)	0.91 (0.79–1.04)
Mean age of doctors (years)		
≤ 45	1	1
45–49	0.72 (0.50–1.03)	0.66 (0.45–0.97)*
50–54	0.68 (0.47–0.98)*	0.61 (0.42–0.89)*
55–59	0.54 (0.34–0.86)*	0.45 (0.29–0.71)*
60–64	0.52 (0.31–0.86)*	0.43 (0.26–0.72)*
≥65	0.39 (0.17–0.90)*	0.25 (0.10–0.61)*
Number of doctors		
2	1	1
3	0.97 (0.84–1.13)	0.99 (0.77–1.27)
4	1.17 (0.95–1.45)	1.15 (0.90–1.45)
5	1.03 (0.82–1.30)	1.08 (0.77–1.51)
>5	1.05 (0.76–1.37)	1.03 (0.69–1.53)
Number of patients per doctor		
<1347	1	1
1347–1575	0.96 (0.82–1.12)	0.97 (0.82–1.15)
1576–1756	1.12 (0.94–1.34)	1.16 (0.96–1.34)
>1756	0.86 (0.69–1.07)	0.88 (0.70–1.11)
Gender of doctors		
Male	1	1
Predominantly male	1.05 (0.87–1.27)	0.99 (0.77–1.27)
Equal male/female	1.07 (0.89–1.29)	1.04 (0.85–1.28)
Predominantly female	1.05 (0.84–1.32)	0.94 (0.73–1.26)
Female	1.07 (0.81–1.42)	1.04 (0.76–1.42)

*P-value < 0.05 **Adjusted for patient factors and practice characteristics.

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established doctor group. Practices were defined single-handed practices if only one established doctor was registered, and partnership practices if two or more established doctors were registered. The majority of the temporary doctors in general practice were junior doctors having six months’ residency in practice, and practices with these doctors listed in the time period were defined training practices. The number of patients per doctor was defined as the practice’s patient list size divided by the number of established doctors. In single-handed practices the doctor’s age and gender were extracted, in partnership practices we calculated the mean age of the established doctor group and assessed whether their gender was exclusively male or female, predominantly male or female or equally mixed. For each practice we calculated a “spirometry proportion” defined as the proportion of adult patients within the practice receiving first-time prescriptions for medication targeting obstructive lung disease who had spirometry performed in the 18-month interval.

Statistical analysis

Practice characteristics are reported as categorical variables. For each practice characteristic we report the mean and standard deviation of the “spirometry proportion.”

Table 4. Association between practice characteristics and spirometry testing in single-handed practices.

	Model 1	Model 2**
	Crude OR	Adjusted OR
	(95% CI)	(95% CI)
Training practice		
No	1	1
Yes	1.40 (1.06–1.87)*	1.40 (1.10–1.79)*
Age of doctor (years)		
≤ 45	1	1
45–49	1.11 (0.78–1.58)	1.09 (0.73–1.61)
50–54	0.99 (0.78–1.58)	0.96 (0.67–1.38)
55–59	0.79 (0.73–1.35)	0.71 (0.49–1.03)
60–64	0.69 (0.56–1.10)	0.64 (0.43–0.95)*
≥65	0.50 (0.28–0.89)*	0.44 (0.28–0.76)*
Number of patients		
<1347	1	1
1347–1575	1.29 (0.97–1.71)	1.26 (0.95–1.67)
1576–1756	1.30 (0.99–1.72)	1.21 (0.92–1.59)
>1756	1.35 (1.02–1.79)*	1.17 (0.90–1.51)
Gender of doctor		
Male	1	1
Female	0.98 (0.84–1.15)	0.93 (0.77–1.12)

*P-value < 0.05 **Adjusted for patient factors and practice characteristics.

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We used mixed effects logistic regression models with patients nested within practice to calculate odds ratios (ORs) with 95% confidence intervals (CI) for the associations between practice characteristics and having spirometry performed. We used two models. Model one estimated the crude OR for each practice characteristic's association with spirometry testing, model two estimated the OR for each practice characteristic, adjusted for both patient characteristics and the other practice characteristics included in the analysis. Our primary analysis was model 2. Analyses comprised the entire cohort of general practices and were subsequently stratified into single-handed and partnership practices. This stratification was done for two reasons: firstly, we hypothesised that this important organisational factor could interact with other practice characteristics, and secondly, some of the variables like age and gender were average values in partnership practices, but precise values in single-handed practices, and separate analyses were needed. Patient characteristics adjusted for were age, gender, income, highest attained education, labour market affiliation, cohabitation status, number of therapies initiated in the first years and repeat prescription redemption. P-values < 0.05 were considered statistically significant associations. Finally, we conducted subgroup analyses of the association between practice characteristics and spirometry testing among two different subgroups of patients: 1) patients over 45 years of age initiating at least two types of medication and redeeming medication repeatedly; and 2) patients less than 45 years of age initiating only one type of medication. This was done to assess if the associations shown among practice characteristics in the overall group of patients receiving first-time prescription for medication targeting obstructive lung disease were also present in: 1) a subgroup of patients where COPD is more common; and 2) among younger patients with mono therapy. We also repeated

all analyses including peak flow measurements conducted in the time period as peak flow measurements might have been used in asthma patients and this might influence some of associations seen.

All statistical analyses were carried out using STATA 11 (STATA Corp, College Station, TX, USA.)

Ethics

This project is register-based and according to “The Act on Research Ethics Review of Health Research Projects in Denmark” only questionnaire surveys and medical database research projects involving human biological material are required to be notified to the research ethics committee. The research ethics committee has, therefore, not been contacted. The study was approved by the Danish Data Protection Agency, J.nr. 2011-41-5798.

Results

A total of 1,980 practices and 35,677 patients were included in our analysis. Just about half of the patients had spirometry performed in the time period corresponding to 51.2% (18,263/35,677). Among general practices, the mean “spirometry proportion” was 50.8%. The distribution of the “spirometry proportion” among general practice is illustrated in Figure 1 and it demonstrates quite a large variation between practices. An overview of practice characteristics and their mean “spirometry proportion” is shown in Table 1.

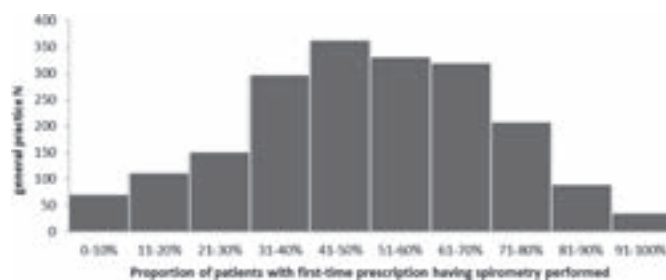


Figure 1. Distribution of the spirometry proportion among general practice in total numbers (N=1980).

When comparing all general practices, partnership practices had a higher OR of performing spirometry compared with single-handed practices (OR 1.24, CI 1.09-1.40), Table 2. In all analyses we saw that increasing age among the group of established doctors decreased the odds of spirometry testing; in the analysis comparing all practices, the smallest OR was seen among doctors over 65 years (OR 0.33, CI 0.22-0.50). The most pronounced effect of doctors' increasing age on spirometry was seen among partnership practices (OR 0.25, CI 0.10-0.61), Table 3. A test for trend showed a significant association between increasing GP age and decreasing spirometry testing. Being a training practice was significantly associated with spirometry testing among single-handed practices (OR 1.40, CI 1.10-1.79), Table 4. There was no significant association between the doctors' gender or number of patients per doctor and having spirometry performed. Further, there was no significant association between number of doctors in a partnership practice and having spirometry performed. Both subgroup analyses demonstrated the same tendency in associations: an increased OR for spirometry testing was seen among partnership practices, practices with younger doctors and among single-handed practices with training practice status (data not shown). These associations were, however, only statistically significant

among patients over 45 years of age initiating at least two types of medication and redeeming medication repeatedly. Adding peak flow measurements to the analyses did not influence the associations significantly.

Discussion

Main findings: This study demonstrated that patients receiving first-time prescriptions for medication targeting obstructive lung disease had higher odds of having spirometry performed if their general practice was a partnership practice. All analysis confirmed decreasing spirometry testing with increasing age of doctors. Among single-handed practices, training practice status was associated with increased spirometry testing. These associations all had an OR above 1.23 or below 0.67 and were considered relevant associations.

Strengths and limitations of this study: The register-based design has the major strength that it allows us to include the entire population and all established general practices in Denmark. The validity of the data in these national registries is considered high, as they are based on administrative data used for reimbursement in the healthcare system²⁷. Due to this economic incentive, spirometry recording is quite complete, although a slight under- or over-recording cannot be entirely excluded. The low rate of spirometry testing is therefore mainly due to non-use and not to inconsistent recording. The registers do not, however, contain data on how the spirometry was conducted, and we cannot exclude some variation in the quality of these measurements.

The registries enable accurate linkage of detailed information on each practice and patient and make it possible to adjust for numerous patient factors, enhancing the possibility of isolating and assessing practice characteristics' influence on spirometry testing in our cohort. Nonetheless, it is important to remember that influence of patient characteristics cannot be entirely excluded; the registers cannot provide complete information on all sociodemographic patient characteristics.

Another challenge was that patient data could only be linked on the level of general practice, preventing us from identifying the doctor within the practice who is primarily responsible for each patient. This complicates the assessment of the influence of doctors' age and gender on spirometry testing when dealing with partnership practices. Mean age of established doctors is a compromise and is not as informative as an individual doctor's age. Also, "patients per doctor", a proxy for workload, may be inaccurate, as doctors in Denmark can schedule their own work. General practitioners with few listed patients may work part-time and still have a high workload in practice.

Newly established and closing practices were excluded in these analyses, and it is important to remember that our data underrepresent these practices, but this was done deliberately. Firstly, forming and closing practices were quite unstable in the time period with regard to both number of doctors and number of patients, making categorisation quite difficult, and secondly, we hypothesised that forming and closing practices could confound our results in favour of larger practices.

Other potential influential variables could have been interesting to include in our study if they were available in our databases. The presence of a practice nurse and the practice's location (rural or urban area, distance to outpatient clinics) could

influence spirometry testing and were very relevant to include in our study. However, the registers contain no data on employed staff in general practice, and the limited data on practice location were not adequate for assessing either rural or urban location or distance to relevant outpatient clinics.

Interpretation of findings in relation to previously published work:

Two studies tested if quality of care scores in asthma patients were influenced by practice size, but found no association.^{28,29} Other studies have found single-handed practices and small practice size to be associated with increased acute admission rates to hospitals for asthma, but not for COPD.^{30,31} Our measure for practice size was divided into two variables: number of doctors and number of patients per doctor. When looking solely at the number of doctors, we found that single-handed practices had lower odds of performing spirometry compared to partnership practices in concordance with the above mentioned studies. Among partnership practices, however, there was no association between number of doctors and odds of spirometry testing, indicating that size of partnership practices was not associated with spirometry testing. Further, we found no association between number of patients per doctor and spirometry testing. Although partnership practices and larger practices have been associated with higher scores for quality of care in several chronic diseases,^{19,20} studies are not consistent with regard to this issue, as the opposite has also been shown,³² and it is interesting that patient satisfaction has been reported to be in favour of single-handed practices.^{33,34}

Increasing age among doctors has been reported to be associated with decreasing quality of care scores in studies^{35,36} and these findings are in concordance with our study, where we found a clear tendency between increasing age and decreasing OR for spirometry testing. Our study does not clarify why older doctors perform fewer spirometry tests in patients initiating medication, but general practitioners' age has been shown to influence clinical practice patterns, with older GPs providing more home visits, doing fewer procedures and having higher prescribing rates.²² We found no association between GP gender and spirometry testing. Other studies have reported that when assessing quality scores, female physicians are more often among high scorers and the majority of the lowest scoring physicians are men.^{35,37} Specifically, female GPs have been reported to attain higher scores in evaluation of antenatal care and more often refer to bone mineral density testing.^{23,38} We therefore hypothesised that female GPs performed more tests as shown by Ioannidis et al.,²³ but our data showed no indication of this pattern.

Training practices have also been shown to influence quality of care^{19,35} and in our study we also saw this tendency, but only among single-handed practices. Why training practice status influences single-handed practices, but not partnership practices, is unknown, but we suggest that this difference in effect is due to a greater interaction between the single-handed practitioner and the resident doctor compared to the interaction seen in a partnership practice with several doctors.

Overall, we conclude that the variation in spirometry testing between practices was quite large and some of this variation can be associated with practice characteristics. Concluding whether the variation shown in spirometry testing is due to a variation in quality of care is more challenging. Although spirometry is essential for diagnosing obstructive lung disease and could

therefore be used as a marker of good quality, it may not be relevant for all patients receiving first-time prescriptions for medication targeting obstructive lung disease to have spirometry performed. Among some patients it may be clinically meaningful not to conduct spirometry testing, for example among patients who are unable to cooperate sufficiently. However, the variations shown could indicate a potential room for quality improvement and further studies should be conducted to clarify this issue. Also, assessing changes in spirometry testing over time in general practice would be relevant, as improvements have been seen in outpatient clinics in recent years.³⁹

Conclusions

Some of the variations in the frequency of spirometry testing are associated with practice characteristics. Young age among doctors, being a partnership practice, or if a single-handed practice, being a training practice, were all factors associated with increased odds of performing spirometry when patients receive first-time prescriptions for medication targeting obstructive lung disease.

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to place a tracheal tube for airway protection. This discussion was occurring but was not settled when I left Renown but my observations were this; when PiP started to exceed 18-20 cmH₂O and the infant needed a backup rate greater than 30 or was riding that rate, there tended to be other issues going on such as sepsis or fatigue. When PiPs exceeded 18-20 it was difficult to control oral leaks and with the infant requiring rates higher than 30 what was the calorie expenditure vs. work of breathing. Should infants be fed while on NIV? Should infants be held or "kangarooed" while on NIV? What frequency should lab work or cxr's be with NIV? Should it be more or less than with invasive ventilation? What criteria should be used and what thresholds established to define failure/fatigue on NIV?

Paying careful attention to these and other questions will go a long way in helping to develop an effective NIV strategy in the NICU.

Low tidal volume...continued from page 32

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Predictors of cardiovascular disease in asthma and chronic obstructive pulmonary disease

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Abstract

Background: Cardiovascular disease (CVD) is a common comorbidity in patients with chronic airway obstruction, and is associated with systemic inflammation and airway obstruction. The aim of this study was to evaluate the predictors of CVD in two different conditions causing chronic airway obstruction, asthma and COPD.

Methods: Lung function tests, clinical and echocardiographic data were assessed in 229 consecutive patients, 100 with asthma and 129 with COPD. CVD was classified into: pressure overload (PO) and volume overload (VO). Sub-analysis of patients with ischemic heart disease (IHD) and pulmonary hypertension (PH) was also performed.

Results: CVD was found in 185 patients (81%: 51% COPD and 30% asthmatics) and consisted of PO in 42% and of VO in 38% patients. COPD patients, as compared to asthmatics, had older age, more severe airway obstruction, higher prevalence of males, of smokers, and of CVD (91% vs 68%), either PO (46% vs 38%) or VO (45% vs 30%). CVD was associated with older age and more severe airway obstruction both in asthma and COPD. In the overall patients the predictive factors of CVD were age, COPD, and male sex; those of PO were COPD, BMI, VC, FEV1 and MEF50 and those of VO were age, VC and MEF50. In asthma, the predictors of CVD were VC, FEV1, FEV1/VC%, and PaO₂, those of PO were VC, FEV1 and FEV1/VC%, while for VO there was no predictor. In COPD the predictors of CVD were age, GOLD class and sex, those of VO age, VC and MEF50, and that of PO was BMI. Sub-analysis showed that IHD was predicted by COPD, age, BMI and FEV1, while PH (found only in 25 COPD patients), was predicted by VO (present in 80% of the patients) and FEV1. In subjects aged 65 years or more the prevalence of CVD, PO and VO was similar in asthmatic and COPD patients, but COPD patients had higher prevalence of males, smokers, IHD, PH, lower FEV1 and higher CRP.

Conclusions: The results of this study indicate that cardiovascular diseases are frequent in patients with chronic obstructive disorders, particularly in COPD patients. The strongest predictors of CVD are age and airway obstruction.

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COPD patients have higher prevalence of ischemic heart disease and pulmonary hypertension. In the elderly the prevalence of PO and VO in asthma and COPD patients is similar.

Background

Asthma and chronic obstructive pulmonary disease (COPD) are the most common airway disorders with a high morbidity and mortality.^{1,2} According to the Global Initiative for Asthma (GINA), approximately 300 million people suffer from asthma¹ with a prevalence ranging from 1 to 18%. COPD prevalence is around 6%, but data are highly variable, depending on survey methods and diagnostic criteria.³

Both asthma and COPD are characterized by inflammation, which in asthma, particularly the eosinophilic phenotype, is predominantly confined to the airway, while in COPD the inflammation may spill-over from the lungs to the systemic circulation and initiate systemic inflammation, as a consequence of exposure to indoor or outdoor air pollution, cigarette smoke, or diesel exhaust fumes.⁴ A recent observation indicates that patients with neutrophilic asthma often have systemic inflammation.⁵ Elevated serum levels of reactive C-reactive protein (CRP) are considered markers of systemic inflammation either in COPD or in asthma^{5,6}. Systemic inflammation may be pathogenically related to many of the comorbidities seen in chronic obstructive airway diseases, including cardiovascular disease (CVD). Cardiovascular complications in COPD have been attributed to the systemic effects of smoking.⁷ Several observations suggest that reduced pulmonary function, no matter what cause, is associated with increases in myocardial infarction and arrhythmia.⁸⁻¹¹ Forced expiratory volume in one second (FEV1) is ranked second to smoking and above blood pressure and cholesterol as a predictor of all-cause and cardiovascular mortality.¹² In this regard, it has been suggested that a reduction in FEV1 combined with smoking history better predicts cardiovascular mortality than cholesterol.¹³

The aim of this study was to evaluate prevalence and predictors of CVD in two common airway obstructive diseases with quite different phenotypes, asthma and COPD.

Methods

Consecutive adult outpatients with asthma and COPD, diagnosed according to international guidelines,^{1,2} were recruited from those attending the Respiratory Pathophysiology clinic of the University Hospital San Giovanni, Turin, Italy, between January 2011 and June 2012. Inclusion criteria were: age over 40 years, no

acute exacerbation of COPD and asthma in the last two months, no active pulmonary tuberculosis or other clinically relevant lung disease. Patients aged below 40 years were excluded because in this age range the risk of COPD is low.¹⁴

Study design

Patients underwent recording of demographic data including age, full smoking history (current, former and never-smokers), recording of symptoms and medication use, clinical examination, assessment of lung function tests, arterial blood gas analysis and venous blood sampling for serum determination of CRP. Body mass index was calculated on the basis of height and weight (BMI)¹⁵. Asthma and COPD severity were classified according to GINA¹ and GOLD² criteria, respectively. Among COPD patients, those with predominant chronic bronchitis and predominant emphysema were identified.

Coexistent cardiovascular disease was assessed on the basis of history, clinical and echocardiographic data. CVD included: prior myocardial infarction and cardiovascular accidents, documented ischaemic heart disease, pulmonary or systemic arterial hypertension, heart valve disease, echocardiographic diagnosis of pulmonary hypertension.

According to the criteria of the American Heart Association,¹⁶ heart disease was classified as follows:

- pressure overload (PO), causing diastolic dysfunction with preserved systolic function, including all the conditions causing concentric left ventricle hypertrophy, such as systemic arterial hypertension and aortic valve disease
- volume overload (VO), including all the conditions causing left ventricle dilatation and systolic dysfunction, such as mitral or aortic incompetence and ischemic heart disease.

Sub-analysis was done on patients with ischemic heart disease (IHD) and pulmonary hypertension (PH).

Lung function tests were measured using the Baires System (Biomedin, Padua, Italy). The values of vital capacity (VC), forced expiratory volume in one second (FEV1), and their percentage ratio (FEV1/VC%), and maximum expiratory flow at mid VC (MEF50) were computed and expressed as percentage of the predicted value, according to the European Respiratory Society guidelines.¹⁷

Arterial blood gases, that is oxygen and carbon dioxide partial pressures (PaO₂ and PaCO₂ respectively) were measured using the analyzer GEM 4000 PREMIERE (Instrumentation Laboratory Lexington USA).

Table 2. Comparisons among patients without cardiovascular disease (no CVD), with pressure overload (PO) and volume overload (VO) in the overall study population.

ASTHMA + COPD	no CVD N. 44	PO N. 97	VO N. 88	Univariate ANOVA	no CVD vs PO	no CVD vs VO	PO vs VO
Age, years	53.3 ± 1.3	64.3 ± 1.0	69.1 ± 1.1	< 0.0001	< 0.0001	< 0.0001	0.002
Male, n (%)	18 (40.9)	43 (44.3)	39 (44.3)	NS	NS	NS	NS
BMI	24.7 ± 0.7	26.9 ± 0.6	25.5 ± 0.5	0.038	0.028	NS	NS
VC, % pred.	93.4 ± 2.2	85.1 ± 1.7	83.5 ± 2.4	0.011	0.005	0.006	NS
FEV1, % pred.	82.6 ± 2.5	70.7 ± 2.1	64.8 ± 2.4	< 0.0001	0.001	< 0.0001	NS
FEV1/VC %	67.6 ± 1.7	61.5 ± 1.5	56.7 ± 1.6	< 0.0001	0.015	< 0.0001	0.032
MEF50, % pred	49.5 ± 4.1	35.8 ± 2.3	25.8 ± 2.3	< 0.0001	0.002	< 0.0001	0.003
CRP, mg/ml	3.1 ± 0.6	5.9 ± 0.6	7.3 ± 1.0	0.011	0.009	0.007	NS

Table 1. Comparison between general characteristics of patients with asthma and with COPD.

	ASTHMA N. 100	COPD N. 129	P
Age, years	59 ± 1.1	69 ± 0.9	< 0.0001
BMI	25.6 ± 0.5	26.2 ± 0.45	0.010
Male, n (%)	22 (22.0)	78 (60.5)	< 0.0001
Smokers			
current, n (%)	10 (10)	72 (55.8)	< 0.0001
past, n (%)	8 (8)	42 (32.6)	< 0.0001
Atopy, n (%)	65 (73.1)	10 (7.7)	< 0.0001
Cardiovascular disease, n (%)	68 (68)	117 (90.7)	0.00002
Pressure overload, n (%)	38 (38.0)	59 (45.7)	NS
Volume overload, n (%)	30 (30.0)	58 (45.0)	0.021
Subgroup IHD, n (%)	8 (8.0)	50 (38.8)	< 0.001
Subgroup PH, n (%)	0 (0.0)	25 (19.4)	< 0.001
VC*, % predicted	88.9 ± 1.7	83.6 ± 1.8	0.033
FEV1*, % predicted	78.0 ± 2.0	64.6 ± 1.9	< 0.0001
FEV1/VC* %	65.7 ± 1.3	57.1 ± 1.3	< 0.0001
MEF50*, % predicted	41.8 ± 2.4	29.5 ± 2.1	< 0.0001
PaO ₂ , mmHg	74.5 ± 1.6	71.4 ± 1.0	NS
PaCO ₂ , mmHg	38.4 ± 0.5	39.8 ± 0.5	NS
CRP, mg/ml	3.4 ± 0.4	7.6 ± 0.7	< 0.0001
Beta adrenergic therapy, n (%)	94 (94.9)	97 (75.2)	0.0001
Corticosteroid therapy, n (%)	95 (96)	90 (69.8)	< 0.0001
Anticholinergic therapy, n (%)	22 (22)	76 (58.9)	< 0.0001

Statistical analysis

Data were analyzed using the SPSS software package, version 20.0 (SPSS Inc, Chicago, IL, USA) for Windows. Discrete variables are presented as counts and percentages. Continuous variables are presented as means ± SEM, as appropriate. Comparisons between asthmatics and COPD patients, and between patients with predominant chronic bronchitis and predominant emphysema were performed by the unpaired Student's t-test. Comparisons among CVD, PO and VO patients with univariate ANOVA. Nominal variables were compared with the Fisher's exact test and Pearson's χ^2 . A stepwise backward selection procedure was used to evaluate factors influent on heart disease, using a linear regression models. The models had as dependent variables CVD, PO or VO and as independent predictors: disease (asthma or COPD), age, sex, BMI, smoking habits, GINA or GOLD class, prebronchodilator lung function tests, PaO₂, CRP. The same models were used to evaluate predictors for asthma

and COPD separately and for the sub-analysis of patients with IHD or PH.

Statistical significance was assumed at $p < 0.05$.

Results

The subjects enrolled were 100 asthmatic patients and 129 COPD patients. CVD was found in 185 patients (81%), and consisted of pressure overload in 97 (42%) and of volume overload in 88 (38%). IHD was found in 58 patients (25%), 8 asthmatics and 50 COPD, and PH in 25 (11%), all with COPD. The general characteristics of asthmatic and COPD patients are compared in Table 1. The COPD group was older, and had higher prevalence of men and of both present and past smokers, more severe airway obstruction and higher prevalence of heart disease, including PO, VO, IHD and PH. Moreover, COPD patients had higher CRP values than asthmatics, suggestive of systemic inflammation. No significant difference in PaO₂ and PaCO₂ was found between the two groups.

The comparisons among subgroups with no cardiovascular disease (No CVD), with PO and VO in the overall patients, in asthma and in COPD are reported in the Tables 2, 3 and 4.

In the overall patients (Table 2), both PO and VO, as compared with no CVD, were associated with older age and lower VC, FEV₁, FEV₁/VC and MEF50 and higher CRP. The same associations (apart from CRP) were found in asthmatic patients (Table 3). In COPD patients (Table 4) the significant associations were with age and MEF50, %.

The results of linear regression analysis are shown in Table 5 for the whole patients, in Table 6 for asthmatic patients and in Table 7 for COPD patients. In the overall patients predictive factors of CVD were: age, COPD, and sex; those of PO were COPD, BMI, VC, FEV₁ and MEF50 and those of VO were age, class of disease severity, VC and MEF50. In asthma, the strongest predictors of CVD were VC, FEV₁ and FEV₁/VC%, and PaO₂, those of PO were VC, FEV₁ and FEV₁/VC%; no predictor was found for VO. In COPD the predictors of CVD were age, GOLD class and sex; those of VO were age, VC and MEF50, while the only predictor of PO was BMI.

As shown in Table 8, the predictors of IHD were COPD, age, BMI and FEV₁ and those of PH, found only in COPD patients, were VO (present in 80% of the patients) and FEV₁.

The distributions of PO and VO by severity of asthma (GINA) and COPD (GOLD) are reported in Figure 1. In asthma, there is a clear increase in the prevalence of both PO and VO with increasing the severity class, while in COPD the prevalence of each type of CVD is similar in all classes. The comparison between chronic bronchitis and emphysema patients, shown in Table 9, showed that the latter ones had older age, lower BMI, more severe airway obstruction and higher prevalence of heart volume overload and of pulmonary hypertension.

As one of the stronger predictors of CVD was age, we made a sub-analysis on subjects with an age equal to 65 years or higher. As shown in Table 10, the prevalence of CVD, PO and VO was similar in asthmatic and COPD patients; the latter had higher prevalence of men, smokers, lower FEV₁, higher CRP and of IHD and PH. The results of linear regression analysis in these older patients are reported in Tables 11, 12 and 13.

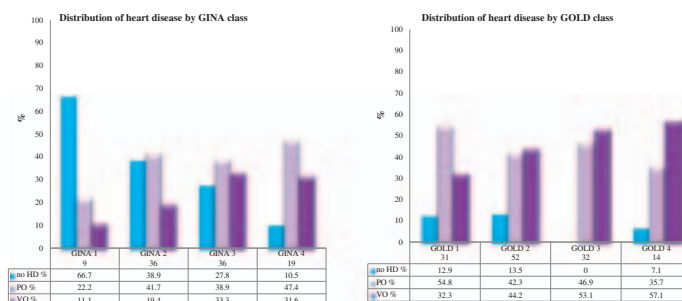


Figure 1. Distributions of heart pressure overload (PO) and volume overload (VO) by GINA asthma severity class (left graph), and by GOLD COPD severity class (right graph).

Discussion

The results of this study show that patients with chronic airway obstructive disorders, either asthma or COPD, have increased prevalence of cardiovascular diseases as compared to the general population of similar age.¹⁸ The comparison between the two disorders, (see Table 1) showed that CVD, particularly with volume overload, was more frequent in COPD patients, who had also older age, higher BMI, heavy smoking history, increased CRP and greater airway obstruction. This finding is in agreement with prior observations that in COPD comorbidities are frequent and are sustained by systemic inflammation and by smoking.^{4,6,7} The comparison among patients without CVD, with PO and VO, showed that both pressure and volume overload were associated with older age and increased airway obstruction, either in asthma or in COPD, (see Tables 2, 3 and 4). These findings are in agreement with prior observations in COPD.^{8-13,19} Unfortunately, relatively little research has been done in asthma.¹⁴ It is generally believed that the link between asthma and CVD is less strong than that for COPD^{14,20,21} and this applies particularly to ischemic heart disease in asthmatic males. By contrast, in women adult-onset asthma has been found to be a significant risk factor for IHD and stroke.^{21,22} Although only 8 of our asthmatic patients had IHD, as many as 6 of them (75%) were never smoking women. However, the strongest predictors of IHD were COPD, age, BMI and FEV₁, as previously suggested.^{19,23} The strong association of COPD with IHD is attributed to the effect of cigarette smoking,¹⁹⁻²⁴ and about 90% of our COPD patients were past or present smokers. The subanalysis of COPD patients with predominant chronic bronchitis or emphysema, (see Table 9), showed that the emphysema phenotype was associated with older age, lower BMI, more severe airway obstruction and higher prevalence of pulmonary hypertension and of volume overload. Unfortunately, there are no data in the literature comparing CVD in the two COPD phenotypes.

As mentioned above, age and COPD were the strongest predictors of CVD, but the two factors were closely linked to each other, as COPD patients were significantly older than asthmatics. To clarify this point, we performed a sub-analysis on patients with an age equal to or higher than 65 years. As shown in Table 10, older asthmatics had the same prevalence of CVD than COPD patients (91% versus 95%). However, also in the elderly, the prevalence of IHD and PH was higher in COPD. Pulmonary hypertension deserves a special comment. PH in COPD is classically attributed to severe hypoxia causing raised pulmonary pressures, but other factors such as endothelial dysfunction or left heart disease, are deemed to play a role²⁴. In our patients, the predictors of PH were FEV₁ and volume overload, suggesting that both airway obstruction and post capillary mechanisms participated in increased pulmonary

Table 3. Comparisons among patients without cardiovascular disease (no CVD), with pressure overload (PO) and volume overload (VO) in asthma.

ASTHMA	no CVD N. 32	PO N. 38	VO N. 30	Univariate ANOVA	no CVD vs PO	no CVD vs VO	PO vs VO
Age, years	51.3 ± 1.4	60.7 ± 1.6	63.1 ± 2.1	< 0.0001	< 0.0001	< 0.0001	NS
Male, n (%)	9 (28.1)	6 (15.8)	7 (23.3)	NS	NS	NS	NS
BMI	24.5 ± 0.8	26.5 ± 0.9	25.7 ± 0.7	NS	NS	NS	NS
VC, % pred.	94.0 ± 2.8	84.7 ± 2.2	89.0 ± 3.7	NS	0.011	NS	NS
FEV1, % pred.	85.4 ± 2.9	76.7 ± 2.9	73.8 ± 4.5	0.029	0.041	0.032	NS
FEV1/VC %	68.9 ± 1.7	65.7 ± 2.0	61.2 ± 2.9	0.042	NS	0.010	NS
MEF50, % pred	51.3 ± 4.2	37.8 ± 3.5	35.8 ± 4.5	0.017	0.016	0.015	NS
CRP, mg/ml	2.5 ± 0.5	4.1 ± 0.8	3.5 ± 0.8	NS	NS	NS	NS

Table 4. Comparisons among patients without cardiovascular disease (no CVD), with pressure overload (PO) and volume overload (VO) in COPD.

COPD	no CVD N. 12	PO N. 59	VO N. 58	Univariate ANOVA	no CVD vs PO	no CVD vs VO	PO vs VO
Age, years	58.5 ± 2.6	66.7 ± 1.3	72.4 ± 1.0	< 0.0001	0.012	< 0.0001	0.001
Male, n (%)	9 (75)	37 (62.7)	32 (55.2)	NS	NS	NS	NS
BMI	25.4 ± 1.5	27.1 ± 0.7	25.4 ± 0.6	NS	NS	NS	NS
VC, % pred.	91.8 ± 3.12	85.3 ± 2.4	80.0 ± 2.9	NS	NS	NS	NS
FEV1,% pred	75.2 ± 4.8	66.3 ± 2.8	60.1 ± 2.8	0.048	NS	0.023	NS
FEV1/VC %	61.5 ± 3.8	58.8 ± 2.0	54.4 ± 1.9	NS	NS	NS	NS
MEF50, % pred	44.6 ± 10.2	34.5 ± 3.1	20.18 ± 2.1	< 0.0001	NS	< 0.0001	< 0.0001
CRP, mg/ml	4.4 ± 1.4	7.0 ± 0.9	8.9 ± 1.4	NS	NS	NS	NS

Table 5. Results of linear regression analysis for predictors of cardiovascular disease (CVD) in the overall patients.

Asthma + COPD	Non standardized coefficients		Standardized coefficient	t	Sig.
	B	SD Error			
CVD					
Constant	.948	.248		3.829	.000
Age	.012	.003	.340	4.357	.000
COPD	.137	.063	.169	2.195	.030
Sex	.116	.058	.144	1.991	.048
VC, % pred	-.003	.002	-.124	-1.784	.076
MEF50, % pred	-.002	.001	-.131	-1.728	.086
Pressure overload					
Constant	1.066	.264		4.031	.000
COPD	.217	.074	.225	2.939	.004
BMI	.017	.007	.183	2.482	.014
VC, % pred	-.006	.003	-.213	-2.031	.044
FEV1, % pred	.007	.003	.322	2.162	.032
MEF50, % pred	-.006	.002	-.305	-2.668	.008
Volume Overload					
Constant	1.318	.446		2.954	.004
Age	.015	.004	.310	3.529	.001
GINA/GOLD class	-.118	.056	-.227	-2.113	.037
VC, % pred	-.006	.003	-.197	-2.244	.027
MEF50, % pred	-.005	.002	-.227	-2.094	.038

vascular resistance. Actually, VO was present in 80% of patients with PH.

Conclusions

In conclusion, the results of this study indicate that

Table 6. Results of linear regression analysis for predictors of cardiovascular diseases (CVD) in asthma

ASTHMA	Non standardized coefficients		Standardized coefficient	t	Sig.
	B	SD Error			
CVD					
Constant	8.291	1.056		7.851	.000
Age	-.009	.005	-.270	-1.981	.059
BMI	.016	.008	.223	1.874	.073
VC, % pred	-.060	.009	-2.402	-6.630	.000
FEV1, % pred	.073	.011	3.667	6.894	.000
FEV1/VC, %	-.094	.013	-3.499	-7.021	.000
PaO2	-.010	.005	-.278	-2.268	.033
PRC	.016	.009	.209	1.797	.085
Pressure Overload					
Constant	6.668	1.082		6.163	.000
VC, % pred	-.060	.012	-1.874	-5.078	.000
FEV1, % pred	.067	.013	2.626	5.107	.000
FEV1/VC, %	-.077	.016	-2.237	-4.690	.000
Volume Overload					
Constant	-.116	.693		-.167	.869
Age	.019	.011	.320	1.822	.079

cardiovascular disease are frequent in patients with chronic obstructive disorders, particularly COPD. The strongest predictors of CVD are age and severity of airway obstruction. In older patients the prevalence of CVD is similar in asthma and COPD, apart from ischemic heart disease and pulmonary

Table 7. Results of linear regression analysis for predictors of cardiovascular diseases (CVD) in COPD.

COPD	Non standardized coefficients		Standardized coefficient	t	Sig.
	B	SD Error			
CVD					
Constant	.686	.393		1.747	.084
Age	.007	.003	.228	2.143	.035
GOLD Class	.076	.036	.241	2.089	.040
Sex	.121	.061	.203	1.983	.050
PaO2	.006	.003	.209	1.826	.071
Pressure Overload					
Constant	1.237	.229		5.414	.000
BMI	.020	.008	.244	2.337	.022
Volume Overload					
Constant	1.317	.519		2.539	.013
Age	.017	.005	.334	3.311	.001
VC, % pred	-.006	.003	-.220	-2.076	.041
MEF50, % pred	-.006	.003	-.305	-2.351	.021

Table 8. Results of linear regression analysis for predictors of ischemic heart disease (IHD) and pulmonary hypertension (PH).

IHD	Non standardized coefficients		Standardized coefficient	t	Sig.
	B	SD Error			
IHD					
Constant	-1.486	.667		-2.229	.028
COPD	.450	.134	.412	3.351	.001
Age	.012	.004	.246	2.834	.005
BMI	.016	.008	.177	2.095	.038
FEV1, % pred	.007	.003	.309	2.127	.036
GOLD class	.150	.083	.294	1.810	.073
PH					
Constant	1.127	.244		4.613	.000
VO	.246	.045	.442	5.468	.000
GOLD class	-.105	.041	-.273	-2.584	.011
FEV1, % pred	-.004	.002	-.239	-2.222	.028

Table 9. Comparison between general characteristics of patients with chronic bronchitis and emphysema.

	Chronic bronchitis	Emphysema	P
	N. 102	N. 27	
Age, years	68 ± 1.0	73 ± 1.5	0.017
BMI	27.2 ± 0.5	22.1 ± 0.6	< 0.0001
Male, n (%)	58 (56.9)	20 (74.1)	NS
Smokers			
current, n (%)	55 (53.9)	17 (63)	NS
past, n (%)	33 (32.4)	9 (33.3)	NS
Cardiovascular disease, n (%)	92 (90.2)	25 (92.6)	NS
Pressure overload, n (%)	51 (50)	8 (29.6)	NS
Volume overload, n (%)	41 (40.2)	17 (63)	0.034
Subgroup IHD n (%)	39 (39.4)	11 (40.7)	NS
Subgroup PH n (%)	15 (4.7)	10 (37)	0.009
GOLD class			
1	30 (29.4)	1 (3.7)	0.005
2	44 (43.1)	8 (29.6)	NS
3	19 (18.6)	13 (48.1)	0.0016
4	9 (8.8)	5 (18.5)	NS
VC, % predicted	82.7 ± 2	85.5 ± 4.3	NS
FEV1, % predicted	68.1 ± 2.2	51.9 ± 3.1	0.001
FEV1/VC %	60.2 ± 1.4	46.56 ± 2.6	< 0.0001
MEF50, % predicted	33.7 ± 2.5	13.6 ± 2.1	< 0.0001
PaO2, mmHg	71.2 ± 1.1	70.1 ± 2.1	NS
PaCO2, mmHg	40.1 ± 0.6	39.0 ± 0.8	NS
CRP, mg/ml	7.9 ± 1.0	6.8 ± 1.2	NS

Table 10. Comparisons between general characteristics of patients 65 years old or more.

	ASTHMA N. 33	COPD N. 92	P
Age, years	71.8 ± 0.8	73.6 ± 0.6	NS
Male, n (%)	5 (15.2)	60 (65.2)	< 0.0001
Smokers			
Current n(%)	4 (13)	45 (51)	< 0.0001
Past n (%)	4 (13)	36 (41)	< 0.0001
BMI	25.8 ± 0.8	26.2 ± 0.5	NS
CVD, n (%)	30 (90.9)	87 (94.6)	NS
Pressure overload, n (%)	15 (45.5)	38 (41.3)	NS
Volume overload, n (%)	15 (45.5)	49 (53.3)	NS
Ischemic heart disease, n (%)	6 (18.2)	42 (46.7)	0.0054
Pulmonary hypertension, n (%)	0	21 (22.8)	0.0026
VC, % predicted	86.1 ± 2.6	82.7 ± 2.2	NS
FEV1, % predicted	73.3 ± 3.3	63.5 ± 2.3	0.023
FEV1/VC %	61.63 ± 2.5	56.4 ± 1.5	NS
MEF50, % predicted	30.8 ± 3.4	26.6 ± 2.3	NS
CRP, mg/l	4.1 ± 0.7	8.2 ± 1.0	0.018

Table 11. Results of linear regression analysis for predictors of cardiovascular disease in the overall patients 65 years old or more.

Asthma + COPD	Non standardized coefficients		Standardized coefficient	t	Sig.
	B	SD Error			
CVD					
Constant	.879	.421		2.087	.040
Age	.020	.006	.380	3.581	.001
VC, % predicted	-.005	.002	-.308	-2.813	.006
CRP	-.006	.003	-.190	-1.707	.092
Pressure overload					
Constant	.895	.328		2.731	.008
Sex	.217	.094	.255	2.310	.024
BMI	.022	.011	.226	2.047	.044
Volume overload					
Constant	.293	.874		.335	.739
Age	.024	.011	.229	2.091	.040
VC, % predicted	-.006	.003	-.207	-1.883	.063

Table 12. Results of linear regression analysis for predictors of cardiovascular disease in asthmatic patients 65 years old or more.

Asthma	Non standardized coefficients		Standardized coefficient	t	Sig.
	B	SD Error			
CVD					
Constant	7.203	.662		10.885	.000
VC, % pred	-.058	.007	-2.909	-8.345	.000
FEV1, % pred	.064	.008	4.069	7.728	.000
FEV1/VC, %	-.084	.011	-3.472	-7.509	.000
Pressure overload					
Constant	3.616	1.487		2.432	.035
Age	.028	.015	.250	1.913	.085
Sex	.864	.152	.864	5.691	.000
GINA class	-.380	.138	-.629	-2.766	.020
VC, % pred	-.032	.010	-1.209	-3.306	.008
FEV1, % pred	.033	.012	1.566	2.661	.024
FEV1/VC, %	-.043	.015	-1.333	-2.785	.019
PaO2	-.017	.006	-.392	-2.954	.014
Volume overload					
Constant	.293	.874		.335	.739
Age	.024	.011	.229	2.091	.040

Table 13. Results of linear regression analysis for predictors of cardiovascular disease in COPD patients 65 years old or more.

COPD	Non standardized coefficients		Standardized coefficient	t	Sig.
	B	SD Error			
CVD					
Constant	.542	.464		1.169	.247
Age	.018	.006	.373	3.259	.002
BMI	.011	.006	.200	1.748	.085
VC, % predicted	-.003	.002	-.198	-1.724	.090
Pressure overload					
Constant	1.110	.330		3.366	.001
BMI	.025	.012	.263	2.060	.044
Volume overload					
Constant	.928	.480		1.932	.058
Sex	.384	.148	.341	2.598	.012
Smoking	.289	.112	.339	2.576	.013
VC, % predicted	-.006	.004	-.212	-1.763	.083

hypertension, which are strongly associated with COPD.

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Value of serum and induced sputum surfactant protein-D in chronic obstructive pulmonary disease

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Abstract

Background: Surfactant Protein D (SP-D) is an important marker in chronic obstructive pulmonary disease (COPD). Serum SP-D levels increase while lung production of SP-D decreases in COPD. SP-D is a specific biomarker for monitoring COPD, assessment of exacerbation frequency and arrangement of treatment modalities. In the present study, we aimed to investigate the correlation between serum and induced sputum SP-D levels with severity and acute exacerbations of COPD.

Method: 20 healthy subjects, older than 40 years, with at least 10 pack/years smoking history (group 1), 20 stage I-II COPD patients (group 2), and 20 stage III-IV COPD patients (group 3) were enrolled in the study. All subjects performed pulmonary function tests. Venous blood samples were taken to determine complete blood count, C-reactive protein(CRP) and serum SP-D levels. Induced sputum samples were obtained to determine SP-D level. COPD patients were followed up for acute exacerbations for 6 months.

Results: Serum SP-D levels of group 3 were the highest and induced sputum SP-D levels of group 2 were the lowest among the three groups. SP-D levels of induced sputum decreased in patients with increasing number of cigarette pack/years ($p=0.03$, $r=0.115$), whereas serum SP-D levels increased in these patients ($p=0.0001$, $r=0.6$). Induced sputum SP-D levels in COPD patients receiving inhaled corticosteroid treatment were significantly higher than in patients who were not receiving inhaled corticosteroid treatment ($p=0.005$). An inverse correlation between serum SP-D levels and FEV1 (%) was found and there was a positive correlation between the serum SP-D levels and exacerbations frequency in 6-month follow up period ($p=0.049$, $r=0.252$; $p=0.0001$, $r=0.598$ respectively).

Conclusion: Our study demonstrates the adverse effects of smoking on local SP-D levels since low levels of induced sputum

SP-D were found in the group of current smokers, who were not receiving inhaled corticosteroid treatment. Relationship between serum SP-D and COPD exacerbations frequency suggests that serum SP-D level may be used as a lung-specific biomarker during the follow up and progression of COPD.

Background

Chronic obstructive pulmonary disease (COPD) is a complex chronic inflammatory disease that involves the activity of various inflammatory cells and mediators.¹ Both local and systemic inflammatory reactions are observed in COPD. There are ongoing researches trying to find out different markers in COPD course. For instance, surfactant protein D (SP-D) is one of the most frequently studied markers contributing to immune and inflammatory regulation within lungs. SP-D is a 43kDa member of the collectin family that is produced from collagenous glycoprotein in type II pneumocyte cells. SP-D is a protein responsible for homeostasis which has an important protective role in the immune system against inhaled microorganisms and allergens. It plays a part in protection against viral, bacterial, and fungal infections, as well as apoptotic cells.² Serum SP-D concentration exhibits an increase together with the decrease in bronchoalveolar lavage in COPD. Furthermore, serum SP-D level and FEV1 display a negative correlation in COPD.³ Higher serum SP-D levels have been found³ in advanced COPD cases with worsening health and aggravating shortness of breath. SP-D is thought to play a role in the pathogenesis and progression of COPD.⁴ SP-D level declines as the disease progresses. There are also some studies indicating the increase of BAL SP-D level using inhaled corticosteroids. The association between decreased SP-D level in lungs and smoking has also been demonstrated in previous studies.^{5,6} Therefore, SP-D is a promising biomarker that might help to determine the health status of patients with lung diseases, particularly with respect to progression of dyspnea and decreasing pulmonary functions.

SP-D of serum and BAL or induced sputum may be used as a lung specific biomarker in the assessment of COPD progression and management. The number of studies investigating the relationship between local and systemic SP-D levels with COPD is not as high as it should be. Therefore, in the present study we aim to investigate the relationships between COPD severity and acute exacerbations frequency with serum and induced sputum SP-D levels.

Methods

This study was approved by the Research Committee of the

The authors are with Ataturk Chest Diseases and Thoracic Surgery Training and Research Hospital. Department of Pulmonary Diseases, Afyon Kocatepe University Faculty of Medicine. Faculty of Medicine, Department of Pulmonary Diseases, Baskent University. Faculty of Medicine, Department of Biochemistry, Baskent University. Reprinted from BioMedCentral, Multidisciplinary Respiratory Medicine 2013. This is an Open Access article distributed under the terms of the Creative Commons Attribution License. Authors would like to thank Alper Murat Ulasli, MD, for his professional support in the statistical analysis of the present study and Elif Erdem for her technical assistance.

Table 1 Demographic characteristics and respiratory function test results of the study population

	Group 1 (control subjects) (n = 20)	Group 2 (stage 1 and 2 COPD patients) (n = 20)	Group 3 (stage 3 and 4 COPD patients) (n = 20)	p
Mean Age (year)	44.85 ± 5.80	60.35 ± 9.40	63.70 ± 8.60	p = 0.001
Gender (F/M)	8/12	0/20	3/17	p = 0.004
Mean BMI (kg/m ²)	33.36 ± 5.70	32.8 ± 6.70	29.6 ± 5.90	p = 0.148
Smoking status				
Active smokers	16 (80%)	10 (50%)	2 (10%)	p = 0.001
Ex-smokers	4 (20%)	10 (50%)	18 (90%)	
Cigarette pack years	23 ± 13 (20)	51 ± 28 (45)	51 ± 33(45)	p = 0.001
Inhaled steroid use	0	6	18	p = 0.001
Mean FVC (%)	131.5 ± 15.1	101.7 ± 19	76.7 ± 16.8	p = 0.001
Mean FEV ₁ (%)	123 ± 14	75.7 ± 16.4	39.7 ± 7.24	p = 0.001
Mean FEV ₁ /FVC (%)	78.9 ± 4.8	59.75 ± 10.8	43.3 ± 11.3	p = 0.001
Mean FEF ₂₅₋₇₅ (%)	94.5 ± 23.4	33.5 ± 18.6	12.5 ± 4.54	p = 0.001
Mean VC (%)	130 ± 16.9	94.5 ± 19	80.8 ± 19	p = 0.001
Mean RV (%)	120 ± 29	156 ± 37	150 ± 77	p = 0.001
Mean SpO ₂ (%)	96.6 ± 1.1	94 ± 1.9	92.1 ± 2.1	p = 0.001
Mean CRP level (mg/L)	2.52 ± 2.4	8.3 ± 10	8.1 ± 9.49	p = 0.014
Mean Hb (g/dl)	14.21 ± 1.55	14.7 ± 1.43	14.6 ± 14	p = 0.282
Mean WBC (/μL)	7.449 ± 1.704	7.291 ± 1.084	8.402 ± 1.694	p = 0.102
Mean PMNL (/μL)	4.272 ± 1.166	4.310 ± 956	5.519 ± 1.205	p = 0.003

The results are expressed as mean ± standard deviation.

BMI Body mass index, CRP C-reactive protein, FEV₁ forced expiratory volume, FRC functional residual capacity, FVC forced vital capacity, Hb hemoglobin, PMNL polymorphonuclear leukocyte, RV residual volume, TLC total lung capacity, VC vital capacity, WBC white blood cell count.

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Our study sample comprised of 60 subjects in total: a control group including 20 individuals (16 smokers and 4 ex-smokers) above 40 years of age (mean age: 44.85 ± 5.80 years) and with a history of at least 10 pack/year cigarette consumption (mean cigarette pack/year: 23 ± 13 pack/year) (Group 1), 20 mild and moderate COPD patients (Group 2), and 20 severe and very severe COPD patients (Group 3) based on GOLD classification.⁷

The patients below 40 years of age and those with a history of COPD exacerbation/infection within the last 4 weeks, cardiac disease, chronic liver and kidney failure, asthma, malignancy, hypertension, diabetes mellitus, and any additional medical disorders were excluded from the study.

In our study all patients and control subjects performed pulmonary function tests (PFT). Furthermore, venous blood sample was collected from each participant for evaluating complete blood count (CBC), C-reactive protein (CRP), and serum SP-D level. Induced sputum specimen was obtained and also tested for induced sputum SP-D level. COPD patients were followed for 6 months to determine exacerbation frequency. Acute exacerbation of COPD was defined as a sustained (lasting 48 hours or more) worsening of dyspnea, cough or sputum production leading to an increase in the use of maintenance medications and/or supplementation with additional medications.^{7,8} The data concerning the exacerbation frequency were collected via hospital visits and telephone calls.

Measurement of biochemical parameters

Venous blood sample was obtained from each patient. 3 ml venous peripheral blood specimen was put into a tube with K₃-EDTA for CBC and 5 ml venous peripheral blood specimen was

Table 2 Treatment modalities of COPD patients

	Group 2 (stage 1 and 2 COPD patients) (n = 20)	Group 3 (stage 3 and 4 COPD patients) (n = 20)
Short acting β ₂ agonist	6	12
Long acting β ₂ agonist	12	18
Long acting anticholinergic	7	15
Inhaler steroid	6	18
N-acetyl cystein	2	7
Long term oxygen therapy	2	10
Pulmoner rehabilitation	0	7

Table 3 Comparison of SP-D levels and cell viability among the study groups

	Group 1 (control subjects) (n = 20)	Group 2 (stage 1 and 2 COPD patients) (n = 20)	Group 3 (stage 3 and 4 COPD patients) (n = 20)	p
Serum SP-D (ng/ml)	86.2 ± 49	108.9 ± 65	129 ± 71	p = 0.10
Sputum SP-D (ng/ml)	33.1 ± 34	28 ± 15.2	30.42 ± 12.8	p = 0.83
Viability %	73.5 ± 12.1	79.8 ± 11.2	80.1 ± 19	p = 0.86

The results were expressed as mean ± standard deviation.

COPD Chronic obstructive pulmonary disease, SP-D surfactant protein D.

put into an additive-free tube for analysis of CRP and SP-D levels. Serum samples were prepared by collecting blood in a vacuum tube and allowing it to clot for 30 minutes at room temperature. About 1mL of serum was obtained after centrifugation at 1100g for 10 minutes and stored in small aliquots at -80°C until analysis. SP-D level was studied by ELISA immunoassay method. Serum CRP level was measured by an ultrasensitive latex-enhanced immunoassay method, using CRP Ultra reagent (Sentinel Diagnostics, Milan, Italy) in Abbott Architect C8000 Analyzer according to the manufacturer's specifications. The detection limit was 0.2 mg/L. The inter- and intra-assay variability were 8.22% and 4.84%, respectively. CBC was carried out with Abbott Cell-Dyne 3700 System device (Abbott Diagnostics, Santa Clara, CA, USA).

Pulmonary function test

Pulmonary function test was performed with a clinical spirometer (SensorMedics Vmax spectra 229, Bithoven, The Netherlands) according to the ERS standards.⁹ We carried out forced vital capacity (FVC) and forced expiratory volume (FEV1) measurements, and calculated the FEV1/FVC ratio. Total lung capacity (TLC), residual volume (RV), functional residual capacity (FRC), and vital capacity (VC) were measured by the multiple nitrogen washout method. Twenty healthy individuals having normal PFTs and 40 patients diagnosed as mild, moderate, severe, and very severe COPD based on the current Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines using postbronchodilator FEV1 values (post bronchodilator values were obtained after 400 mcg salbutamol inhalation), were enrolled in the study.⁷

Induced sputum analysis

The patients were informed about the process and FEV1 values were measured before the bronchodilatation. Then, 10 minutes after inhaling 400 µg salbutamol, post-bronchodilator FEV1 values were measured. Induction was started with 3% NaCl in patients with FEV1 value >1 L or >60%. This was continued for a period up to 20 minutes by incremental doses applied with nebulizer at 5 minute intervals and FEV1 values were measured after each induction. If 20% or more decrease in FEV1 values was detected, process was terminated.

The induction started using 0.9% NaCl with nebulizer in patients with a FEV1 value <1 L or <60%. The induction was carried out for 30 seconds, 1 minute, and 5 minutes. At the end of these time intervals, FEV1 value was re-measured and induction was

discontinued if there was a decrease of 20% or more. Induction with higher concentration was not applied to patients when adequate material could be obtained at this concentration. If the patient failed to produce sputum and/or adequate sputum at these concentrations, induction was applied using 3% NaCl with nebulizer and it was carried out for 30 seconds, 1 minute, and 2 minutes. At the end of these time intervals, FEV1 value was measured again and induction was discontinued if there was a decrease of 20% or more. Induction with a higher concentration was not applied to patients when adequate material could be obtained at this concentration. If the patient failed to produce sputum and/or adequate sputum at this concentration, induction was applied with 4.5% NaCl and it was carried out for 30 seconds, 1 minute, 2 minutes, and 4 minutes. At the end of these times, FEV1 value was measured again and induction was discontinued if there was a decrease of 20% or more. Following each induction, participants were asked to rinse their mouth with water and produce sputum by cough.

The processing of induced sputum

The induced sputum was immediately analyzed following the acquirement. Firstly, the specimen was weighed. Sputum was treated with Sputalysin (0.1% DTT) by mixing the agent in a 1:1 ratio with the specimen. The mixture was vortexed for 15 minutes at room temperature and thereafter it was filtered through a 48µm-thick nylon filter. The resulting filtrate was weighed. The cell viability of the filtrate was evaluated by Trypan blue and total cell count (TCC) was calculated on a Thoma slide. TCC was calculated by following the formula: Average number of cells in one large square x dilution factor* x 104 (*dilution factor is 2x2 = 4 (1:1 dilution with Sputalysin and 1:1 dilution with trypan blue)). The filtrate (790µg) was centrifuged at 4°C for 10 minutes. The resultant supernatant was separated and put into Falcon tubes. These tubes were stored at -20°C.

Induced sputum and serum SP-D level determination

Surfactant protein D concentration in serum and induced sputum samples was determined by a sandwich enzyme-linked immunosorbent assay (ELISA) system (SP-D; Biovendor, Brno, Czech Republic). For SP-D, the inter- and intraassay CV were 3.7% and 2.3%, respectively, and the sensitivity was 0.01 ng/ml.

Statistical analysis

The statistical analyses of our study were performed using SPSS statistical software version 15.0. The variables were investigated using visual (histograms, probability plots) and

Table 4 Comparison of patients with and without inhaled corticosteroid therapy

	COPD patients receiving inhaled steroid (n = 24)	COPD patients not receiving inhaled steroid (n = 16)	p
Serum SP-D (ng/ml)	132 ± 71	99 ± 59	0.038
Sputum SP-D (ng/ml)	35.5 ± 14	20 ± 7.8	0.005

The results were expressed as mean ± standard deviation.

COPD Chronic obstructive pulmonary disease, SP-D surfactant protein D.

Table 5 Multiple linear regression models

Multiple linear regression model for six month exacerbation frequency by serum and induced sputum SP-D levels				
	Coefficient B	Standard error	t	p
Constant	-0.37	0.32	-1.15	0.25
Serum SP-D levels	0.008	0.002	4.22	0.0001
Sputum SP-D levels	0.011	0.009	1.18	0.247
Multiple linear regression model for induced sputum SP-D levels by six month exacerbation frequency and number of years on inhaled steroid treatment.				
	Coefficient B	Standard Error	t	p
Constant	16.948	3.78	4.4	0.0001
Six month exacerbation frequency	1.38	2.14	0.64	0.525
Number of years on inhaled steroid treatment	2.848	0.53	5.37	0.0001
Multiple linear regression model for serum SP-D levels by age, FEV1 (%) and six month exacerbation frequency				
	Coefficient B	Standard error	t	p
Constant	17.660	70.64	0.25	0.80
Age	1.461	1.08	1.35	0.187
FEV1(%)	-0.61	0.45	-1.36	0.182
Six month exacerbation frequency	42.598	9.85	4.32	0.0001

FEV₁, forced expiratory volume, SP-D surfactant protein D.

analytical methods (Kolmogorov-Smirnov test) to determine the normality of distributions. The results were expressed as mean±standard deviation and median value. For continuous variables without normal distribution Mann-Whitney U test was used for the comparison of the two groups (patients receiving inhaler steroids or not receiving inhaler steroids), whereas Kruskal-Wallis test for the comparison of parameters between 3 groups. T-test was used for the comparison of parameters with normal distribution between 2 groups and ANOVA together with Bonferroni correction was used for the comparison of continuous parameters with normal distribution among the three groups. The parameters affecting 6 month exacerbation frequency, induced sputum and serum surfactant protein D levels were investigated using Spearman correlation analysis. Multiple linear regression models were used to identify independent predictors of 6 month exacerbation frequency, serum and induced sputum surfactant protein D levels. The model fit was assessed using appropriate residual and goodness of fit statistics. A 5% type-I error level was used to infer statistical significance.

Results

The demographic characteristics, PFT parameters and complete blood count results of our study groups are reported in Table 1. CRP levels of group I were the lowest among study groups ($p=0.03$).

Smoking status (active, ex-smoker) of the groups was also evaluated. 80% of the healthy individuals ($n=16$) in Group 1, 50% of patients ($n=10$) in Group 2, and 10% of patients ($n=2$) in Group 3 were active smokers. The amount of cigarette consumption (pack/years) was 20 pack/years in Group 1, 45 pack/years in Group 2, and 45 pack/years in Group 3. When we asked the ongoing bronchodilator and/or oxygen therapy of COPD patients, 24 patients were found to be on inhaled corticosteroid therapy and 12 patients on nasal oxygen therapy due to type I respiratory failure (Table 2). Mean duration of inhaled steroid treatment was 5.31 ± 3.81 years.

The serum and sputum SP-D values of subjects in all three groups were compared (Table 3). Serum SP-D levels of Group 3

were the highest and serum SP-D levels of Group 2 were higher than Group 1. However, there was no statistically significant difference among the three groups in terms of serum SP-D level ($p=0.099$). In addition, we did not find statistically significant differences among the three groups in terms of induced sputum SP-D levels ($p=0.836$). Although, induced sputum SP-D levels in Group 2 were the lowest, they did not achieve to the significance level.

The groups were also evaluated in terms of relationships between cigarette consumption (pack/year) and serum/sputum SP-D levels. While sputum SP-D and cigarette consumption demonstrated a negative correlation ($p=0.03$, $r=-0.115$), serum SP-D and cigarette consumption showed a positive correlation ($p=0.0001$, $r=0.6$). No significant difference was observed between genders in terms of serum/sputum SP-D levels and cell viability.

Serum SP-D levels were significantly correlated with FEV1 (%) ($p=0.049$; $r=-0.252$). However no significant correlation was found between FEV1 (%) and induced sputum SP-D levels ($p=0.92$, $r=-0.013$).

Induced sputum and serum SP-D levels were significantly different between patients with and without inhaled corticosteroid therapy ($p=0.005$ and 0.038 respectively). The COPD patients receiving inhaled corticosteroid therapy had higher SP-D levels compared to those not receiving inhaled corticosteroid therapy (Table 4). The number of years on inhaled steroid treatment was significantly correlated with induced sputum SP-D levels whereas no significant correlation was evidenced with serum SP-D levels ($p=0.0001$, $r=0.800$; $p=0.59$, $r=0.104$ respectively).

We also evaluated the relationships between serum/sputum SP-D levels and 6-month exacerbation frequency in COPD patients of Groups 2 and 3. There was no significant correlation between sputum SP-D levels and 6-month exacerbation frequency ($p=0.051$; $r=0.342$). However, patients with increased serum SP-D levels had significantly higher 6-month exacerbation frequency

($p=0.0001$; $r=0.59$). The other parameters such as BMI, cigarette pack/years, FEV1(%) and number of years on inhaled steroid treatment were not correlated with 6-month exacerbation frequency ($p=0.39$, $r=0.152$; $p=0.117$, $r=-0.278$; $p=0.177$, $r=-0.241$; $p=0.137$, $r=0.294$ respectively).

Multiple linear regression analyses were conducted after adjusting for age, cigarette pack/years, BMI, FEV1 (L), FEV1(%), number of years on inhaled steroid treatment, serum and induced sputum SP-D levels; only serum SP-D levels were found to be significantly associated with acute exacerbation frequency ($p=0.0001$). Sputum surfactant protein D level was found to be significantly associated with number of years on inhaled steroid treatment ($p=0.0001$). Serum surfactant protein D level was significantly related with 6 month exacerbation frequency ($p=0.0001$) (Table 5).

Discussion

In this study, we investigated the relationships between local and systemic SP-D levels, and course of COPD by evaluating serum and induced sputum SP-D levels. In the literature review, no study including both induced sputum and serum SP-D measurement in COPD patients has been found according to our knowledge.

Induced sputum analysis has been recently recognized as a valuable method for revealing the pathogenesis of inflammatory airway diseases such as COPD and asthma, and monitoring the activity and treatment response in these pathologies.¹⁰⁻¹³ Currently, induced sputum is recognized to reflect lower respiratory tract inflammation.^{10,13} Therefore, we preferred to use induced sputum specimens, also known as cost-effective diagnostic tool, in evaluating the courses of local and systemic inflammation in COPD.

Previous studies have demonstrated a positive correlation between cigarette consumption (pack/year) and serum SP-D levels. Serum SP-D concentrations have been found to be higher in current smokers than in ex-smokers.^{2,14} In our study, among COPD patients, there was a negative correlation between induced sputum SP-D levels and cigarette consumption (pack/year), whereas serum SP-D levels and cigarette consumption (pack/year) showed a positive correlation.

The comparison of induced sputum SP-D levels among three groups revealed no statistically significant difference. Sputum SP-D concentrations of Group 2 were lowest among study groups. Furthermore, 50% of patients in Group 2 were currently active smokers. Inhaled corticosteroid treatment was more common in Group 3 due to increased airway obstruction level and exacerbation frequency of severe and very severe COPD patients. Sputum SP-D levels were significantly different between patients with and without inhaled corticosteroid therapy in the present study. Moreover, significant correlation was also found between number of years on inhaled corticosteroid treatment and induced sputum SP-D levels in linear regression analysis. These results also support the fact that the use of inhaled corticosteroids indirectly contributes to the local SP-D levels in a positive way.¹⁵ Ishikawa et al. found increased induced sputum SP-D levels in 28 COPD patients compared to subjects with prolonged cough.¹⁶ They included patients with mild, moderate and severe COPD patients, and subjects with prolonged cough as control group and did not mention the medications of the subjects. Different results might be due to the fact that study

populations and medications in the study by Ishiwaka et al. were different from those in present study.

In COPD patients, serum SP-D levels and FEV1 show a negative correlation, whereas lung SP-D levels and FEV1 exhibit a slightly positive correlation.³ In the present study, serum SP-D levels were negatively correlated with FEV1(%) and group 3 had the highest serum SP-D levels among study groups. Group 2 had higher serum SP-D levels than Group 1, although, these differences did not reach to significance level. We believe that low number of patients in all groups was a limitation for the statistical comparison.

We had a higher number of males than females in study groups (F/M:11/49). In a recent study COPD rate was reported as four times higher in males than females in our country and total smoking, biomass, and occupational exposure were also found to be overwhelmingly higher in males than females (16.1% and 3.9% respectively).¹⁷ Therefore, these results could be attributed to a higher incidence of COPD in males as higher incidence of smoking and environmental/occupational exposure in our country.

Acute exacerbations that are observed during the course of the COPD are significant causes of morbidity and mortality.^{18,19} Some COPD patients exhibit a higher acute exacerbation frequency mostly due to the infections of tracheobronchial tree. Some studies demonstrate that increased airway inflammation incidence may have a role in the elevated acute exacerbation frequency.¹⁸ Our patients were followed up for 6 months for acute exacerbations. In 20 (50%) of our COPD patients in group 2 or 3, the acute exacerbation frequency varied between 1 and 3 within a 6 month follow-up period. 85% of 20 patients with a history of exacerbation were moderate, severe, and very severe COPD cases. This finding is consistent with the fact that raised airway inflammation increases the frequency and number of acute exacerbations.

In advanced COPD patients especially with frequent acute exacerbations, markers of systemic inflammation such as cytokines, chemokines, and acute phase proteins have been used.¹⁸⁻²⁰ SP-D, has also been proposed to be a lung-specific biomarker in COPD cases.²¹ Elevated serum SP-D levels can show the poor health status of COPD patients within a 3 month period.³ Also Shakoori TA et al. demonstrated in COPD patients higher levels of serum SP-D levels during acute exacerbation than during stable period.²² In our study, we determined a significant relationship between serum SP-D level and number of acute exacerbations within a 6 month period. In addition, we strengthen our hypothesis in linear regression analysis and found that the only significant determinant of 6 month exacerbation frequency was serum SP-D. These findings also suggest that SP-D level may be a lung-specific biomarker that can be used for monitoring COPD and its progression.

Limitations

The limitations of our study were the unequal number of female and male patients, the absence of a non-smoker healthy control group, and the failure to convince higher number of patients to participate in the study. Further studies with larger sample sizes are needed to confirm and explore the findings of the present study.

Conclusions

In conclusion, we believe that our preliminary study demonstrates a significant relationship between serum SP-D and COPD exacerbation frequency which suggests that serum SP-D level may be used as a lung-specific biomarker during the follow-up and progression of COPD.

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Wireless Capabilities Key in Choosing Blood Analysis System

Chris Campbell

When Children's Hospital Central California (CHCC), a specialty pediatric medical center, was looking to upgrade its POCT system, an extensive investigation was launched to study everything from patient needs to technology to how much it would cost per test.

Kevin Kitzmiller, POCT Coordinator Department of Pathology and Laboratory Medicine, for the CHCC, said this "complex process" was necessary to take advantage of the latest advances in blood analysis technology.

It turns out that the CHCC began investigating POCT way back in the late 1980s.

"As more and more patient-care providers began requesting bedside testing," Kitzmiller said, "it became clear that easy-to-perform tests that could provide timely test results along with immediate clinician access to these results would likely play a significant role in the delivery of health care in the future."

According to Kitzmiller's findings, by the mid-1990s, technologic advances and the availability of the first generation of POCT devices paved the way for CHCC to incorporate point-of-care blood gas, and electrolyte testing into its health-care system.

Kitzmiller said CHCC derived similar process improvements with POCT as those found by Theodore Bailey and colleagues in a four-year study at Methodist Clinical Laboratory Services, which was published in 1997. "In addition, we realized multiple patient-care benefits associated with time-sensitive testing throughout the health-care system."

Requested tests from patient-care providers were actually performed in a timely manner at the patient's bedside, and gained immediate access to critical test results, he said, and testing of freshly collected blood samples at the point of care eliminated the errors often introduced to tests for pH, blood gases, glucose, lactate, and ionized calcium by metabolic activity within the blood sample and exposure of the sample to ambient air that is inherent to performing tests at a remote laboratory location.

Patient throughput has also improved through the use of POCT in the emergency department and busy outpatient sites.

"By eliminating the need for patients to make trips to the laboratory for blood draws and care providers having to wait for the laboratory to receive a sample and return a test result,

patient visits were shortened," Kitzmiller said. "More than just convenience, this efficient patient throughput improved patient care and business efficiency while increasing patient access to CHCC's very specialized and busy outpatient clinics."

The center's study found that more patients were seen each day and patients were able to schedule appointments at earlier dates.

So with the CHCC needing to upgrade its POCT system, the process was heavily influenced by the needs of the patient population it served, Kitzmiller said.

"Children with medical problems require specialized care that enables a rapid recognition of their immediate medical needs," Kitzmiller said. "In a pediatric population, rapid turnaround times are required for emergent situations with minimal blood loss to the patient."

The system would be required to accommodate a large demand for results, including more than 1,000 operators, as it would be placed in all NICUs, including satellite NICUs located within 3 general hospitals in 3 other central California cities, the pediatric intensive care unit, surgery, cardiac catheterization, transport, and emergency departments, and all inpatient acute care units.

"After examining several options, we chose the epoc blood analysis system," Kitzmiller said. "Its wireless capabilities and low cost per test were deciding factors in our purchasing decision."



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