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BILIRUBIN/LACTIC ACID TESTING
CO-OXIMETRY
BLOOD GAS ANALYSIS
SURVIVING SEPSIS

The Clinical Utility of Bilirubin Testing with ABGs in the Neonatal Setting

Doug Wilder, RRT

Introduction

Jaundice is a yellowish discoloration of the whites of the eyes, skin and mucous membranes caused by deposition of bile salts (bilirubin) in these tissues. Increased bilirubin in neonates and premature infants, if left untreated can cause mental retardation and death. In jaundice of newborns this occurs when total bilirubin values are greater than 12 mg/dL.[1] This condition is known as hyperbilirubinema. Jaundice is common in 25 - 50 % of all full term neonates and there is an increased occurrence in premature babies, that is infants born after a gestation period of less than 37 weeks. It is important to determine if this condition is due to physiologic conditions which is normal or an underlying pathologic condition which is abnormal and requires immediate intervention.[2]

Pathology

Bilirubin is a biproduct of red cell breakdown. The total bilirubin is metabolized into two biproducts, carbon monoxide and unconjugated bilirubin. Once released into the blood stream the unconjugated bilirubin is transported to the liver for conversion. The unconjugated bilirubin enters the liver and undergoes a series of reactions with glucose and oxygen. The converted conjugated form of bilirubin is then removed from the neonate or infant.

Contributory factors to hyperbilirubinemia in neonates and premature infants are poor liver function due to liver development, increased red cell volume and reduced oxygen or decreased glucose levels due to delayed lung development. The result can be an increased level of bilirubin in the blood stream. And since unconjugated bilirubin is not water soluble but is very soluble in fat, the excess bilirubin is deposited in the fatty tissues, mucous membranes and especially brain tissue.[2]

Discussion

With the increasing number of cases of hyperbilirubinemia in neonates and premature infants, the American Academy of Pediatrics and JCAHO guidelines recommend transcuteanous monitoring of all neonates and premature infants for hyperbilirubinema. They require any monitoring value that excesses 12 mg/dL to be verified by an accepted clinical chemistry method.[3] By running a complete ABG panel with metabolites this enables the healthcare provider to determine the root cause of hyperbilirubinema and immediately map the best course of treatment by not only assessing the bilirubin level but also by assessing the glucose, PO_2 and O_2 saturation.

Recommendation

The cobas b 221 blood gas system correlates with accepted clinical chemistry methods for bilirubin testing and can provide a much larger clinical picture from just one blood draw reducing blood loss and improving patient care and outcomes at the point-of-care.

References

1 Clinical Guide to Lab Tests, Third Edition, Nobert Tietz, M.D., 1995
2 Basic Pathology, Stanley L. Robbins, M.D., 1976
3 JCAHO Sentential Event Alert, Issue 31 August 2004

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The Clinical Utility of Lactic Acid Testing with ABGs in the Neonatal Setting: A Case Study

Doug Wilder, RRT

Case

A 19 year old female presented to the hospital with increasing labor pains and delivered an otherwise normal 3 lb neonate. The neonate was placed under an infant warmer with an Oxyhood at 100% O_2.

After a period of one hour the patient's respiratory rate increased to 60 with mild retractions noted.

A blood gas was ordered and run on the Roche cobas b 221 blood gas system.

The following results were reported:

Parameter	Reported Value	Neonatal Normal Ranges
pH	7.331	7.35 – 7.50
PCO_2	44.3	35 – 45
PO_2	225.0	50 – 80
HCO_3	22.9	22 – 26
tHb	20.5	13 – 22
SO_2	99.5%	< 90
Glu	60	80 – 120
Lac	6.2	< 2.0

Assessment

The patient had a normal SO_2 of 99.5% normal PCO_2, normal HCO_3, and all electrolytes were in normal range. Based on ABG values and physical appearance, the patient appeared normal with increased respirations attributed to its premature condition. Upon closer review of the ABG results along with the lactic acid level of 6.2 mmol which is three times the upper limits of the normal range, the patient was diagnosed with Infant Respiratory Distress Syndrome. This syndrome increases the breathing rate in response to incomplete lung development characterized by reduced amounts of lung surfactant, cyanosis, the formation of a glassy membrane over the alveoli and pulmonary collapse. As respiration increases inspiratory muscles work harder to provide oxygen. The increased muscle activity results in utilization of glucose and increase in lactic acid in the bloodstream due to the inefficiency of the neonatal liver to convert the lactic acid to pyruvic acid.

Treatment

The patient was transferred to the NICU, administered bicarbonate, glucose, surfactant and placed on nasal CPAP overnight. The nasal CPAP was removed the next day.

Conclusion

Lactic acid and glucose as part of a neonatal ABG panel provides greater diagnostic capabilities in assessing and treating Infant Respiratory Distress Syndrome and related conditions.

Recommendation

All NICU blood gas analyzers should have the ability to run lactic acid and glucose like the Roche cobas b 221 system. All neonatal blood gas panel should include lactic acid and glucose as a standard of care in the neonatal setting.

The Clinical Utility of Lactic Acid Trending with ABGs in the Critical Care Setting: A Case Study

Doug Wilder, RRT

Introduction

With today's blood gas technology such as the Roche cobas b 221 blood gas system healthcare providers can trend any four of the eighteen parameters including metabolites such as glucose and lactic acid. This provides a diagnostic platform for a number of clinical applications. For example trending lactic acid gives the clinician the ability to not only monitor the level of lactic acid but also the ability to intervene early on in cases of tissue hypoxia, sepsis and the onset of myocardial infarction. The following study is a case in point.

Case

A 65 year old female presented to ED with the following clinical findings: shortness of breath, evaluated temperature 101, blood pressure 110/70, swollen ankles. The patient also has a history of COPD and CHF. The patient was given bronchodilator therapy, diuretics, chest x-ray and a blood gas was drawn at 14:39 with the following results:

pH	7.31
$PaCO_2$	50
PO_2	55
HCO_3	28.8
Lac	1.2

The patient was admitted to the hospital and placed on oxygen, bronchodilator therapy, treatment for CHF and antibiotic therapy. A second blood gas was drawn at 20:55 on LPM with the following results:

pH	7.32
$PaCO_2$	48
PO_2	74
HCO_3	14.2
Lac	8.8

After the results were called to the physician the patient was placed on non-invasive ventilation overnight. At 07:59 another blood gas was drawn with the patient 40% O_2 with the following results:

pH	7.35
$PaCO_2$	45
PO_2	80
HCO_3	16.1
Lac	7.4

At this point the patient seemed to be responding to the therapy. At 12:30 the patient's oxygen saturation started to drop and another blood gas was run with the following results:

pH	7.31
$PaCO_2$	55
PO_2	60
HCO_3	10.1
Lac	13.3

Following this blood gas, the patient was moved to the intensive care unit placed on 100% oxygen via mask and another blood gas was drawn to 13:52 with the following results:

pH	7.30
$PaCO_2$	65
PO_2	59
HCO_3	15.3
Lac	13.8

Now the patient was placed on a ventilator and an infectious disease physician was consulted. At 15:15 another blood gas was drawn with the following results:

pH	7.35
$PaCO_2$	50
PO_2	80
HCO_3	10.2
Lac	15.1

At 18:30 a final blood gas was drawn with the following results:

pH	7.35
$PaCO_2$	50
PO_2	84
HCO_3	14
Lac	18.9

The patient was transferred to another facility.

Treatment

At the new facility the patient was placed on the ventilator for several more days and treated for a septic pulmonary infection and finally discharged 2 weeks later.

Conclusion

The respiratory staff had received several in-services on lactic acid prior to the admission of this patient. This knowledge and training was instrumental in providing the physicians with trending data that improved patient care and resulted in a positive patient outcome. Any critically ill patient should have blood gases with electrolytes and a direct measurement of lactic acid. Trending should be considered in cases where sepsis, tissue hypoxia and myocardial infraction are suspected. The hospital should consider blood gas lactic acid testing and trending as a standard of care when dealing with critically ill patients.

Point-of-Care Lactate Testing as a Predictor of Mortality in a Heterogeneous Emergency Department Population

Audwin Joseph Garcia, Robert L. Sherwin, Robert N. Bilkovski.

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Background: Point-of-care (POC) lactate testing has been shown to correlate with serum measurements of lactate. In certain disease states, early lactate measurement is recommended.

Objective: To demonstrate that addition of POC lactate testing predicts mortality better than traditional clinical and laboratory markers.

Methods: This was a post-hoc analysis of a data set from a prospective, double-blind cohort study involving a convenience sample of heterogeneous patients presenting to an urban emergency department (ED). Patients presenting in cardiac arrest were excluded. POC lactate level R4 mmol/L (POC4) was compared with several clinical and biological values. Using descriptive statistics, we analyzed the impact of systemic inflammatory response syndrome (SIRS) criteria and POC4 on mortality rates. Logistic regression for mortality analysis was performed on POC4, systolic blood pressure, shock index, anion gap, base excess, and serum bicarbonate concentration. A composite score (the lactate-SIRS product, or LSP) involving the cross-product of the number of SIRS criteria (#SIRS) and POC was calculated. Likelihood ratios for in-hospital mortality were also calculated for #SIRS, LSP (R8), and POC4.

Results: Data were collected from 116 patients. Mortality for the entire population was 15%. POC <4 mmol/L mortality was 7.1% and POC4 mortality was 36.7%. Patients with 3 and 4 SIRS criteria had mortality rates of 16% and 33.3%, respectively. With the addition of POC4 to 3 and 4 SIRS criteria, mortality increased to 33.3% and 100%. Logistic regression demonstrated the POC4 to be the only variable to predict mortality independently ($p = 0.049$). Calculated positive likelihood ratios (LRs) for R2 SIRS criteria, LSP, and POC4 were 1.2, 2.25, and 3.3, respectively.

Conclusions: POC lactate testing is more useful than other clinical or laboratory results for predicting death in a heterogenous ED population. POC lactate added to SIRS criteria defines a population with a greater mortality than SIRS criteria alone.

CO-Oximetry Q&A

An interview with Larry Healy, Blood Gas Marketing Manager

What new or improved analysis tools are available for co-oximetry?
In the critical care setting, spectroscopic analysis of hemoglobin and its derivatives (co-oximetry), in combination with blood gas analysis, provides immediate, actionable information about oxygen transport in human blood. The accuracy of the hemoglobin and bilirubin results depends on the performance of the co-oximetry technology.

The co-oximetry module of the Roche cobas b 221 blood gas system measures both hemoglobin derivatives and bilirubin (spectrophotometrically, in the visible spectrum range [460nm to 660nm]). Absorbance of the sample is measured at a total of 512 discrete wavelengths. The concentrations of hemoglobin, hemoglobin derivates and bilirubin are determined by applying an accepted mathematical algorithm.[1] This enables the cobas b 221 system's co-oximetry technology to detect the presence of light-absorbing substances not covered by the reference spectra and to prevent incorrect values due to interfering substances from being reported.[3] This advanced co-oximetry design helps improve the accuracy of patient test results, which is demonstrated by a high correlation with results from accepted clinical chemistry test methods.[2]

References

1 cobas b 221 reference manual version 8.0 pp 20, 21.
2 Rolinski, Boris et al. Evaluation of Total Bilirubin Determination in Neonatal Whole-Blood Samples by Multiwavelength Photometry on the Roche OMNI S Point-of-Care Analyzer. Point-of-Care, The Journal of Near Patient Testing and Technology; Volume 4, March 2005.
3 Schweiger, Gerd. Technical Aspects: Determination of Bilirubin on the Roche OMNI S, International Evaluation Workshop, October , 23 2003, Deutschlandsberg, Austria.

What is the impact of improved analysis for patient care?
Blood gas operators that use the cobas b 221 blood gas system facilitate patient diagnosis and expedite treatment decision-making at point-of-care by delivering up to 18 test results – including blood gases, electrolytes, tHb, O2Hb, HHb, COHb, MetHb, Hct, bilirubin, glucose, lactate and BUN – from one 210 µL sample.* This menu, coupled with automated acid-base mapping trending and patient trending, provides clinicians in the ER, ICU and other critical care environments with immediate actionable information for improved health outcomes. The trending display and result display help answer questions for the healthcare provider: "Is my patient getting better? Has the patient condition changed?"

* Roche cobas b 221 Instruction for Use v. 8.0

What's the latest in the Surviving Sepsis campaign?
In the Journal of Critical Care Medicine [Volume 36, No. 1], the Internal guidelines for management of severe sepsis and septic

shock: 2008 special article was published to provide an update to the original Surviving Sepsis Campaign clinical guidelines published in 2004. [See the summary in this supplement – Ed.]

Key level 1 recommendations, include early recognition of sepsis, early goal-directed resuscitation of the septic patient during the first 6 hours after recognition and administration of broad-spectrum antibiotic therapy within 1 hour of diagnosis.

What results are you starting to see?
In an effort to recognize sepsis in its early stage, healthcare providers in the ED, ICU and NICU are trending metabolites such as glucose and lactate along with other blood gas parameters at the point-of-care along with the recommended laboratory tests from the Surviving Sepsis Campaign clinical guidelines published earlier this year.

There have been several case studies presented this year in this journal that illustrate the clinical utility of such testing and trending of results at the point-of-care.

Discuss advances in bilirubin testing and/or applications of results.
In the August/September issue of the journal Neonatal Intensive Care, a neonatal application utilizing bilirubin, glucose and ABGs was presented. [See this supplement.] With the increasing number of cases of hyperbilirubinemia in neonates and premature infants, the American Academy of Pediatrics and JCAHO guidelines recommend transcutaneous monitoring of all neonates and premature infants for hyperbilirubinema. They require any monitoring value that excesses 12 mg/dL to be verified by an accepted clinical chemistry method. By running a complete ABG panel along with metabolites, this enables the healthcare provider to determine the root cause of hyperbilirubinema and immediately map the best course of treatment by not only assessing the bilirubin level but also by assessing the glucose, PO_2 and O_2 saturation.

What are the latest benchmarks you are aiming for in research and development?
Roche blood gas systems have had a history of continuous innovation with a number of firsts such as: The first to offer a blood gas analyzer with electrolytes, the first to incorporate a photometry to determine tHb and Hb derivatives, the first to design an analyzer with a full color touch screen, liquid calibration eliminating gas tanks and Auto QC, the first to utilize SMART reagents with RF technology and zero maintenance electrodes and the first with polymer thick film technology sensors for metabolite detection. Research and development is now incorporating these advances to create a new generation blood gas system that meets and exceeds the needs of the decentralized areas of the hospital to provide actionable information at the point-of-care.

BLOOD GAS ROUNDTABLE

Roche Diagnostics Corporation

Response provided by Larry Healy, Blood Gas Marketing Manager.

How does your product help implement quality control in the point-of-care setting?
The Roche cobas b 221 blood gas system offers customers the tools necessary to implement quality control and meet compliance standards at the point-of-care. The cobas b 221 blood gas system's Auto QC has onboard capacity for up to 40 days of QC material. The flexibility of cobas b 221 onboard QC programming provides user-defined programs to meet specific QC protocols. For example, the program manager can program the analyzer to run range studies for the new lot of QC while the current lot of QC is in use. With 20 gigabytes of onboard storage, the cobas b 221 system maintains an average of five years' worth of QC, calibration and patient data for review and reporting. Our real-time peer review QC program, eQAP, helps ensure performance and regulatory compliance. OMNILink Instrument manager software provides real-time screen sharing and allows immediate access to QC, calibration and system status of all connected decentralized systems.

What features of your product help reduce error rates?
To help avoid unnecessary errors, the cobas b 221 blood gas system has a run mode that reduces the number of screens the operator uses. This is called the POC or Point-of-Care mode. The mode is configured by the RT director, lab manager and POC coordinator and helps provide ease of operation to up to 3,000 qualified users in the decentralized setting. The barcode reader allows for patient IDs to be entered automatically, helping to avoid transcription errors. Barcode entry of all consumables helps document lot numbers, stores ranges and helps prevent use of reagents past their manufacturer or onboard expiration date, assures correct lot number, ranges and expiration date. QC and calibration default settings for all parameters prevent patient samples from being run until QC and calibration are in range. Continuous self-monitoring of consumables tracks expiration dates and automatically helps prevent the use of expired controls, reagents and electrodes. And continuous electronic monitoring provides operational status between calibration intervals, alerting the operator to the problem or re-running a calibration to maximize uptime.

What educational materials do you provide to help avoid equipment usage error?
Roche provides a number of educational materials to help ensure proper use of the system. The cobas b 221 blood gas system comes with onboard video tutorials to instruct the user in the proper operation of the system. A Short Instructions for Use guide supports the tutorials and a customer-based training CD ROM, along with the Instruction for Use and Reference manuals, provides detailed instructions to help avoid equipment usage error.

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Life needs answers

How can automated acid-base mapping help you deliver a more precise diagnosis and therapy monitoring?

Accurate, graphical acid-base mapping on the **cobas b** 221 blood gas system can help clinicians:

- Rapidly identify metabolic and respiratory acid-base disturbances without the need for a calculator
- Efficiently assist physicians to monitor the effectiveness of therapy
- Easily distinguish between compensatory responses and mixed acid-base disturbances
- Differentiate between acute and chronic patient conditions in complex environments such as the ED or ICU

Automated acid-base mapping on the cobas b 221 system creates a graphical representation of patient results.

Roche Diagnostics

How does your product provide for accuracy in measurement?

In addition to the details described above, Roche cobas b 221 customers can be reassured that results are available only from valid calibrations; that errors are detected and, when possible, corrected before alerting the operator; and that QC is automatically run on time to help ensure only accurate measurements are available. In the critical care setting, spectroscopic analysis of hemoglobin and its derivatives (co-oximetry), in combination with blood gas analysis, provides immediate, actionable information about oxygen transport in human blood. The accuracy of the hemoglobin and bilirubin results depends on the performance of the co-oximetry technology. The co-oximetry module of the Roche cobas b 221 blood gas system measures both hemoglobin derivatives and bilirubin (spectrophotometrically, in the visible spectrum range (460nm to 660nm)). Absorbance of the sample is measured at a total of 512 discrete wavelengths. The concentrations of hemoglobin, hemoglobin derivates and bilirubin are determined by applying an accepted mathematical algorithm.[1] This enables the cobas b 221 system's co-oximetry technology to detect the presence of light-absorbing substances not covered by the reference spectra and to prevent incorrect values due to interfering substances from being reported.[3] This advanced co-oximetry design helps improve the accuracy of patient test results, which is demonstrated by a high correlation with results from accepted clinical chemistry test methods.[2]

References

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2 Rolinski, Boris et al, Evaluation of Total Bilirubin Determination in Neonatal Whole-Blood Samples by Multiwavelength Photometry on the Roche OMNI S Point-of-Care Analyzer, Point-of-Care, The Journal of Near Patient Testing and Technology; Volume4, March 2005

3 Schweiger, Gerd. Technical Aspects: Determination of Bilirubin on the Roche OMNI S, International Evaluation Workshop, October , 23 2003, Deutschlandsberg, Austria.

What features of your product help clinicians interpret blood gas data?

Blood gas operators that use the cobas b 221 blood gas system facilitate patient diagnosis and expedite treatment decision-making at point-of-care by delivering up to 18 test results — including blood gases, electrolytes, tHb, O2Hb, HHb, COHb, MetHb, Hct, bilirubin, glucose, lactate and BUN—from one 210 µL sample.* This menu, coupled with automated acid-base mapping trending and patient trending, provides clinicians in the ER, ICU and other critical care environments with immediate actionable information for improved health outcomes. The trending display and result display help answer questions for the healthcare provider: "Is my patient getting better? Has the patient condition changed?" [* Roche cobas b 221 Instruction for Use v. 8.0.]

Does your equipment readily connect with most hospital information systems; if so, which ones; are there any problematic issues with connectivity?

The cobas b 221 blood gas system with IT solutions has been designed to provide connectivity for both centralized and decentralized settings. These solutions enable connectivity with most hospital LIS/HIS systems.

- OMNILink – Software that provides the key operator command and control of instruments even if they are remotely placed in decentralized settings.
- DataCare POC – Data management platform recognized for its clinical and report capabilities for all centralized and decentralized customers through HL7.
- MAS RALS Plus – Single IT connectivity and data management solution recognized for its multiple point-of-care program functionality for decentralized customers.
- Middleware – Direct interface for current Roche chemistry customers in the laboratory to an HIS/LIS.
- Direct Interface – uni-directional output capability from the cobas b 221 blood gas system.
- A dedicated team of agents are available to resolve interface questions.

How does your product address patient safety at the point-of-care?

Operators of the cobas b 221 blood gas analyzer have access to a broad menu of analytes from one sample. This minimizes the amount of blood or number of blood draws a patient needs to generate accurate results. The ability to provide acid-base map trending and patient result trending can help operators inform healthcare providers, potentially resulting in enhanced patient treatment and outcomes. Patient safety goals, as announced by the Joint Commission, include accurate patient identification. The use of barcodes for patient ID and the incorporation of an admission, discharge, transfer data stream can help ensure that the right results are run and reported on the right patient. The cobas b 221 system is designed with a turn-and-dock sample port, without an external needle, to help minimize exposure of the operator to bio-hazardous samples in the critical care setting. This port allows sample aspiration from a syringe and capillary or injection from a syringe. The sample port is automatically rinsed before and after the sample is introduced. All sample waste is pumped to closed wastecontainer housed in the system for proper disposal and helps protect the operator from potential biohazards.

What technical support programs do you have in place to maximize equipment uptime?

The cobas b 221 blood gas system with OMNILink Instrument Manager software allows RT directors, Lab managers and POC coordinators to meet compliance requirements with centralized command and control of analyzer operation, documentation and reporting. The system provides remote real-time monitoring of calibration data, QC, maintenance and operator activity of all connected analyzers from one central location—without interrupting analyzer workflow. With this software and available site permissions, the Roche call center can also access and share the analyzer's screen. This helps facilitate faster troubleshooting and resolution, maximizing analyzer uptime for patient result reporting.

Blood Gas Analysis: The Pros and Cons of Point-of-Care Testing

Beth Wegerbauer

Since the first system was invented in 1957, blood gas analysis has revolutionized clinical medicine and patient care. During the 1960s, blood gas analysis became almost universally available, and blood gases were considered "the most important laboratory test for critically ill patients," according to a www.bloodgas.org article by Dr John Severinghaus, inventor of the blood gas analysis system.

Blood gas tests determine whether a patient has enough oxygen in his blood and whether or not that blood is pH balanced. The tests reveal levels of pH (indicating blood's acid/base status), pO_2 (how much oxygen is dissolved in blood), PCO_2 (how much carbon dioxide gas is dissolved in blood), as well as other parameters like O_2 saturation and HCO_3. Blood samples are collected from an artery, usually the radial artery in the wrist, but also can be taken from the brachial or femoral arteries. For infants, capillary blood may be taken from a heelstick. In addition to arterial sampling, blood gas panels can be ordered on blood drawn through a central venous line to estimate cardiac output.

Blood gas analysis is performed by trained health-care providers in a hospital, emergency room, or large clinical laboratory. These tests are "stat" tests, meaning they should be done as quickly as possible after sample collection. For arterial blood gases (ABGs), the collected sample degrades quickly and, if any testing delay is expected, it should be kept on ice and rewarmed later for accurate analysis. If, after sample collection, any air bubbles remain in the top of the syringe, they must be removed. After the needle is capped, the syringe is then placed on ice and transported for immediate analysis.

To reduce transport as well as turnaround time, especially for the most seriously ill patients, many analyzers are located in or near selected patient care settings, such as intensive care units (ICUs), operating rooms (ORs) and emergency departments. Because ABGs are the most common tests ordered in ORs and ICUs, immediate results are critical. Therefore, many healthcare providers are choosing blood gas analysis that is performed via point-of-care testing (POCT), using handheld units that give a quick result at the bedside or operating table. Such handheld units can be used in non-traditional settings such as rural clinics and in ambulance or helicopter transport situations.

POCT can offer several benefits, most importantly the instant implementation of treatment decisions rather than waiting, sometimes for several hours, for the results from a more traditional central laboratory-based analyzer. By the time those results become available, the condition of the patient may have changed. In the case of POCT, immediate results mean immediate care. Specimen transport time is minimized as no staff have to leave the OR or bedside to carry a sample to the lab. In some cases, there may even be a reduction in pneumatic tube traffic. POCT also reduces the risk of preanalytical errors that may accompany traditional laboratory testing, such as the handling, labeling, and transport of samples.

Another advantage to POCT is a decrease in phlebotomy-related blood loss, an important feature in settings like the OR or ICU, where blood conservation is key. Some analyzers used in central laboratories have menus that require a minimum sample size, whereas POCT devices use smaller samples.

The reality of POCT, despite all of these benefits, is that the advantages of POCT are lost when a sample is mishandled or testing is done incorrectly. Therefore, implementation of point-of-care tests inherently demands structure and regulation (per JCAHO and CLIA regulation) to ensure quality results. POCT places a burden on department and site directors to properly identify the training needs of non-laboratorians, and to ensure that they are met. Additionally, non-laboratorian staff trained on POCT methods must be monitored following the trainings in order to insure their competency with the tests. Training a diverse non-laboratorian staff (including MDs, RNs and RTs) across multiple shifts, instruments, methods, and then monitoring their competency over time is a formidable task which increases with each test introduced and with department size. It is easier to decentralize the test itself than it is to decentralize the specialized laboratory knowledge and training that goes with each test.

Lack of adequate documentation may be considered another drawback to POCT. Results from POCT devices usually appear on a screen with temporary printouts available. Those results may get mishandled or misplaced and never find their way into the patient's permanent medical record. This lack of documentation may also have an affect on potential reimbursement issues.

As healthcare providers must consider each advantage and disadvantage to POCT, its technology continues to develop. The analyzers are getting faster, smaller, easier to use, and show the ability to perform accurate testing with smaller blood samples.

Of course, the decision to use POCT instead of a central laboratory depends on various factors unique to a particular hospital or health-care setting. One thing is for certain, the transfer of blood gas analysis from the laboratory to the ICU and OR will profoundly effect critical care, just as the introduction of laboratory-based blood gas analyzers did more than 40 years ago.

Beth Wegerbauer is Contributing Editor to Bio-Medicine and a medical writer and editor with 12 years of experience covering the clinical laboratory field. This article has been edited for Respiratory Therapy's readers.

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Life needs answers

Why is a 1-minute bilirubin test especially important in the NICU?

Timely monitoring of critical newborns can reduce the risk of potentially life-threatening diseases and enhance neonatal care for hyperbilirubinemia.

Kernicterus is a serious condition that can occur in infants with elevated bilirubin levels (>20 mg/dL).[1] The **cobas b** 221 blood gas system can help reduce the risk of kernicterus by delivering fast, actionable bilirubin results in the NICU.

The cobas b 221 system delivers bilirubin results in 1 minute or less.

Roche Diagnostics

Bilirubin Determination in Neonatal Blood by Multiwavelength Photometry

A Case Study with the Roche OMNI S Point-of-Care Analyzer

The authors investigated the performance of the Roche OMNI S blood gas analyzer. Results were evaluated in comparison to routine clinical chemistry methods and another point-of-care testing device. Four hundred ninety-six heparinized blood samples were drawn from newborns up to 39 days of age. An aliquot of the sample was measured on the Roche OMNI S and on another analyzer. Plasma was prepared from the remaining sample for routine lab analysis. Results showed agreement between bilirubin concentrations measured in whole blood on the Roche OMNI S, the other analyzer, and the routine comparison analyzers. Direct spectrophotometric measurement of bilirubin gave results that compared well with those from routine clinical chemistry methods. The advantages of the Roche were the very small volume of blood required and the brief turnaroud time. The authors concluded: "The Roche OMNI S analyzer represents a suitable method for monitoring neonatal jaundice at the point-of-care."

Background

Hyperbilirubinemia in the newborn is caused by increased hemoglobin turnover combined with immature hepatic glucuronidation. About 60% of infants manifest with jaundice in their first weeks, and just over 30% of breastfed infants have bilirubin levels above 12 mg/dL, with neonatal plasma bilirubin concentrations in neonates rising to as high as 40 mg/dL. The condition usually resolves by itself in the first weeks. However, at higher concentrations, bilirubin can enter the central nervous system, causing kernicterus, exacerbated by immaturity of the blood-brain barrier and impaired binding to albumin. As a result, jaundiced infants need to be monitored for bilirubin levels from every 4 hours to every other day. Thus, monitoring at the point-of-care, using small volumes of whole blood, needs to be fast and reliable.

The information in this article is from the Symposium Article, Evaluation of Total Bilirubin Determination in Neonatal Whole-Blood Samples by Multiwavelength Photometry on the Roche OMNI-S Point-of-Care Analyzier, by Boris Rolinski, MD; Anthony O. Okorodudu, PhD; Gerald Kost, MD; Markus Roser, MD; Jiaxi Wi, MD, PhD; Ada Goerlach-Graw, PhD and Helmut Kuester, MD. The original article was published in Point of Care, Volume 4, Number 1, March 2005, © 2005 by Lippincott William & Wilkins. The information has been edited for our readers. Access to the complete article is available from Williams & Wilkins via Medline and other search engines.

Methodology

This was a multicenter study in four hospital NICUs, UC Davis, UTMB, Universitatsklinikum Greifswald, and Stadtisches Krankenhaus Munhen-Harlaching, Munich. Four hundred ninety-six blood samples were analyzed; the age of 353 newborns ranged up to 39 days, with a median age of four days. Sample types were venuous and venous/capillary. An aliquot was measured immediately on the Roche and the other similar analyzer and the samples taken to the lab, where bilirubin in plasma was measured by wet chemistry and dry chemistry. Ten sets of comparison data were obtained, and assessments of imprecision, inaccuracy and recovery were performed with four materials.

Results

Bilirubin concentrations covered the range needed for diagnostic decisions (0.2 to 23.7 mg/dL). There was good agreement between bilirubin measured on the Roche OMNI S and those from comparison methods. Small differences were observed in values measured with some of the comparison methods, but ultimately, the data sets fit correctly. The wet chemistry methods correlated well, once adjustments were made for methods of testing. Dry chemistry bilirubin also correlated closely with the Roche OMNI S. The authors report that, taken together, the differences between testing methods were minor and much less than those reported in daily routine. The authors also noted that quality control is a difficult issue when using whole-blood samples, and that daily preparation of whole-blood controls may have increased minor imprecisions.

Conclusions

Bilirubin measurement has been well-known to be unreliable, and until recently, there has been no standardization between assays of various reagent suppliers, with target values varying widely, depending on the assay used. Direct photometry of neonatal whole-blood samples in a blood gas analyzer provides fast, reliable results from a small sample volume. This study demonstrated that the accuracy and precision of the Roche OMNI S met the expectations for a routine laboratory method and allowed for a reliable determination of bilirubin concentrations in neonatal whole-blood samples at the point-of-care.

Surviving Sepsis

The surviving sepsis campaign is a cooperative effort by numerous sponsoring organizations to provide clinical management guidelines. This article provides an update on the original guidelines, published in 2004. The article on which this feature is based is titled: Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008, © 2007 by the Society of Critical Care Medicine. It was published in Crit Care Med 2008 Volume 36, Number 1, © Lippincott Williams & Wilkins. The information below has been edited for the readers of Respiratory Therapy and this supplement. For more information regarding the article, type "Surviving Sepsis Campaign" for an internet search or e-mail Dellinger-Phil@CooperHealth.edu.

Overview

Guidelines were assembled through consensus conferences of 55 international experts and the Surviving Sepsis committee, which made a series of strong to weak recommendations. The authors emphasized that the grade of strong or weak is considered of greater clinical importance than a difference in letter level of quality of evidence. Recommendations are grouped into those directly targeting severe sepsis, recommendations targeting general care of the critically ill patient that are considered high priority in severe sepsis, and pediatric considerations. Key recommendations include: early goal-directed resuscitation of the septic patient during the first 6 hours after recognition; blood cultures prior to antibiotic therapy; imaging studies to confirm potential source of infection; administration of broad-spectrum antibiotic therapy within an hour of diagnosis of septic shock or sepsis; reassessment of antibiotic therapy with microbiology and clinical data to narrow coverage, as needed; 7–10 days of antibiotic therapy guided by clinical response; source control with attention to the balance of risks and benefits of the chosen method; administration of either crystalloid or colloid fluid resuscitation; fluid challenge to restore mean circulating filling pressure; reduction in rate of fluid administration with rising filing pressures and no improvement in tissue perfusion; vasopressor preference for norepinephrine or dopamine to maintain an initial target of mean arterial pressure ≥ 65 mm Hg; dobutamine inotropic therapy when cardiac output remains low despite fluid resuscitation and combined inotropic/vasopressor therapy; stress-dose steroid therapy given only in septic shock after blood pressure is identified to be poorly responsive to fluid and vasopressor therapy; and recombinant activated protein C in patients with severe sepsis and clinical assessment of high risk for death. In the absence of tissue hypoperfusion, coronary artery disease, or acute hemorrhage, target a hemoglobin of 7–9 g/dL; a low tidal volume and limitation of inspiratory plateau pressure strategy for ALI and ARDS; application of at least a minimal amount of positive end-expiratory pressure in acute lung injury; head of bed elevation in mechanically ventilated patients unless contraindicated; avoiding routine use of pulmonary artery catheters in ALI/ARDS; to decrease days of mechanical ventilation and ICU length of stay, a conservative fluid strategy for patients with established ALI/ARDS who are not in shock; protocols for weaning and sedation/analgesia; using either intermittent bolus sedation or continuous infusion sedation with daily interruptions or lightening; avoidance of neuromuscular blockers, if possible; institution of glycemic control targeting a blood glucose < 150 mg/dL after initial stabilization; equivalency of continuous veno-veno hemofiltration or intermittent hemodialysis; prophylaxis for deep vein thrombosis; use of stress ulcer prophylaxis to prevent upper GI bleeding using H2 blockers or proton pump inhibitors; and consideration of limitation of support where appropriate.

Recommendations for pediatric severe sepsis include: greater use of physical examination therapeutic end points; dopamine as the first drug of choice for hypotension; steroids only in children with suspected or proven adrenal insufficiency; a recommendation against the use of recombinant activated protein C in children.

There was strong agreement among a large cohort of international experts regarding many level 1 recommendations for the best current care of patients with severe sepsis. Evidenced-based recommendations regarding the acute management of sepsis and septic shock are the first step toward improved outcomes for this important group of critically ill patients.

Severe sepsis and septic shock are major healthcare problems, affecting millions of individuals around the world each year. The speed and appropriateness of therapy administered in the initial hours after severe sepsis develops are likely to influence outcome. In 2004, an international group of experts in the

diagnosis and management of infection and sepsis, representing 11 organizations, published the first internationally accepted guidelines that the bedside clinician could use to improve outcomes in severe sepsis and septic shock. These guidelines represented Phase II of the Surviving Sepsis Campaign (SSC), an international effort to increase awareness and improve outcomes in severe sepsis. Joined by additional organizations, the group met again in 2006 and 2007 to update the guidelines document using a new evidence-based methodology system for assessing quality of evidence and strength of recommendations. Most of the recommendations are appropriate for the severe sepsis patient in both the ICU and non-ICU settings. The committee noted that the greatest outcome improvement can be made through education and process change.

Severe sepsis: resuscitation: The authors recommend the protocolized resuscitation of a patient with sepsis-induced shock, defined as tissue hypoperfusion (hypotension persisting after initial fluid challenge or blood lactate concentration equal to or greater than 4 mmol/L). This protocol should be initiated as soon as hypoperfusion is recognized and should not be delayed pending ICU admission. During the first 6 hrs of resuscitation, the goals of initial resuscitation of sepsis-induced hypoperfusion should include all of the following as one part of a treatment protocol: central venous pressure (CVP): 8–12 mm; Hg; mean arterial pressure (MAP) ≥ 65 mm Hg; urine output ≥ 0.5 mL.kg^{-1}. hr $^{-1}$; central venous or mixed venous oxygen saturation ≥ 70% or ≥ 65%, respectively (Grade 1C). Early goal-directed resuscitation has been shown to improve survival for emergency department patients presenting with septic shock in a randomized, controlled, single-center study. Resuscitation directed toward the previously mentioned goals for the initial 6-hr period of the resuscitation was able to reduce 28-day mortality rate. In mechanically ventilated patients or patients with known pre-existing decreased ventricular compliance, a higher target CVP of 12–15 mm Hg is recommended to account for the impediment to filling. Similar consideration may be warranted in circumstances of increased abdominal pressure or diastolic dysfunction. Recently published observational studies have demonstrated an association between good clinical outcome in septic shock and MAP ≥ 65 mm Hg as well as central venous oxygen saturation ($ScvO_2$, measured in superior vena cava, either intermittently or continuously) of ≥ 70%. Many recent studies support the value of early protocolized resuscitation in severe sepsis and sepsis-induced tissue hypoperfusion. Studies of patients with shock indicate that SvO_2 runs 5–7% lower than central venous oxygen saturation ($ScvO_2$) and that an early goal directed resuscitation protocol can be established in a non-research general practice venue. Technologies currently exist that allow measurement of flow at the bedside. Future goals should be making these technologies more accessible during the critical early resuscitation period and research to validate utility. These technologies are already available for early ICU resuscitation.

During the first 6 hrs of resuscitation of severe sepsis or septic shock, if $S_{CV}O_2$ or SvO_2 of 70% or 65% respectively is not achieved with fluid resuscitation to the CVP target, then transfusion of packed red blood cells to achieve a hematocrit of ≥ 30% and/or administration of a dobutamine infusion (up to a maximum of 20 µg.kg^{-1}.min^{-1}) should be utilized to achieve this goal.

Diagnosis: Obtaining appropriate cultures before antimicrobial therapy should be initiated if such cultures do not cause significant delay in antibiotic administration. At least two blood cultures should be obtained prior to antibiotics with at least one drawn percutaneously and one drawn through each vascular access device, unless the device was recently inserted. Cultures of other sites such as urine, cerebrospinal fluid, wounds, respiratory secretions, or other body fluids that may be the source of infection should also be obtained before antibiotic therapy if not associated with significant delay in antibiotic administration. Imaging studies should be performed promptly to confirm a potential source of infection. Sampling of potential sources of infection should occur as they are identified; however, some patients may be too unstable to warrant certain invasive procedures or transport outside of the ICU. Bedside studies are useful in these circumstances.

Antibiotic therapy: IV therapy should be started within the first hour of recognition of septic shock and severe sepsis. Appropriate cultures should be obtained before initiating antibiotic therapy, but should not prevent prompt administration of antimicrobial therapy. Recently used antibiotics should generally be avoided. Clinicians should be cognizant of the virulence and growing prevalence of oxacillin (methicillin) resistant Staphylococcus aureus (ORSA or MRSA). Clinicians should also consider whether Candidemia is a likely pathogen when choosing initial therapy. When deemed warranted, the selection of empiric antifungal therapy will be tailored to the local pattern of the most prevalent Candida species, and any prior administration of azoles drugs. Risk factors for candidemia should also be considered when choosing initial therapy. Because patients with severe sepsis or septic shock have little margin for error in the choice of therapy, the initial selection of antimicrobial therapy should be broad enough to cover all likely pathogens. There is ample evidence that failure to initiate appropriate therapy correlates with increased morbidity and mortality. An experienced physician or clinical pharmacist should be consulted to ensure that serum concentrations are attained that maximize efficacy and minimize toxicity. The antimicrobial regimen should be reassessed daily. The duration of therapy should be between 7 to 10 days; longer courses may be appropriate in special cases. Clinicians should be aware that blood cultures will be negative in more than 50% of cases of severe sepsis or septic shock, yet many of these cases are very likely caused by bacteria or fungi. Thus, the decisions to continue, narrow, or stop antimicrobial therapy must be made on the basis of clinician judgment and clinical information.

Source control: The principles of source control include a rapid diagnosis of the specific site of infection, and identification of a focus of infection amenable to source control measures. Foci of infection readily amenable to source control measures include an intra-abdominal abscess or gastrointestinal perforation, cholangitis or pyelonephritis, intestinal ischemia or necrotizing soft tissue infection, and other deep space infection such as an empyema or septic arthritis. The source control objective should be accomplished with the least physiologic upset possible. The selection of optimal source control methods must weigh benefits and risks of the specific intervention as well as risks of transfer. Source control interventions may cause further complications such as bleeding, fistulas, or inadvertent organ injury. Surgical intervention should be considered when lesser interventional approaches are inadequate, or when diagnostic uncertainty persists despite radiological evaluation.

Fluid therapy: The conferees recommend fluid resuscitation

with either natural/artificial colloids or crystalloids. Fluid resuscitation should initially target a CVP of at least 8 mm Hg (12 mm Hg in mechanically ventilated patients). A fluid challenge technique should be applied, wherein fluid administration is continued as long as the hemodynamic improvement continues. Fluid challenge must be clearly separated from simple fluid administration.

Vasopressor therapy is required to sustain life and maintain perfusion in the face of life-threatening hypotension, even when hypovolemia has not yet been resolved. Some patients may require vasopressor therapy to achieve a minimal perfusion pressure and maintain adequate flow. Supplementing end points such as blood pressure with assessment of regional and global perfusion, such as blood lactate concentrations and urine output, is important. Adequate fluid resuscitation is a fundamental aspect of the hemodynamic management of patients with septic shock, and should ideally be achieved before vasopressors and inotropes are used, but using vasopressors early as an emergency measure in patients with severe shock is frequently necessary. When that occurs great effort should be directed to weaning vasopressors with continuing fluid resuscitation. Dobutamine is the first-choice inotrope for patients with measured or suspected low cardiac output in the presence of adequate left ventricular filling pressure (or clinical assessment of adequate fluid resuscitation) and adequate mean arterial pressure. Septic patients who remain hypotensive after fluid resuscitation may have low, normal, or increased cardiac outputs. Therefore, treatment with a combined inotrope/vasopressor such as norepinephrine or dopamine is recommended if cardiac output is not measured.

Intravenous hydrocortisone should be given only to adult septic shock patients after blood pressure is identified to be poorly responsive to fluid resuscitation and vasopressor therapy. The ACTH stimulation test should not be used to identify the subset of adults with septic shock who should receive hydrocortisone. Patients with septic shock should not receive dexamethasone if hydrocortisone is available. The daily addition of oral fludrocortisone (50 µg) is suggested if hydrocortisone is not available and the steroid that is substituted has no significant mineralocorticoid activity. Clinicians should wean the patient from steroid therapy when vasopressors are no longer required. Doses of corticosteroids comparable to > 300 mg hydrocortisone daily should not be used in severe sepsis or septic shock for the purpose of treating septic shock, nor should corticosteroids be administered in the absence of shock.

Recombinant Human Activated Protein C: Adult patients with sepsis induced organ dysfunction associated with a high risk of death should receive rhAPC if it is deemed safe to do so. Patients with low risk of death should not.

Blood product administration: Red blood cell transfusion should occur when hemoglobin decreases to < 7.0 g/dL (< 70 g/L) to target a hemoglobin of 7.0–9.0 g/dL (70–90 g/L) in adults. Erythropoietin should not be used as a specific treatment of anemia associated with severe sepsis, but may be used when septic patients have other accepted reasons for administration of erythropoietin such as renal failure-induced compromise of red blood cell production. In patients with severe sepsis, it is suggested that platelets should be administered when counts are < 5000/mm^3 (5×10^9/L) regardless of apparent bleeding.

Supportive Therapy

In mechanical ventilation of sepsis-induced ALI and ARDS, it is recommended that clinicians target a tidal volume of 6 ml/kg (predicted) body weight. The use of lung protective strategies for patients with ALI is supported by clinical trials and has been widely accepted, but the precise choice of tidal volume for an individual patient with ALI may require adjustment for such factors as the plateau pressure achieved, the level of PEEP chosen, the compliance of the thoracoabdominal compartment and the vigor of the patient's breathing effort. Some clinicians believe it may be safe to ventilate with tidal volumes higher than 6 ml/kg PBW as long as the plateau pressure can be maintained ≤ 30 cm H_2O. High tidal volumes that are coupled with high plateau pressures should be avoided in ALI/ARDS. Clinicians should use as a starting point the objective of reducing tidal volumes over 1–2 hrs from its initial value toward the goal of a "low" tidal volume (≈ 6 mL per kilogram of predicted body weight) achieved in conjunction with an end-inspiratory plateau pressure ≤ 30 cm H_2O. No single mode of ventilation has been consistently shown advantageous when compared with any other that respects the same principles of lung protection. It is recommended that hypercapnia be allowed in patients with ALI/ARDS if needed to minimize plateau pressures and tidal volumes, and that PEEP be set so as to avoid extensive lung collapse at end-expiration. It is also recommended that NIV only be considered for ALI/ARDS patients with mild-moderate hypoxemic respiratory failure. It is also recommended that a weaning protocol be in place, and mechanically ventilated patients with severe sepsis undergo spontaneous breathing trials on a regular basis to evaluate the ability to discontinue mechanical ventilation when they are arousable, hemodynamically stable, meet low ventilatory and end-expiratory pressure requirements, and meet F_IO_2 requirements that could be safely delivered with a face mask or nasal cannula. The use of the pulmonary artery catheter for patients with ALI/ARDS is discouraged.

Sedation, Analgesia, Neuromuscular Blockage: A growing body of evidence indicates that the use of protocols for sedation of critically ill ventilated patients can reduce the duration of mechanical ventilation and ICU and hospital length of stay. Currently, however, there is not a clearly superior sedation evaluation methodology against which these sedation scales can be evaluated. The administration of intermittent sedation, daily interruption, and retitration or systemic titration to a predefined end point have been demonstrated to decrease the duration of mechanical ventilation. Although NMBAs are often administered to critically ill patients, their role in the ICU setting is not well defined. No evidence exists that maintaining neuromuscular blockade in this patient population reduces mortality or major morbidity.

Glucose Control

The campaign recommends that, following initial stabilization, patients with severe sepsis and hyperglycemia who are admitted to the ICU receive IV insulin therapy to reduce blood glucose levels. Targeted glucose levels should be in the < 150 mg/dl range. Blood glucose should be monitored every 1-2 hours until glucose values and insulin infusion rates are stable, and then every 4 hours thereafter. The consensus on glucose control in severe sepsis was achieved at the first committee meeting and subsequently approved by the entire committee. Two observational studies report an association of mean glucose levels with reductions in mortality, polyneuropathy, acute renal failure, nosocomial bacteremia, and number of transfusions,

and suggest a glucose threshold for improved mortality lies somewhere between 145 and 180 mg/dl. Several factors may affect the accuracy and reproducibility of point-of-care testing of blood capillary blood glucose, including the type and model of the device used, user expertise, and patient factors including hematocrit (false elevation with anemia), PaO_2, and drugs. Some protocols may be more effective than other protocols. Thus, the use of a validated and safe intensive insulin protocol is important not only for clinical care but also for the conduct of clinical trials to avoid hypoglycemia, adverse events, and premature termination of these trials before the efficacy signal, if any, can be determined. Further study of protocols that have been validated to be safe and effective for controlling blood glucose concentrations and blood glucose variation in the severe sepsis population are needed.

The surviving sepsis study also discusses renal replacement, bicarbonate therapy, deep vein thrombosis prophylaxis, stress ulcer prophylaxis, and selective digestive tract decontamination.

Limitation of support: Advance care planning, which includes a communication of likely and realistic goals, is also recommended. "Too frequently, inadequate physician/family communication characterizes end-of-life care in the ICU. The level of life support given to ICU patients may not be consistent with their wishes. Early and frequent caregiver discussions with patients who face death in the ICU and with their loved ones may facilitate appropriate application and withdrawal of life-sustaining therapies. A recent RCT demonstrated reduction of anxiety and depression in family members when end-of-life meetings were carefully planned, conducted, included advance care planning, and provided relevant information about diagnosis, prognosis, and treatment."

Pediatric considerations: The overall mortality from severe sepsis in children is much lower than in adults, estimated at about 10%. Antibiotics should be administered within an hour of the identification of severe sepsis. Children normally have a lower blood pressure than adults, and fall in blood pressure can be prevented by vasoconstriction and increasing heart rate. Therefore, blood pressure by itself is not a reliable end point for assessing the adequacy of resuscitation.

Glycemic control: Infants are at risk for developing hypoglycemia when they depend on intravenous fluids. This means that a glucose intake of 4–6 $mg.kg^{-1}.min^{-1}$ or maintenance fluid intake with glucose 10%/NaCl containing solution is advised. Associations have been reported between hyperglycemia and an increased risk of death and longer length of stay. A recent retrospective PICU study reported associations of hyperglycemia, hypoglycemia, and glucose variability with length of stay and mortality rates. Insulin therapy to avoid long periods of hyperglycemia seems sensible in children as well, but the optimal goal glucose is not known. However, continuous insulin therapy should only be done with frequent glucose monitoring in view of the risks for hypoglycemia.

Conclusion

The sepsis campaign noted that optimum treatment of severe sepsis and septic shock "is a dynamic and evolving process. New interventions will be proven and established interventions, as stated in the current recommendations, may need modification. This publication represents an ongoing process. The Surviving Sepsis Campaign and the consensus committee members are committed to updating the guidelines on a regular basis as new interventions are tested and published in the literature." The committee went on to note growing evidence that protocol implementation associated with education and performance feedback does change clinician behavior and may improve outcomes in and reduce costs in severe sepsis. The Campaign also offers significant program support and educational materials at no cost to the user, at survivingsepsis.org.

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Roche Diagnostics

Pleural Fluid pH Analysis in the Blood Gas Laboratory

This article is specifically addressing the role of the Respiratory Care Practitioner (RCP) in the role of body fluid analysis and specifically pleural fluid pH. Before we take an in depth look at this analyte we must first look at the pathophysiology of this pneumonic process.

Pleural effusion is the accumulation of fluid in the chest between the lung and the chest cavity. Normally there is no space between the parietal pleura, which covers the chest wall, and the visceral pleura, which covers the lung. The normal fluid that is present facilitates the mechanics of ventilation that maintains a negative intrapleural pressure therefore allowing the lungs to remain expanded. For a diagnosis of pleural effusion, 75% of those patients will have a diagnosis made at the onset of the clinical findings presented. 25% of those patients will have a positive cytology or positive culture of the aspirate analyzed. Fifty percent of those patients have a presumptive diagnosis prior to the laboratory findings. Fifteen to 20% of the patients will not have a diagnosis made prior to diagnostic studies. The history and physical (H & P) exam are critical in guiding the evaluation of the pleural effusion and it is imperative that an extensive H & P be obtained from the patient. Chest examination demonstrates dullness to percussion and diminished breath sounds, which may be, but are not necessarily gravity dependent. Confirmation of a pleural effusion may include an Anterior-Posterior radiograph, lateral decubitus whereby the patient lays on their side, and/or CT of the chest and abdomen. The interpretive physician is looking for clear radiographic findings that suggest a pleural space infiltrate. The definitive diagnosis is a thoracentesis whereby the physician performs a needle aspirate to a local anesthetized area of the chest wall and inserts the needle into the pleural space now occupied by an infiltrate. The sample must be obtained under anaerobic conditions, iced, and analyzed within two hours preferentially through the "gold standard" Blood Gas Analyzer (BGA). If the sample is not iced, in vitro glycolysis will occur resulting in a false low pH. If the sample is exposed to room air, then a false high pH will occur due to gas equilibration. The sample, by most clinical standards of medical practice, should include a diagnostic order for LDH, Protein, Glucose, Amylase, Cell Count, Cytology, and cultures in addition to pH analysis. There are about 1 million cases per year of pleural effusions and primarily are subcategorized as transudate (movement of fluid into the pleural space due to imbalance of hydrostatic and oncotic pressures) or exudative (caused by inflammation of the lung or pleura) effusions. Trasudative effusions normally have a pH 7.40-7.55 and exudative effusions normally have a pH less than 7.45. Categorically, most of the effusions are by congestive heart failure, malignancy, infections, and pulmonary emboli, requiring urgent evaluation and treatment. It is interesting to note that 25% of the pleural effusions are resolved within 48 hours with aggressive diuretic therapy. Cirrhosis, pulmonary embolus, infection, malignancy, immunologic disorders, lymphatic abnormalities, non-infectious inflammation and nephritic syndrome are other common etiologies of transudative pleural effusions. Decreased glucose in the pleural fluid may indicate a malignancy, empyema, and a complicated parapneumonic effusion, or tuberculosis to name just a few disease entities. Normal pH of pleural fluid is 7.60. American College Chest Physicians (ACCP) and the British Thoracic Society agree that pH values less than 7.20 are a critical value with a parapneumonic infection and will require immediate drainage via chest tube insertion. 20-25% of pneumonia patients have a parapneumonic infection and will resolve with aggressive antibiotic therapy. Decreased glucose with a decreased pH signals the possible diagnosis of a malignant pneumonic process. A pH less than 7.28, with a malignant pneumonic process, has a 39% mortality after 3 months. Two negative cytologys with a low pH indicate possible tuberculosis or rheumatoid pleurisy.

Several analytical methods have historically been performed over the years. The methods that have been and currently are being utilized are the pH meter, pH indicator strips, and the Blood Gas Analyzer (BGA). In studies reported in Chest (1998), pH meters and pH indicator paper reported significantly higher mean pH than the BGA; therefore the clinical and research findings as stated earlier in this article were that the BGA is the gold standard for pleural fluid pH analysis. Blood Gas Laboratories must meet regulatory standards as set forth by CLIA and other regulatory agencies such as College of American Pathologists (CAP). The method of testing falls into three CLIA classifications of waived, moderately complex, and highly complex categories. The BGA fall into either the moderately complex or high CLIA complexity category depending upon whether the BGA has undergone 510K FDA clearance for analyzing pleural fluid pH. It is each laboratory's responsibility to determine if their BGA has met the FDA clearance for analyzing pleural fluid pH. If your instrument is 510 K FDA cleared, then CLIA recognizes this instrument's analyte as a moderately complex instrumentation. If the BGA is not FDA cleared which is referred to as "off-label," then the analyte is considered to be reported from high complexity instrumentation and must meet the 6 point high complexity CLIA category. Pleural fluid pH analyte reported from a moderate complex BGA has less regulatory requirements from CLIA as opposed to an "off-label" BGA that must meet more CLIA regulations. CLIA does not recognize the waived category for pleural fluid pH so to use litmus paper you must meet CAP guidelines of proficiency testing, daily QC, method validation, and personnel training and competency validations. The use of litmus paper is compromised by the fact that the test results cannot be reported in hundredths (X.XX) and the accuracy needs to be reported to this mathematical expression, as accuracy is the critical factor in reporting pleural pH. Litmus paper relies on colorimetric determinations and has a falsely reportable high value as previously mentioned in Chest. PH meters expose the anaerobic sample to room air and have falsely high reportable pH as well. Pleural fluid samples when analyzed through the BGA should be cautiously analyzed with the addition of a clot catcher between the syringe and the BGA sample inlet port or an internal clot catcher as the pleural sample presents a small risk of BGA clotting contaminates much like other blood samples introduced

into a BGA such as neonatal or patients with polycythemia. Critical values must be determined to meet CAP standards and documented like any other critical value in your laboratory. We have established any value less than 7.20 as a critical result and must be called and read back to the ordering physician to meet CLIA, CAP, JCAHO, and other accreditation standards.

Body fluids must meet proficiency testing just like any other analyte and can be ordered from the CAP web site. These are performed twice a year and reported using similar proficiency testing methodologies.

In summary, pH pleural fluid testing provides the physician with a valuable diagnostic test that complements the clinical decisions necessary to provide excellence in patient outcomes. Not only does the diagnostic testing provide a diagnostic tool, but also from the financial aspect it is a revenue stream within your departmental operations.

Literature Review

A look at recent papers of interest to our readers.

Hemoglobin Estimation at Point-of-Care

The paper, Point-of-Care estimation of hemoglobin in neonates was published this year in the Archives of Disease in Childhood, a study by L.E. Hinds, C.L. Brown and S.J. Clark with the Paediatric Department, Barnsley Hospital Foundation Trust, Barnsley, UK , [Arch Dis Child Fetal Neonatal Ed 2007 Sep;9295):F378-80 Epub 2007 Feb 14, © Arch Dis Child].

The objective of the study was to evaluate whether measurement of hemoglobin concentration in neonates using point-of-care testing agrees with laboratory measurement. One hundred twenty-seven paired blood samples taken from babies on a neonatal intensive care unit for full blood count and blood gas analysis by point-of-care testing were reviewed according to current practice. A comparison was made between the laboratory and blood gas analyzer hemoglobin measurements to assess limits of agreement and look for any systematic difference. Results from blood samples were reviewed and comparisons made between laboratory and point-of-care testing of hemoglobin concentrations. The mean laboratory hemoglobin concentration was 155 g/l (range 30-226 g/l); the mean point-of-care testing hemoglobin concentration was 157 g/l (range 30-228 g/l). The mean (SD) difference between paired samples was 2 (11) g/l; 95% CI -4.0 to 0.1 g/l; and limits of agreement -23 to 19 g/l. The authors concluded that the blood gas analyzer on the neonatal unit gave a useful estimation of hemoglobin concentration compared with laboratory measurement, with smaller sample volume. A follow-up letter in a subsequent issue of Arch Dis Child [2008 Apr;93(4):353-4] noted that POC estimation was useful not just for hemoglobin. The respondents Owen J. Arthurs and A.W. Kelsall with the NICU at Rosie Hospital in Cambridge, noted that "blood gas analyzers have become more sophisticated and are now able to perform many different analyses on a single blood sample including electrolytes, calcium, glucose, lactate and bilirubin measurement." The respondents came to their conclusions based on their assessment of the Roche OMNI S blood gas analyzer used in their NICU. Their hospital's system includes the Ascensia Elite XL blood glucometers, bilimeters and hematocrit readers, against laboratory tests and across a wide range of hematological markers.

POC and Critical Care

Crit Care Med, in an older study from the archives, published: Multicenter study of oxygen-insensitive handheld glucose point-of-care testing in critical care/hospital/ambulatory patients in the United States and Canada, by G.J. Kost, H.T. Vu, J.H. Lee, P. Bourgeois, F.L. Kiechle, C. Martin, S.S. Miller, A.O. Okorodudu, J.J. Podczasy, R. Webster and K.J. Whitlow, with the University of California, Davis. [Crit Care Med 26 (3):581-90, Wolters Kluwer/ Lippincott Williams & Wilkins.]

In this study, the primary objectives were to introduce a new glucose dehydrogenase (GD)-based electrochemical biosensor for point-of-care testing; determine the oxygen-sensitivity of GO- and GD-based electrochemical biosensor test strips; and evaluate the clinical performance of the new GD-based glucose meter system in critical care/hospital/ambulatory patients. Multicenter study sites compared glucose levels determined with GD-based biosensors to glucose levels determined in whole blood with a perchloric acid deproteinization hexokinase reference method. One site also studied GO-based biosensors and venous plasma glucose measured with a chemistry analyzer. Biosensor test strips were used with a handheld glucose monitoring system. Bench and clinical oxygen sensitivity, hematocrit effect, and precision were evaluated. The study of 1,248 patients was performed at eight US medical centers and one Canadian medical center. The GO-based biosensor was oxygen-sensitive. The GD-based biosensor was oxygen-insensitive. GD-based biosensor performance was acceptable, with 96.1% of glucose meter measurements within a normative range compared with the whole-blood reference method results. With the GD-based biosensor, the percentages of glucose measurements that were not within the error tolerance were comparable for different specimen types and clinical groups. The authors concluded that the performance of GD-based, oxygen-insensitive, handheld glucose testing was technically suitable for arterial specimens in critical care patients, cord blood and heelstick specimens in neonates, and capillary and venous specimens in other patients. The authors recommended that physiologic changes, preanalytical factors, confounding variables, and treatment goals be taken into consideration when interpreting glucose results, especially in critically ill patients, for whom arterial blood glucose measurements will reflect systemic glucose levels.

A related, more recent study by the same principle author and others looked at point-of-care testing in critical care. [Multicenter study of whole-blood creatinine, total carbon dioxide content,

and chemistry profiling for laboratory and point-of-care testing in critical care in the United States, G.J. Kost, H.T. Vu, M. Inn, R. DuPlantier, M. Fleisher, M.H. Kroll, J.C. Spinosa, UC Davis, Health System and Point-of-Care Testing Center for Teaching and Research, published in Crit Care Med 2000 Jul;28(7):2379-89, © Wolters Kluwer/Lippincott Williams & Wilkins.] The objectives were to introduce a creatinine biosensor and a total carbon dioxide content method for whole-blood measurements, to evaluate the clinical performance of a new transportable analyzer that simultaneously performs these two and six other tests (Na+, K+, Cl-, glucose, urea nitrogen, and hematocrit), and to assess the potential of the new analyzer for point-of-care testing in critical care by comparing results obtained by nonlaboratory personnel and by medical technologists. Multicenter sites compared whole-blood measurements with the transportable analyzer to plasma measurements from the same specimens with local reference instruments. One site compared whole-blood results produced by nonlaboratory personnel vs medical technologists and evaluated day-to-day and within-day precision at the point-of-care at four medical centers in the US. Venous and arterial specimens were taken from 710 critically ill patients with a variety of diagnoses. Point-of-care testing was in the emergency room and operating room. The performance of the creatinine biosensor and the TCO_2 method was found to be acceptable for whole-blood samples. Comparisons of whole-blood results from the transportable analyzer and plasma results from the local reference instruments revealed analyte biases that may have been attributable to differences between direct whole-blood analyses and indirect-diluted plasma measurements and other factors. Performance of nonlaboratory personnel and medical technologists was equivalent for point-of-care testing in critical care settings. The authors concluded that a whole-blood analyzer should be useful when patient care demands immediate results.

Lab VS POC

Am J Crit Care recently published: Comparison of point-of-care and laboratory glucose analysis in critically ill patients, by T. Lacara, C. Domagtoy, D. Lickliter, K. Quattrocchi, L. Snipes, J. Kuszaj and M. Prasnikar, [Am J Crit Care 2007 Jul;16(4):336-46 (quiz); 2007 Nov;16(6):531-2 (author reply). The authors are with Rex Healthcare, Raleigh, NC, abstract and article © Am J Crit Care].

The objectives were to examine agreement between point-of-care and laboratory glucose values and to determine effects of hematocrit, serum carbon dioxide, and mean arterial pressure on the accuracy of point-of-care values. Point-of-care values were compared with laboratory values. In 49 critically ill patients, blood was obtained first from a catheter for laboratory testing and then from the catheter and via fingerstick for point-of-care testing. Bias, precision, and root-mean-square differences were calculated to quantify differences in values between the 2 methods. A t test was used to determine differences in values between each point-of-care blood source and the laboratory value. Multiple regression analysis was used to determine if serum level of carbon dioxide, hematocrit, and/or mean arterial pressure significantly contributed to the difference in bias and precision for the point-of-care blood sources. Mean laboratory glucose level was 135 (SEM 5.3, range 58-265) mg/dL. In point-of-care testing, bias ± precision and root-mean-square differences were 2.1 ± 12.3 and 12.35, respectively, for fingerstick blood and 0.6 ± 10.6 and 10.46 for catheter blood. Values for point-of-care and laboratory tests did not differ significantly. For catheter samples, hematocrit and serum carbon dioxide contributed significantly to difference scores between point-of-care and laboratory values ($P < .001$). The authors concluded that glucose values for point-of-care samples did not differ significantly from laboratory values. For catheter samples, hematocrit and serum carbon dioxide levels accounted for the difference between point-of-care and laboratory glucose values.

Intraoperative POC and Lab Testing

Anesth Analg recently published: Changes in utilization of intraoperative laboratory testing associated with the introduction of point-of-care testing devices in an academic department, by D.B. Wax and D.L. Reich, Department of Anesthesiology, Mount Sinai School of Medicine, New York, [Anesth Analg 20007 Dec;105(6):1711-3, © Anesth Analg].

The authors tested the hypothesis that frequency of intraoperative blood testing (IBT) would increase in association with installation of POCT devices in our surgical suites. A retrospective analysis was made of 38,115 electronic anesthesia records for cases performed in the year before and the year after POCT installation. For each case, the frequency of IBT was tabulated and the change in frequency of IBT between the study periods was calculated for individual anesthesiologists, for the department as a whole, and for clusters of anesthetizing locations. For the department as a whole, there was no significant change between the before and after study periods in the 13% proportion of cases in which IBT was obtained. For cases in which IBT was used, there was no significant increase in the number of IBTs per case. The authors found no significant increase in the overall utilization of IBT associated with POCT presence in noncardiothoracic operating rooms.

More About Point-of-Care

The article, Cost-Benefit of Point-of-Care Blood Gas Analysis notes that point-of-care testing allows laboratory tests to be independent of hospital-based resources and power. This study indicated that the technology is cost-effective and can reduce stabilization times. The authors concluded, "The technology would be ideal for medical management during disasters." (Prehosp Disast Med 2000;15(3):s105.) Blood Gas Org reported, in its article, Laboratory Supervision of Point-of-Care Blood Gas Testing, that training in the use of POC yielded valuable results: "The... training of nurses and physicians has greatly improved and intensified the contacts between the laboratory and the wards concerned." The continuous monitoring of the instruments is considered a major improvement, both by the nurses performing the analyses and by the MLTs." (From the Blood Gas Org article, "Laboratory supervision of point-of-care blood gas testing," June 2000, Dirk Bernard, et al.)

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