Wednesday, July 29, 2015

Poster Session: 9:30 AM - 5:00 PM

Electrolytes/Blood Gas/Metabolites

B-041

Evaluation of GEM Premier 4000 Total Hemoglobin Test Accuracy Using Cyanmethemoglobin Reference Procedure and a Hospital Lab Reference Method

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Background: Whole blood total hemoglobin (tHb) measurement using Co-Oximetry methodology in hospital labs and at the point-of-care has become common practice for rapid evaluation of patients at-risk for bleeding or with suspected anemia. Reliability of tHb results is essential for patient care management and lack of inter-method harmonization of tHb results in hospital settings may cause confusion in tHb result clinical interpretation. Recently, differences in CO-Oximetry-derived tHb results using GEM Premier 4000 (Instrumentation Laboratory, Bedford, MA) versus Radiometer ABL 800 series analyzers (Radiometer, Westlake, OH) were identified and prompted enhanced efforts in tHb result harmonization. Cyanmethemoglobin (CNmetHb) based total hemoglobin (tHb) assay is recognized as a reference procedure by Clinical Laboratory Standards Institute (CLSI H15 A3) and International Council for Standardization in Hematology (ICSH). The GEM Premier 4000 tHb assay, similar to other CO-Oximetry analyzers, is traceable to CNmetHb procedure through its calibration reagents. CNmetHb procedure works well with hemoglobin standards and it has challenges with whole blood tHb measurements due to errors at different blood hemoglobin levels from turbidity or dilution issues from blood viscosity. Appropriate controls to minimize such errors in whole blood CNmetHb assay are implemented. The aim of this study was to evaluate GEM Premier 4000 tHb test accuracy in an industry setting compared with a CNmetHb reference procedure and in a hospital setting at 1 institution compared with Radiometer ABL 800 series analyzers.

Methods: At IL, lithium-heparinized blood was collected and the plasma to RBC ratio was adjusted to prepare five samples with increasing tHb concentration (range 3-21 g/dL). THb concentrations in the 5 samples were measured in triplicate using the CNmetHb reference procedure (CLSI H15A3) and GEM Premier 4000 analyzers. At the University of North Carolina (UNC) Hospital lab (Chapel Hill, NC), lithium-heparinized whole blood samples (n=110) sent to the lab for routine tHb testing were analyzed using Radiometer ABL 800 series analyzers, and residual whole blood from these samples was used for tHb measurement using GEM Premier 4000 analyzers.

Results: Linear regression analyses of tHb results yielded the following equations: [GEM 4000] = 1.001[CNmetHb] + 0.0947, (r2 = 0.9993, Range 3 -21 g/dL); [GEM 4000] = 0.9608[ABL 800] + 0. 4885, (r2 = 0.9868, Range 6.8 -16.7 g/dL). Bland Altman analysis of tHb results measured using GEM Premier 4000 compared with Radiometer ABL 800 series yielded a mean bias in 0.08 g/dL with a 95% confidence interval of ± 0.59 g/dL.

Conclusions GEM Premier 4000 tHb assay demonstrated excellent correlation compared with the CLSI and ICSH recognized CNmetHb reference procedure. Excellent correlation and good accuracy in tHb measurement was similarly observed between the GEM Premier 4000 and the Radiometer ABL 800 series tHb assays in a hospital setting. Taken together, these data indicate that using CO-Oximetry based tHb methods with calibration traceable to the CNmetHb reference procedure support inter-instrument harmonization of tHb results.

B-042

Evaluation of the Piccolo Xpress Implemented in an Ebola Bio-Containment Laboratory

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Background: The 2014 Ebola epidemic, the largest in history, revealed the need of medical institutions around the world to be able to provide medical care for patients potentially infected with highly contagious and dangerous infectious diseases. The University of Chicago Medicine (UCM) is one of fifty-five designated Ebola Treatment Centers in the United States by the Centers for Disease Control and Prevention. The challenge for UCM clinical laboratories is to provide quality laboratory results on highly virulent specimens with minimal risks to the medical technologists. The Piccolo Xpress (Abaxis, Union City, CA) is a small bench-top analyzer performs up to 14 chemistry tests on a single self-contained reagent disc. The complete test menu comprises of 31 different tests divided among 16 different panels.

Methods: The MetLac 12 (ALB, BUN, Ca, Cl-, CRE, GLU, K+, LAC, Mg, Na+, Phos, tCO2) and Hepatic Function (ALB, ALP, ALT, AST, DBIL, TBIL, TP) panels were evaluated and compared to the central lab's Roche Cobas 8000 chemistry analyzers. Precision studies were performed with low and high QC material (BioRad, CA) and linearity was assessed using linearity standards (Main Standards, ME; BRT, FL). Pooled patient samples were used in the interference studies and 51 plasma samples were used in the comparison study.

Results: The inter-assay precision for all assays varied from <0.01-16.4% CV for the low and high QC materials. The analytical measuring range for all analytes were linear (r2 = 0.9971-0.9999) over the testing range (ALB: 2.1-5.9 g/dL, BUN: 6-116 mg/dL, Ca: 4.4-13.6 mg/dL, Cl-: 89-135 mmol/L, CRE: 0.3-15.7 mg/dL, GLU: 28-701 mg/dL, K+: 1.9-7.3 mmol/L, LAC: 0.49-8.12 mmol/L, Mg: 0.6-6.5 mg/dL, Na+: 114-163 mmol/L, Phos: 1.2-14.8 mg/dL, tCO2: 11-39 mmol/L, ALP: 20-1758 U/L, ALT: 17-1400 U/L, AST: 16-1558 U/L, DBIL: 0.3-15.4 mg/dL, TBIL: 0.5-31.1 mg/dL, TP: 2.9-9.9 g/dL). Interference studies showed no significant interference for all analytes up to an H-index of 200 (except for LAC, DBIL, and TBIL) and an L-index of 212 (except for Phos and DBIL). Comparisons studies using Passing-Bablok linear regressions and Bland-Altman difference plots showed good overall agreement to the Cobas 8000 values except: ALB (y=0.85x+0.23), Ca (y =0.85x+1.38), Cl- (y=0.90x+14.10), Na+ (y=0.95x+6.90), tCO2 (y =1.20x-2.12), ALP (y=0.85x+0.16), ALT (y=0.89x+5.33), AST (y=0.93+8.80), and DBIL (y=0.56x+0.16). The calculated anion gap using the Piccolo Xpress values was significantly different from the central laboratory mainly due the positive biases in Cl- and tCO2. The reference ranges for ALB, Cl-, tCO2, AGAP, ALP, ALT, and AST required adjustment to account for the observed biases.

Conclusion: The overall analytical performance of the Piccolo Xpress is acceptable for use in a biocontainment laboratory. Despite the observed higher analytical imprecision and biases, the Piccolo Xpress has the additional advantages of having a small bench-top footprint, requiring a small sample volume in a self-contained reagent disc in ~13 minutes, minimal maintenance, and ease of operation.

B-043

Performance Evaluation of a New Fructosamine Assay to Measure Serum Glycated Protein on the High-Throughput ADVIA Chemistry Systems

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Background: Monitoring of glycemic status is important in diagnosis and monitoring of diabetes. The glycemic status of an individual can be assessed by measurements of fasting blood glucose, serum fructosamine (glycated protein), or glycated hemoglobin (HbA1c) for short term (daily), midterm (2-3 weeks), or longer (3-month average) periods. Fructosamine is formed by a nonenzymatic Maillard reaction between glucose and amino acid residues of proteins. During this glycation process, an intermediate labile Schiff base is produced which is converted to a more stable ketoamine (fructosamine) via an Amadori rearrangement. A new fructosamine assay [FRUC] has been developed for the measurement of serum or plasma fructosamine on the automated random access ADVIA® Clinical Chemistry Systems [Siemens]. The objective of this study was to evaluate the performance of this new assay on all ADVIA Chemistry Systems.

Methods: In the ADVIA Chemistry FRUC assay, sample is automatically pre-diluted (by 5x) and reacted with the first reagent (R1) for five minutes. The proteinase K in the reagent digests the serum glycated proteins. Fructosaminase and peroxidase in the second reagent (R2) then generates H_2O_2 and color, respectively, using the chromogen N-ethyl-N-sulphohydroxypropyl-m-toluidine (TOOS). The fructosamine concentration in a sample is determined from a linear calibration curve using Siemens ADVIA Chemistry Fructosamine Calibrator. The performance evaluation in this study included precision, interference, linearity, and correlation with a commercially available Diazyme glycated protein assay run on the Hitachi 717. Data were collected for all ADVIA Chemistry Systems (ADVIA 1200, ADVIA 1800, ADVIA 2400 and XPT*), which use the same ADVIA Chemistry FRUC reagent packs, calibrators, and commercial controls.

Results: The imprecision (total %CV) of the new ADVIA Chemistry assays with two-level commercial controls and six serum pools ranging from ~40 to ~750 µmol/L (n = 80) on all ADVIA Chemistry Systems was ≤2.9% (within-run) and 4.4% (total). The analytical range of the new assay is 30 - 1000 µmol/L. The assay correlated well with the Diazyme assay: ADVIA 1650 FRUC = 0.99 [Diazyme] - 13.1 (r = 0.995, n = 110; sample range: 40-737 µmol/L). The new assay demonstrated no interference (<10%) at a fructosamine level of ~150 µmol/L with unconjugated or conjugated bilirubin (5 mg/dL), hemoglobin (250 mg/dL), triglyceride (1000 mg/dL), albumin (6.1 g/dL), ascorbic acid (up to 10 mg/dL), glucose (2800 mg/dL), uric acid (50 mg/dL) and total protein - tested at approximately 490 µmol/L Fructosamine level - (8.4 g/dL). , Minimum on-system stability was 60 days with a calibration frequency of every 28 days.

Conclusion: The data demonstrates good performance of the FRUC assay on the high-throughput ADVIA Chemistry Systems from Siemens Healthcare Diagnostics.*Not available for sale in the U.S. Product availability may vary from country to country and is subject to local regulatory requirements.

B-044

Evaluation of Urine Performance on the VITROS® Cl- Slide Assay*

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Background

* The use of the VITROS Cl- Slide with urine specimens is in development

VITROS Chemistry Products Cl^- Slides (Chloride) quantitatively measure chloride (Cl-) concentration in serum and plasma using the VITROS 250/350/5,1 FS/4600 Chemistry Systems and the VITROS 5600 Integrated System. The VITROS Cl^- Slide is a multilayered, analytical element coated on a polyester support that utilizes direct potentiometry for measurement of chloride ions. Chloride is an essential electrolyte, and testing in urine is conducted to determine if there is an electrolyte imbalance. Testing is especially important in cases of persistent metabolic alkalosis where measured urine chloride levels are low.

Methods

We evaluated the accuracy of 81 patient urine samples (11 - 195 mmol/L) and 7 commercial Urine linearity fluids (1 - 316 mmol/L) diluted 1:1 with the VITROS Calibrator Kit 2, Level 1 on the VITROS 5,1 FS System compared to two commercial methods: titration using a Corning 926S Chloridometer and indirect potentiometry with the Chloride assay on the Siemen's ADVIA 1800 Chemistry System.

Results

The VITROS Cl^- Slides assay showed excellent correlation with both methods. VITROS 5,1 FS System = 0.989*Corning 926S + 3.08; (r) = 0.999 and VITROS 5,1 FS System = 1.001* ADVIA 1800 + 1.68; (r) = 0.997. Accuracy was also evaluated for 100 low chloride urine patient samples (5 - 50 mmol/L) run undiluted on the VITROS 5,1 FS System compared to the Siemen's ADVIA 1800 assay. The VITROS Cl^- Slides assay showed comparable correlation to the ADVIA 1800 assay as was observed in the previous assessment; VITROS 5,1 FS System = 1.053* ADVIA 1800 - 4.03; (r) = 0.987. A 5-day precision study conducted on the VITROS 350 and 5600 Systems with undiluted and diluted samples showed excellent precision with undiluted samples on both chemistry systems. Mean Chloride concentrations of 3.70 mmol/L, 9.99 mmol/L, 32.5 mmol/L, 97.1 mmol/L and 315.4 mmol/L resulted in within-laboratory percent coefficient of variation (%CV) of 2.0%, 0.81 %, 0.60%, 0.42%, and 0.67% respectively on the VITROS 5600 system.

Conclusion

The VITROS Cl^- Slides assay has exhibited good correlation with urine across a broad measuring range compared to commercial titration and indirect potentiometry methods. In addition excellent precision has been observed on the VITROS 350, 5,1 FS, and 5600 Systems with undiluted urine specimens.

B-045

Harmonization of ionized calcium levels in point-of-care blood gas analyzers

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Background: The measurement of ionized calcium has an important role in certain clinical settings such as primary hyperparathyroidism, cardiac and critical care, and patients undergoing major surgery. The aim of this study is to evaluate the differences of ionized calcium level among 6 manufacturers point-of-care blood gas analyzer and to check feasibility of harmonization mathematically.

Methods:A total of 6 kinds of point-of-care blood gas analyzer were used in this study for ionized calcium level measurement; Profile Critical Care Xpress (Nova Biomedical, USA), ABL 90 FLEX analyzer (Radiometer Medical), GEM Premier 3500 (Instrumentation Laboratory, USA), i-STAT System (Abbott Diagnostics), RAPIDPoint 500 Systems (Siemens Healthcare Diagnostics Inc.) and epoc Blood analysis System (Alere). Quality control materials provided by manufacturers were analyzed for 20 days to evaluate the precision according to the CLSI EP5-A2 guidelines. Ionized calcium levels were measured by each analyzer for 120 heparinized whole blood samples. The results were analyzed and compared with Deming regression and bias plot. Regression equation obtained from randomly allocated one group was applied for adjustment of results from another group.

Results: The total coefficients of variation (CV) of 6 instruments for the tested ionized calcium were less than 3.0%. Before adjustment, the slope, intercept and correlation coefficient of correlation equation were 0.881 to 1.124, -0.570 to 0.700, and 0.891 to 0.988, respectively. Adjustment of 6 analyzers made improvement in the slope, intercept, and correlation coefficient (1.011 to 1.054, -0.254 to -0.063, and 0.895 to 0.984, respectively). Three samples showed large bias (>10% of mean) before the adjustment, while all samples were within ±10% of mean after adjustment.

Conclusion:A majority of point-of-care blood gas analyzer showed excellent quality of performance of precision and correlation. This study demonstrates that harmonization may be accomplished technically by establishing adjustment to the overall mean values for a panel of patient samples.

B-046

Comparative precisions of intra-patient ICU blood gas results measured by paired GEM 4000's and Radiometer ABL800's

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Background: Over the last three decades, duplicate blood gas testing has been replaced by singlicate testing, usually by one of multiple blood gas instruments. Between-instrument variation can either falsely indicate trends or obscure real trends. We have developed a methodology that transforms sequential intra-patient results into biologic and analytic variation. We previously derived realistic biologic variation (s_b) parameters of blood gas analytes from ICU blood gas data (from two Radiometer 800 ABL Flex's[Copenhagen, Denmark]). We apply these results to derive the imprecision of two GEM 4000's (Instrumentation Laboratory, Bedford MA)

Methods: A repository provided arterial blood gas results generated by two GEM 4000's on ICU patients in 2012-2013 at Foothills University Hospital in Calgary, Alberta. As results were not linked to the analyzers' identity, sequential results appeared to originate from the same analyzer. For each analyte, we tabulated consecutive pairs of intra-patient results separated by time intervals of 0-2 ,2-4, 4-6, up to 16 hours. The average between pair variations were regressed against time with the y-intercept representing biologic variation and short term analytic variation, including between-instrument and between-cartridge variation: $y^2_{o\ GEM} = s^2_b + s^2_{aGEM}$. Using an equivalent equation for the Radiometer and simple algebra, the imprecision of the two GEM's can be calculated from: $s_{aGEM} = (y^2_{o\ GEM} - y^2_{o\ ABL} + s^2_{aABL})^{1/2}$.

Results: Over the two year period, approximately 60,000 arterial blood gases were analyzed. Regression graphs were derived from around 1800 patients with least 10,000 data pairs grouped into 2 hr intervals. The Table compares the directly measured s_{aABL}, the calculated s_{aGEM}, and corresponding sigmas, calculated from (biologic variation)/(analytic variation).

Conclusion: For a large number of GEM analytes, the effective analytical variation of GEMs used in tandem is on the order of the biologic variation, indicating a significant reduction in the clinical usefulness of the repeated analytes.

Test	S_{aABL}	S_{aGEM}	Sigma ABL	Sigma GEM
Chloride, mmol/L	0.44	0.52	1.8	1.5
Glucose, mmol/L	0.11	0.41	4.7	1.3
HCO_3, mmol/L	0.22	0.60	3.6	1.3
ionized Ca, mmol/L	0.0042	0.033	3.4	0.4
Potassium, mmol/L	0.0244	0.044	7.9	4.4
Sodium, mmol/L	0.38	0.72	2.2	1.2
pCO_2, mmHg	0.34	0.40	6.6	5.6
pH	0.00148	0.029	15.0	0.8
pO_2 ,mmHg	1.36	5.34	9.9	2.5

B-047

High Throughput Immunoassay for Kidney Function Biomarker Symmetric Dimethylarginine (SDMA)

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Symmetric dimethylarginine (SDMA) is a dimethylated derivative of arginine that results from intra-nuclear methylation and subsequent catabolism of proteins. SDMA is a sensitive and specific biomarker for kidney function and correlates well to GFR. Several recent studies have shown SDMA to be an earlier and more accurate marker than serum creatinine. In addition, studies have shown that SDMA is a better indicator of kidney function associated mortality in cardiac and stroke patients further establishing the value of this emerging biomarker. The current report describes a high throughput clinical chemistry immunoassay that has been developed and correlated to the gold standard LC-MS assay using samples from canine and feline models along with healthy and CKD human cohorts.

The LC separation was achieved using X-Bridge RP C-18 column and an ion pairing agent. The API 4000 triple quadrupole mass spectrometer (Applied Biosystems/MDS Sciex) was operated in Multiple Reaction Monitoring (MRM) mode with positive electrospray interface. The MRM transition for SDMA was observed at m/z 203.2 ---> 172.1. As part of the method validation, performance characteristics including sensitivity, carryover and interferences, matrix effect and recovery, linearity, accuracy and precision, ruggedness, stability, robustness and interfering substances were established. All performance metrics were within established FDA guidance.

The clinical chemistry immunoassay utilizes a SDMA-G6PDH conjugate and anti SDMA monoclonal antibody. The antibody is specific to SDMA and has no significant cross reactivity to arginine, monomethyl arginine and asymmetric dimethylarginine. The dynamic range of the assay is between 0 and 100µg/dL and within-run precision across the range is between 5 and 10%.

Accuracy was determined using 351canine and 280 feline and 160 human serum samples from healthy and CKD populations. All the samples were run on both the LC-MS assay and the clinical chemistry immunoassay (Beckman automated clinical chemistry analyzer) and the results were presented in the following table:

Slope Intercept R

Dogs 1 0.2 0.97

Cats 0.96 0.2 0.97

Humans 0.96 1.3 0.99

In conclusion, we have developed and validated a high throughput clinical chemistry immunoassay that correlates to the LC-MS and accurately quantifies SDMA in biological samples from dogs, cats and humans.

B-048

Validation of a Novel High Throughput Immunoassay for the Quantitation of Symmetric Dimethylarginine (SDMA)

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Symmetric Dimethylarginine (SDMA) is derived from intranuclear methylation of L-arginine by protein-arginine methyltransferases (PRMT) and released into the circulation after proteolysis. SDMA is eliminated primarily by renal clearance and is shown to be an accurate and precise biomarker for calculating estimated glomerular filtration rate (eGFR) in humans. Recent studies have also demonstrated its utility as an early and more sensitive biomarker than serum creatinine in assessing renal dysfunction. SDMA represents an emerging biomarker for diagnosing and monitoring chronic kidney disease (CKD). The objective of this study was to validate a new high-throughput, competitive homogeneous immunoassay to quantify SDMA in serum and plasma using a canine model.

The two-reagent system contains an anti-SDMA monoclonal antibody and a G6PDH-SDMA conjugate. Precision, dynamic range, and accuracy were determined following CLSI guidelines using Beckman automated clinical chemistry analyzers across multiple reagent lots. In the range of 10-20 µg/dL, within-run precision was ≤ 7%CV, and total precision was ≤ 10% CV. Dynamic range was shown to be 5 to 100 µg/dL. Accuracy, which was assessed by correlation to the gold standard liquid chromatography mass spectrometry method, showed a slope of 1.0±0.1 and an intercept below the assay limit of detection. No significant interference from lipemia or icterus was observed, and no significant interference from moderate levels (100 mg/dL) of hemoglobin was observed. Related compounds such as arginine, monomethyl arginine and asymmetric dimethylarginine had no significant impact on assay performance. The assay performance was acceptable on both serum and plasma sample.

This SDMA immunoassay demonstrates clinical utility as a novel diagnostic tool in measuring the promising chronic kidney disease biomarker SDMA.

B-049

Evaluation of Photometric Methods on the Siemens ADVIA® Chemistry XPT System

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Introduction

Siemens recently introduced the new ADVIA Chemistry XPT System which joined the ADVIA Chemistry family of analyzers: the ADVIA 2400 and ADVIA 1800 Clinical Chemistry Systems. The ADVIA Chemistry XPT System utilizes identical reagents as the previous analyzers while having a throughput of 2400 tests/hour. For this study we assessed five methods: Hemoglobin A1c_3 Automated Pretreatment (A1C_3), Calcium_2 (CA_2), Cholesterol_2 (CHOL_2), Glucose Hexokinase_3 (GLUH_3), and Creatinine_2 (CREA_2).

Materials & Methods

All studies were completed at a Siemens Healthcare Diagnostics laboratory. Precision was analyzed according to CLSI Guideline EP05-A2 and Method Comparison according to CLSI Guideline EP09-A3. Precision was evaluated on two ADVIA XPT systems with five replicates of commercial controls over ten days, two runs/ day. Method comparison was performed on two ADVIA XPT systems and one ADVIA 2400 Clinical Chemistry System.

Results

Hemoglobin A1c_3 Automated Pretreatment within-lab CVs in whole blood ranged from 2.2% to 2.6% across the concentrations tested.

Calcium_2 within-lab CVs in serum ranged from 1.0% to 1.4% across the concentrations tested. Within-lab CVs in urine ranged 1.2% to 1.6% across the concentrations tested.

Cholesterol_2 within-lab CVs in serum were 1.2% across the concentrations tested.

Creatinine_2 within-lab CVs in urine ranged from 2.7% to 3.2% across the concentrations tested.

Glucose Hexokinase_3 within-lab CVs in serum ranged from 0.7% to 0.9% across the concentrations tested. Within-lab CVs in CSF ranged 1.0% to 1.1% across the concentrations tested.

The method comparison table below shows Weighted Deming fit against the ADVIA 2400 Clinical Chemistry System.

Assay	Matrix	n	Slope	Intercept	r	Sy x	Range	Units
A1C_3	Whole Blood	75	1.00	0.13	0.990	0.030	4.50- 12.80	%
CA_2	Serum	130	0.99	-0.19	0.999	0.021	1.49- 15.22	mg/dL
CA_2	Urine	102	0.98	-0.17	0.999	0.031	2.16- 29.08	mg/dL
CHOL_2	Serum	99	0.98	0.61	0.997	0.033	28- 549	mg/dL
CREA_2	Urine	142	1.05	-0.05	0.998	0.040	3.47- 290.92	mg/dL
GLUH_3	Serum	97	0.99	-0.55	0.999	0.032	43- 659	mg/dL
GLUH_3	CSF	104	0.98	-0.55	1.000	0.019	16- 620	mg/dL

Conclusion

All methods demonstrated equivalent performance for both repeatability and within-lab performance as well as demonstrating agreement for method comparison testing on the ADVIA Chemistry XPT Systems versus the ADVIA 2400 Clinical Chemistry System.

*ADVIA is a registered trademark of Siemens Healthcare Diagnostics, Inc and System availability depends on local regulatory requirements.

B-050

Prevalence of clinically significant errors in sodium measurements due to ion exclusion effect using an indirect ion selective method

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Background: Indirect ion selective electrode (ISE) is the primary method used to measure serum sodium in clinical laboratories. Pseudohyponatremia can occur from the ion exclusion effect due to hyperlipidemia and hyperproteinemia. Reporting erroneous sodium values could impact patient management. Hyperlipidemia can easily be detected using the serum lipemia index on automated chemistry analyzers, while hyperproteinemia requires protein measurement for detection. **Objectives:** (i) Determine the relationship between serum total protein (TP) concentration and the change in sodium concentration observed between indirect and direct ISE methods, (ii) estimate the frequency at which sodium results measured by indirect ISE are clinically re-categorized due to abnormal TP concentration, and (iii) determine whether middleware rules that query test results for combined protein and sodium orders would be effective for error detection. **Methods:** Sodium concentration was measured using indirect ISE (Cobas 8000, Roche Diagnostics) and direct ISE (ABL 825, Radiometer) methods on residual serum from physician-ordered TP testing (Roche Biuret method; n=66, concentration range: 3.6-9.0 g/dL) or protein electrophoresis with confirmed monoclonal protein (n=49, concentration range: 9.5-15.4 g/dL). The difference in sodium concentration (Δ[Na+]) was calculated as follows: ([Na+]indirect-ISE – [Na+]direct-ISE). Retrospective sodium and TP orders and results from the Mayo Clinic (Rochester, MN) from 07/31/2013 to 09/24/2014 were analyzed. Specimens were stratified based on TP reference intervals: low TP (<6.3 g/dL, n=41), normal TP (6.3-7.9 g/dL, n=16), and high TP (>7.9 g/dL, n=57). The sodium reference interval is 135-145 mmol/L. **Results:** Δ[Na+] was inversely proportional to TP concentration (y=-1.22x+7.9, R2=0.835). When TP concentration was <6.3 g/dL the average difference(SD, range) in sodium concentration was 2.2(1.5, -2 to -4) mmol/L. This led to 17% of specimens with sodium concentration within the reference range (normal) by indirect ISE to measure low by direct ISE. The average difference(SD, range) was -5.6(3.3, -13 to 0) mmol/L when TP>7.9 g/dL, which led to 31.5 % of specimens with low sodium to become normal and 1.7 % considered normal to become high when measured by direct ISE. Only 12.8% of routine sodium test orders include an order for TP on the same collection. Of orders including both tests, 19.1% had low TP and 3.2% had high TP. Hematology/oncology and nephrology clinics accounted for 20.2% of low TP results, while general internal medicine and hematology/oncology clinic accounted for 36.6% of all high TP results. Only 5.1% of stat sodium orders include a TP test order; 41.1% had low TP and 1.8% had high TP. **Conclusions:** This study demonstrated that sodium measurement by indirect-ISE can give erroneous results in serum or plasma when TP concentrations are outside the reference interval. In our patient population, sodium is usually not ordered with TP so a middleware rule-based solution that queries TP results would not detect most cases of low or high TP. Health systems that use indirect ISE for sodium measurement need to be aware of the limitation of the method and the potential errors in sodium measurement and misclassification that may occur in patients with abnormal TP concentrations.

B-051

Ion chromatography as candidate reference method for the determination of chloride in human serum

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Background: Serum chloride is the major anion in human body which has to be kept within narrow limit to ensure the maintenance of electrolyte homeostasis in both intra- and extracellular compartments of the organism. The standardization of the measurement of serum chloride is of considerable interest for quality assurance in patient care. In this context, isotope dilution thermal ionization spectrometry (ID-TIMS) and coulometry are recognized as the traditional reference method principles for serum chloride. While, there is at least two independent measurement principles should be used to increase the reliability of the cerified value for reference materials. In this perspective, a simple, rapid, accurate and sensitive method based on ion chromatography, which could be recommended as candidate reference method, has been developed for the determination of serum chloride.

Method: Serum samples were diluted with 10 mmol/L KOH solution and chloride was measured by ion chromatography with a gradient elution procedure using a KOH eluent generator. The measurement accuracy and precision was calculated by analyzing IFCC-RELA samples. Furthermore, the proposed method was compared with inductively coupled plasma mass spectrometry (ICP-MS) by using 27 serum samples from individual patients.

Results: The calibration curve for chloride was linear in the concentration range from 0 - 15 mg/L with a correlation coefficient of 0.99995 under the optimum experimental conditions. The detection limit was found to be 3.5 µg/L. The measurement accuracy and precision is less than 0.8 % by analyzing 2012 and 2013 IFCC-RELA samples. The results were also comparable with the reference values obtained by the inductively coupled plasma mass spectrometry (ICP-MS), which were found to be in good agreement (see Figure 1).

Conclusion: The proposed method could be recommended as candidate reference method for the determination of chloride in human serum.

B-052

Comprehensive Correlation between Siemens Point-of-care and Central Laboratory Blood Gas Systems and ADVIA 1800 Clinical Chemistry System for Electrolytes and Metabolites

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Objective: Determine correlation between Siemens point-of-care (POC) and central laboratory blood gas systems versus the central laboratory ADVIA® 1800 Clinical Chemistry System in order to demonstrate harmonization across the diagnostic product portfolio.

Relevance: AACC's International Consortium for Harmonization of Clinical Laboratory Results has been working with a variety of stakeholders regarding harmonization among results from different methods and laboratories for the same measurand.[1] Malone states, "Harmonization means achieving comparable results among different measurement procedures... When lab measurement procedures give different results for the same specimen, patients may get the wrong treatment, because decision criteria are not appropriate for the procedure in use. In order to do this effectively, results need to be harmonized."

[1]. Malone B. AACC's Thought Leadership Series: Why Harmonization Matters.

*Not available for sale in the U.S. Product availability varies by country.

Methods:

Method comparison studies were performed with whole blood on the POC and central laboratory blood gas systems (RAPIDPoint® and RAPIDLab® Blood Gas Systems) and with plasma on the clinical chemistry system (ADVIA 1800 system) in accordance with the CLSI EP09-A3 guideline. Correlation statistics including regression types, slopes, intercepts, and coefficients of determination (r^2) were generated for the following comparisons:

- RAPIDPoint 500 Blood Gas System vs. ADVIA 1800 Clinical Chemistry System
- RAPIDLab 1265 Blood Gas System vs. ADVIA 1800 Clinical Chemistry System
- RAPIDLab 348EX Blood Gas System* vs. ADVIA 1800 Clinical Chemistry System

Results:

Regression statistics for each comparison across measured intervals for each measurand are shown in Table 1. The slopes for each measurand fell between 0.91 and 1.17, with $r^2 \geq 0.9679$.

Conclusion:

Harmonization at medical decision levels and average concentrations was demonstrated between Siemens POC and central laboratory blood gas platforms with whole blood and the ADVIA 1800 Clinical Chemistry System with plasma for the measurands evaluated.

Comparison	Measurand	n	Median Bias	Regression Type	Slope	Intercept	r^2	Interval
RAPIDPoint 500 Blood Gas System vs. ADVIA 1800 Clinical Chemistry System	Na^+ (mmol/L)	124	0.4	Deming	1.02	-1.2	0.9893	102.0–197.0
	K^+ (mmol/L)	100	3.89%	Weighted Deming	0.96	0.27	0.9979	1.10–9.60
	Cl^- (mmol/L)	124	-1	Deming	0.91	8	0.9916	66–147
	Glu (mg/dL)	100	3%	Weighted Deming	1.04	-2	0.9960	28–693
	Lac (mmol/L)	97	1.76%	Weighted Deming	0.97	0.19	0.9679	0.30–32.67
	nBili (mg/dL)	108	-0.3	Deming	1.14	-1.7	0.9974	2.3–24.7
RAPIDLab 1200 Blood Gas System vs. ADVIA 1800 Clinical Chemistry System	Na^+ (mmol/L)	123	0.9	Deming	1.05	-5.1	0.9865	102.0–197.0
	K^+ (mmol/L)	100	3.64%	Weighted Deming	1.02	0.09	0.9972	1.10–9.60
	Cl^- (mmol/L)	124	2	Deming	0.99	3	0.9908	66–147
	Glu (mg/dL)	100	5%	Weighted Deming	1.02	4	0.9985	28–693
	Lac (mmol/L)	95	-2.47%	Weighted Deming	0.93	0.27	0.9933	0.65–32.67
	nBili (mg/dL)	110	0.8	Deming	1.17	-0.8	0.9763	2.3–24.7
RAPIDLab 348EX Blood Gas System vs. ADVIA 1800 Clinical Chemistry System	Na^+ (mmol/L)	124	3	Deming	0.98	7	0.9851	102–197
	K^+ (mmol/L)	101	5.38%	Weighted Deming	1.03	0.13	0.9972	0.70–9.60
	Cl^- (mmol/L)	124	0	Deming	0.98	2	0.9901	66–147

B-053

Performance of the NephroCheck® for VITROS® Test** on the VITROS® 3600 Immunodiagnostic System

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Acute kidney injury (AKI) is a common disorder with potentially catastrophic complications that can lead to high morbidity and mortality rates. The NephroCheck for VITROS Test** (VITROS) quantitatively measures Tissue Inhibitor of Metalloproteinase 2 (TIMP-2) and Insulin-like Growth Factor Binding Protein 7 (IGFBP-7) to generate an acute kidney injury (AKI) risk index (AKIRISK™ Score). We have evaluated the performance on the VITROS® 3600 Immunodiagnostic Systems. The test is linear across the range of 1.58 to 30.9 ng/mL for TIMP-2 and 20.6 to 647 ng/mL for IGFBP-7 yielding an AKIRISK™ Score range of 0.0325 to 20.0. Limits of Blank (LoB) were determined to be 0.52 ng/mL and 0.110 ng/mL for TIMP-2 and IGFBP-7, respectively. Limits of Detection (LoD) were determined to be 0.243 ng/mL for TIMP-2 and 1.994 ng/mL for IGFBP-7 resulting in LoB and LoD for the AKIRISK™ Score of 2.8×10^{-6} and 0.003 respectively. A 5-day precision study with samples at mean TIMP-2 concentrations of 1.26 ng/mL, 2.63 ng/mL, 9.67 ng/mL, and 10.6 ng/mL resulted in within-laboratory percent coefficient of variation (%CV) of 10.7%, 6.4%, 3.4%, and 3.7% respectively. Similar results were obtained for IGFBP-7 at concentrations of 35.1 ng/mL, 65.7 ng/mL, 138 ng/mL, and 202 ng/mL, resulting in within-laboratory %CV of 5.8%, 6.6%, 7.5%, and 8.0% respectively. The precision of the AKIRISK™ Score based on the two results were 11.5%, 7.9%, 9.0%, and 9.8% at AKIRISK™ Score of 0.04, 0.17, 1.34, and 2.14. The accuracy of the test was evaluated with 50 patient specimens against the Astute Medical NephroCheck® Test System (Astute) The following linear regression statistics were obtained: VITROS TIMP-2 = 1.153*Astute - 1.24; (r) = 0.960; VITROS IGFBP-7 = 1.069*Astute - 1.717; (r) = 0.984. The positive (PPA) and negative (NPA) percent agreement between the two assays were calculated based on the AKIRISK™ Score cutoff of 0.3 established on the Astute Medical NephroCheck® Test System, with AKIRISK™ Score greater than 0.3 being positive and AKIRISK™ Score less than 0.3 being negative. Compared to Astute, the VITROS AKIRISK™ Score had a 93.8% PPA and a 100% NPA. (** under development)

B-054

Asymptomatic severe hypophosphataemia in acute T-cell lymphoblastic leukaemia

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Introduction: Hypophosphatemia is a metabolic disorder that iscommonly encountered in critically ill patients.Hypophosphatemia is defined asplasma phosphate level below 0.80 mmol per litre(mmol/L), and can be further divided into subgroupsof mild (a plasma phosphate of 0.66 to 0.79 mmol/L),moderate (plasma phosphate of 0.32 to 0.65mmol/L) and severe (plasma phosphate of less than0.32 mmol/L).Phosphate has many roles in physiologicalfunctions, thus the depletion of serum phosphatecould lead to impairment in multiple organ systems,which include respiratory system, cardiovascularsystem, neurological system, muscular system,haematological and metabolic functions. The causes of hypophosphatemia include inadequate phosphate intake, decreased intestinal absorption, gastrointestinal or renal phosphate loss, and redistribution of phosphate into cells. Symptomatic hypophosphatemia associated with haematological malignancies has been reported infrequently. We report here a case of asymptomatic severe hypophosphatemia in achild withacute T-cell lymphoblastic leukaemia.

Case report:A 14-year-old Chinese boy initially presented with left lower motor neuron facial nerve palsy and was given oral prednisolone for two weeks. However, his symptom did not improve. After one month, he developed high grade fever and bilateral epistaxis. On physical examination, cardiovascular system was normal and lungs were clear. Abdomen examination revealed hepatosplenomegaly. However, he was noted to have bilateral submandibular and right inguinal lymphadenopathies. Central nervous system showed no other abnormality other than 7th nerve palsy.

His initial complete blood counts showed mild anaemiaand increased total white cellscount of183 x 10^9/L.His peripheral blood picture showed numerousblast cells. Bone marrow examination and immunophenotypingconfirmed the diagnosis of acute T Cell Lymphoblastic Leukaemia (ALL).

His serum biochemistry results were normal except inorganic phosphate and lactate dehydrogenase levels. The serum inorganic phosphate level was 0.1mmol/L and the level was low on repeated analysis.The laboratory notified the requesting clinician about the low phosphate level and enquired about any clinical signs and symptoms related to low phosphate level. The child had no symptoms related to low phosphate level. Since the serum phosphate level was very low without any symptoms for hypophosphatemia, lithium heparin sample was requested to rule out any interference. This confirmed very low serum phosphate level. The possible causes of low phosphate were ruled out and urine Tmp/GFR was normal.Chemotherapy regime was started and the serum phosphate levels started to increase. He was monitored for tumour lysis syndrome.

Hypophosphatemia in leukaemia was attributed due to shift of phosphorus into leukemic cells and excessive cellular phosphate consumption by rapidly proliferating cells. Several reports of symptomatic hypophosphatemia in myelogenous and lymphoblastic leukaemia in adults have been reported. To our knowledge this is the first case of severe asymptomatic hypophosphatemia in a child with ALL.

B-055

Bilirubin interference and bias evaluations of 7 routine creatinine measurement methods compared with ID-LC/MS

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Background:

Serum creatinine is measured in order to estimate glomerular filtration rate. For the measurement of creatinine, alkaline picrate reaction or Jaffe reaction is still widely used in clinical laboratories. However, the Jaffe method is interfered by bilirubin, resulting in falsely low creatinine level. Because enzymatic method is known to be free form the problem of bilirubin interference, reagent based on the enzymatic method can be alternative assay. The aim of this study is to compare enzymatic methods and kinetic Jaffe methods with isotope dilution-liquid chromatography mass spectrometry (ID-LC/MS) to estimate bilirubin interference.

Methods:

Forty clinical serum samples from 31 patients which had serum of total bilirubin concentration above 4.0 mg/dL were collected. The serum creatinine was measured using three enzymatic reagents: Pureauto S CRE-L (SEKISUI MEDICAL CO., LTD, Japan) and L-Type Wako CRE•M (Wako Pure Chemical Industries, Ltd., Japan)

performed on Hitachi 7600 analyzer (Hitachi Co., Japan), and Stat Profile Critical Care Xpress (Nova Biochemical, USA) performed on Critical Care Xpress blood gas analyzer (Nova Biochemical). The serum creatinine was also measured with four kinds of kinetic Jaffe methods of Clinimate CRE (SEKISUI MEDICAL CO., LTD, Japan) using Hitachi 7600, SYNCHRON CREm (Beckman Coulter, Inc., USA) using Unicel DxC880i (Beckman Coulter), CREJ2 (Roche Diagnostics GmbH, Germany) using Cobas c 702 modules (Roche Diagnostics), and AU Creatinine (Beckman Coulter, Inc., USA) using AU680 chemistry system (Beckman Coulter) as well as ID-LC/MS. The total bilirubin values are plotted against percent bias, between serum creatinine values from each reagent and those of ID-LC/MS. In addition, the correlation between serum total bilirubin and percent bias was analyzed in three different ranges of serum creatinine, Low (1.1 mg/dL). Passing-Bablok regressions for method comparison between those 7 reagents and ID-LC/MS were also performed.

Results:

Pureauto S CRE-L, L-Type Wako CRE•M, SYNCHRON CREm and Stat Profile Critical Care Xpress reagents showed no significant serum bilirubin interference. However, Clinimate CRE showed significant negative serum bilirubin interference on the low and medium serum creatinine levels, while CREJ2 and AU Creatinine showed significant positive interference on the low serum creatinine level. Method comparison with ID-LC/MS using Passing-Bablok regression revealed that Pureauto S CRE-L and SYNCHRON CREm reagent had bias beyond the allowable total error at one or two medical decision levels.

Conclusion:

Three enzymatic methods evaluated were free from bilirubin interference while kineteic Jaffe methods showed negative or positive bilirubin interference except one method. However, one enzymatic method showed bias at medical decision level indicating the reagent was not traceable to ID-LC/MS. Therefore, to select an accurate method for creatinine, both traceability to ID-LC/MS and bilirubin interference should be considered.

B-056

Assessment of serum indices implementation on ADVIA Chemistry 2400 System

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Background: Use of hemolyzed, lipemic, and icteric samples can cause critical changes in the results of several laboratories analyzes. The increasing of laboratory examinations, combined with automated processes, reduces the possibility of manual inspection. So, it`s very important that an automated system provides this analysis quickly, accurately and in a standardized way. This study aims to compare the effectiveness of automated spectrophotometric detection with the visual inspection of lipemic and hemolyzed serum samples **Methods:** The study was conducted during the processing of 500 serum samples; 50 samples showed changes in one or more serum indices. For the automatic identification, it was used a specific and standardized protocol for the ADVIA 2400® Systems. At the manual inspection, three experienced laboratory analysts defined the graduation of interferences (According to Siemens Setting Up a Dedicated Serum Indices Method Rev. A, 2008-11 figures). For the comparability of visual reading with the automatic detection of lipemic and hemolyzed serum, it was accepted up to one level of difference for positive samples and no difference in negative samples. **Results:** For hemolysis, there was a complete correlation between the automation and manual classification in 90% of the samples. In 10 % there was a one-grade divergence. For Lipemia, 92% of samples showed no differences in evaluation. In 8% of the samples there was a one-grade difference. All negative samples for the visual reading were also confirmed as negative by the automated testing. **Conclusion:** According to this study, automated identification of serum indices performed by the ADVIA Chemistry 2400® System is considered highly reliable when compared to manual inspection. This eliminates subjective interpretations that may occur in ordinary visual reading. The automation of this process permits availability of the operators to perform high value activities, ensuring the release of the results, making clinical correlations and detecting the presence of interferents in a short time and with a high quality score.

B-057

Evaluation of Electrolyte Performance on the Siemens ADVIA Chemistry XPT System

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Introduction

Electrolytes play an important role in the human body. Analytical determination of electrolytes is a critical function in the clinical laboratory. The Siemens ADVIA® XPT Chemistry System is a floor standing, 2400 test per hour chemistry system engineered for continuous operation and timely, accurate results. We evaluated three electrolytes, sodium (Na), potassium (K), and chloride (Cl), on the ADVIA XPT system.

Materials and Methods

All studies were conducted on two ADVIA Chemistry XPT systems. Precision studies assayed QC material over 10 days. Correlation studies assayed both serum and urine samples over multiple days against an ADVIA® 2400 Clinical Chemistry System. Precision was analyzed according to CLSI Guideline EP05-A2. Correlation was analyzed according to CLSI Guideline EP09-A3.

Results

The method comparison table below shows Weighted Deming fits against the ADVIA 2400 Clinical Chemistry system.

Analyte	Matrix	n	Slope	Y-intercept	r	Syx	Range (mEq/L)
Cl	Serum	117	1.01	0.7	0.998	0.015	50-191
Cl	Urine	137	0.99	2.8	0.999	0.035	15-375
Na	Serum	102	0.98	2.4	0.996	0.012	101-196
Na	Urine	139	0.96	4.13	0.999	0.036	10-377
K	Serum	122	0.97	0.11	0.998	0.021	1.0-9.7
K	Urine	142	1.00	0.07	1.000	0.013	2.4-272.3

For Cl precision, repeatability and within-lab CVs in serum ranged from 0.2% to 0.4% and 0.3% to 0.6%, respectively, across the concentrations tested. Repeatability and within-lab CVs in urine ranged from 0.3% to 0.6% and 0.5% to 0.9% across all concentrations tested.

For Na precision, repeatability and within-lab CVs in serum ranged from 0.2% to 0.3% and 0.3% to 0.6%, respectively, across the concentrations tested. Repeatability and within-lab CVs in urine ranged from 0.3% to 0.8% and 0.5% to 1.1% across the concentrations tested.

For K precision, repeatability and within-lab CVs in serum ranged from 0.2% to 0.9% and 0.5% to 1.1%, respectively, across the concentrations tested. Repeatability and within-lab CVs in urine ranged from 0.4% to 0.6% and 0.7% to 0.9% across the concentrations tested.

Conclusion

The Na, Cl, and K assays all showed good repeatability, within-lab precision and correlation to ADVIA 2400 Clinical Chemistry systems when tested on the ADVIA Chemistry XPT System.

*System availability depends on local regulatory requirements.