Wednesday, August 2, 2017

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

Electrolytes/Blood Gas/Metabolites

B-029

Comparison of Electrolyte Measurement Using Laboratory Autoanalyzer and Blood Gas Analyzer

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Background: In many hospital laboratories, electrolyte values are measured both by laboratory autoanalyzers (AA) and blood gas analyzers (BGA). The BGA gives faster results than the AA but the AA is very widely used, especially in hospital's central laboratory because it uses venous blood and thus, can be done with other clinical chemistry tests. The study aimed to evaluate whether sodium and potassium ion concentrations measured using an AA and a BGA were equivalent and comparable.

Methods: We retrospectively studied outpatient and hospitalized patients between January and December 2014. Of 89,749 samples, we identified 2,104 samples where electrolytes were measured using an AA (Cobas, Roche Diagnostics, Mannheim, Germany) and a BGA (pHOx Stat Profile Plus L, Nova Biomedical, Waltham MA, USA). Statistical analysis to compare the data included Spearman's correlation and Bland-Altman plot.

Results: The median sodium concentrations of AA and BGA were 140 (91-190) mmol/L and 137 (93-192) mmol/L, respectively ($p<0.001$). The median potassium levels of AA and BGA were 4.33 (1.29-16.22) mmol/L and 4.00 (1.26-16.14) mmol/L, respectively ($p<0.001$). Bland-Altman plot showed mean difference of sodium and potassium of 3.9152 and 0.3307, respectively.

Conclusion: We conclude that the AA and the BGA do not yield equivalent sodium and potassium results. Although the mean difference between the results of two assays was within the range given by the US CLIA 1988 guidelines, a difference of 0.3307 mmol/L in potassium level is clinically relevant when intra-individual variation is considered. For electrolyte measurement in clinical practice, we suggest not to use the AA and the BGA interchangeably.

B-030

Performance of the EKF Diagnostics, Stanbio β-Hydroxybutyrate LiquiColor® Assay on the VITROS® 4600 Chemistry System and the VITROS® 5600 Integrated System

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The EKF Diagnostics, Stanbio β-hydroxybutyrate LiquiColor assay quantitatively determines the concentration of β-hydroxybutyrate in serum or plasma. β-hydroxybutyrate, acetoacetate and acetone are three ketogenic byproducts from the metabolism of fatty acids. The byproducts are typically present in low concentration; however in disease state conditions such as diabetic ketoacidosis the levels are elevated, with β-hydroxybutyrate being present in the highest concentration. The traditional method for detecting the ketogenic byproducts is the qualitative nitroprusside test which detects only the ketone bodies acetoacetate and acetone, but fails to detect the ketoacid, β-hydroxybutyrate, the most prominent ketone body. The mechanism for the Stanbio β-hydroxybutyrate LiquiColor assay is as follows: β-hydroxybutyrate in the presence of NAD is converted to acetoacetate and NADH by β-hydroxybutyrate dehydrogenase. NADH produced by this reaction reacts with 3-p-nitrophenyl-2-p-iodophenyl-5-phenylterazolium chloride (INT) in the presence of diaphorase to generate a colorimetric signal at 510nm. We have assessed the performance of the Stanbio β-hydroxybutyrate LiquiColor assay on the VITROS 4600 Chemistry System and the VITROS 5600 Integrated System. The assay was run on the VITROS MicroTip assay processing side of the MicroImmunoassay Center using 4.0uL of patient sample and the two Stanbio LiquiColor reagents. Endpoint absorbance measurements were taken at 510nm and converted to a concentration using a linear calibration model. The absorbance is directly proportional to the concentration of β-hydroxybutyrate in the patient specimen. We evaluated the accuracy of 105 serum and plasma samples (0.05 - 12.56 mmol/L) on the VITROS 4600 and VITROS 5600 Systems compared to the Stanbio SIRRUS Clinical Chemistry Analyzer. The VITROS 4600 and VITROS 5600 Systems showed excellent correlation with the SIRRUS Analyzer. VITROS 4600 System = 0.9542 * SIRRUS - 0.0123; (r) = 0.995. VITROS 5600 System = 0.97 * SIRRUS - 0.0227; (r) = 0.997. A 28-day precision study conducted on the VITROS 4600 and VITROS 5600 Systems showed excellent precision. Mean β-hydroxybutyrate concentrations of 0.191 mmol/L and 4.224 mmol/L resulted in within-laboratory percent coefficient of variation (%CV) of 2.58% and 0.88% respectively, for the VITROS 4600 System and 1.06% and 0.87% respectively, for the VITROS 5600 System. The Limit of Detection (LoD) for the VITROS 4600 and VITROS 5600 Systems is 0.02 mmol/L based on 120 determinations with 2 low-level samples. The Limit of Blank (LoB) is 0.01 mmol/L based on 120 determinations with 2 blank samples. The VITROS 4600 System and VITROS 5600 System results for an endogenous interferent panel evaluated at a β-hydroxybutyrate concentration of 1.50 mmol/L showed no interference to hemolysis (600 mg/dL), conjugated and unconjugated bilirubin (40 mg/dL), and triglycerides (Intralipid,1600 mg/dL). The β-hydroxybutyrate LiquiColor assay run on the VITROS 4600 and VITROS 5600 Systems exhibited excellent correlation with the SIRRUS Clinical Chemistry Analyzer, excellent precision and low end sensitivity. In addition, the assay was free from interference by endogenous substances at a clinically relevant β-hydroxybutyrate concentration.

B-031

P_{50} calculation using IFCC approved equation (Hill's equation); a first report in Korea.

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Background: High oxygen-affinity hemoglobin (Hb) variants and 2,3-diphosphoglycerate (2,3-DPG) deficiency are one of the causes of congenital(familial) erythrocytosis. High oxygen-affinity Hb variants/2,3-DPG deficiency result in low tissue oxygen tension and a left shift of the oxygen dissociation curve, with reduction of the P_{50} (the oxygen tension at which hemoglobin is 50% saturated). Therefore P_{50} is included in diagnostic strategies for erythrocytosis. The acquired secondary (pulmonary, renal, cardiac etc.) and acquired primary erythrocytosis (Polycythemia vera, *JAK2* mutation with low serum EPO level) are excluded. Low serum EPO level with negative *JAK2* mutation is suggestive of primary familial congenital polycythemia (PFCP). In cases of normal or high serum EPO level, P_{50} is recommended to rule out high oxygen-affinity Hb variants and 2,3-DPG deficiency. According to this diagnostic strategies, we found a first Korean case of high oxygen-affinity Hb variant (Hb Heathrow) with low P_{50} (14mmHg). To the best of knowledge, there have been no studies for P_{50} in Korea until now. **Methods:** In this study, we established the P_{50} reference range using International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) approved equation (Hill's equation, using single venous/arterial blood). We selected the 227 blood gas analysis results (oxygen saturation ranged 40 to 90%, Hb<16mg/dL).

Results: Total 143 male and 84 female were enrolled. The mean white blood cell, platelet, Hb levels were followings; 8.0×10^3/uL, 239×10^3/uL, 12.7mg/dL, respectively. The mean±SD and reference range (2.5%-97.5%) of P_{50} were 27.3±2.25mmHg and 23.0-31.2mmHg respectively.

Conclusion: Some previous studies reported P_{50} reference range as 22.6-29.4mmHg. And they suggested that high-affinity Hb variant or 2,3-DPG deficiency should be suspected if the P_{50} level is <20-22.6mmHg. Hill's equation is simple and approved method for P_{50}. Only single venous or arterial blood sample and blood gas analyzer is required to obtain P_{50}. Our study will provide the useful tool for work-up of erythrocytosis.

B-032

Performance of GEM Premier 5000 at High Altitude

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Background: Traditional blood gas analyzers are calibrated with humidified gas mixtures and require correction for barometric pressure. However, cartridge-based systems measuring blood gases typically feature solutions pre-equilibrated with specific gas tensions and sealed in gas-impermeable bags. Barometric pressure correction is not performed on these systems, based on the assumption that ambient pressure has no influence.

Methods: In this study, we compared pH, pO_2 and pCO_2 performance on the GEM Premier 5000 analyzer with Intelligent Quality Management 2 (iQM2) at different altitudes. Two levels of internal Process Control Solutions (PCSs) D and E and five levels of external linearity controls, were analyzed and compared at two elevations. In addition, six levels of tonometered whole blood were run at low altitude (near sea level) and seven levels were run at high altitude. The low elevation test was performed at Instrumentation Laboratory (IL) facilities, Bedford, MA (elevation = 135 ft/41m). The high elevation test was performed at St. Vincent's Hospital, Leadville, CO (elevation = 10,152 ft/3,094 m).

Results: The bias between high and low altitude results for pH and blood gases in both aqueous controls and tonometered whole blood samples was within total allowable error specifications (TEa) for all levels tested. Whole blood results at Medical Decision Levels (MDLs) were calculated from a linear regression against a reference method (tonometry for gases and GEM Premier 3000 for pH) and compared at both altitudes as shown in Table 1. Aqueous controls at high altitude compared to aqueous controls at low altitude are also shown in Table 1.

Table 1: Whole blood and aqueous results at High vs. Low Altitude:

Sample	pH 3,094m	pH 41m	pH bias (±0.04)	pO_2 (mmHg) 3,094m	pO_2 (mmHg) 41m	pO_2 bias (±9 or 10%)	pCO_2 (mmHg) 3,094m	pCO_2 (mmHg) 41m	pCO_2 bias (±5 or 8%)
WB-MDL1	7.30	7.30	0.001	35	31	4.4	37	36	0.3
WB-MDL2	7.35	7.34	0.002	50	45	4.8	52	51	1.3
WB-MDL3	7.44	7.44	0.004	65	60	5.1	72	70	3.9%
QC-L1	6.62	6.63	-0.008	31	35	-4.0	132	129	2.0%
QC-L3	7.22	7.22	0.002	90	91	-0.4	67	65	2.4%
QC-L5	7.73	7.73	0.003	565	556	1.7%	18	18	0.2
PCS-D	7.35	7.35	0.000	64	67	-2.9	24	24	0.0
PCS-E	7.21	7.21	-0.005	104	105	-1.1%	67	68	-0.8%

Conclusion: Based on the results obtained in this study, gas tensions in sealed PCS bags on the GEM Premier 5000 cartridge PAK demonstrated analytical stability, independent of altitude.

B-033

Surrogate Prognostic Marker for Diabetic Nephropathy by NMR-based Urine Metabolomics

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Background: Chronic kidney disease (CKD) is a major health issue worldwide. Patients with varying stages of CKD have high risks for end-stage renal disease (ESRD), cardiovascular disorders and death. Diabetic nephropathy is the leading cause of CKD, which is one of the most significant long-term complications in terms of morbidity and mortality for patients with diabetes. Early diagnosis and treatment are important in preventing the progression of CKD. Urine metabolites can offer direct insights into the pathophysiology of kidney. Elucidation of characteristic metabolic alterations during diabetic nephropathy progression is critical to identify potential markers and therapeutic targets. The purpose of this study is to investigate the change of metabolites at different stage of CKD in diabetic patients and apply these metabolites as potentially predictive surrogate markers for the detection of early kidney deterioration.

Methods: Patients from various stage of CKD referred to a medical center for diabetes monitoring were recruited with informed consent from September 2013 to September 2015. Urine samples were collected and metabolites were assessed by using ^{1}H nuclear magnetic resonance (NMR) spectroscopy coupled with multivariate statistical analysis. Metabolites were identified and quantified using the 600 MHz Library within Chenomx NM suite 7.5 professional software.

Results: A total of 77 participants (42 males and 35 females) were separated into five CKD stages according to the K/DOQI guideline. After creatinine normalization, 15 metabolites had significant differences in the advanced CKD stage comparing to the early CKD stage including 1-methylnicotinamide, 3-hydroxyisovalerate, Alanine, Choline, Dimethylamine, Formate, Hippurate, Isobutyrate, Lactate, Myo-inositol, N-phenylacetylglycine, O-acetylcarnitine Trigonellin, Tyrosine, and Valine.

Conclusion: We have analyzed urine metabolomes by NMR metabolomics from patients at different stages of CKD to find association between the consecration of metabolites and the degeneration of renal function. These metabolomic-based prognostic urine markers may improve CKD management with the potential of predicting the risk of rapid progression to ESRD and can be potential therapeutic targets.

B-034

Determination of serum calcium levels by ^{42}Ca isotope dilution inductively coupled plasma mass spectrometry

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Background: Serum calcium level is an important clinical index that reflects pathophysiological states. However, detection accuracy in laboratory tests is not ideal; as such, an improved reference method is needed.

Methods: We developed a candidate reference method for measuring serum calcium levels by isotope dilution inductively coupled plasma mass spectrometry (ID ICP-MS), using ^{42}Ca as the enriched isotope. Serum was digested with 69% ultrapure nitric acid & diluted to a suitable concentration. The ^{44}Ca/^{42}Ca ratio was detected in H_2 mode; spike concentration was calibrated by reverse IDMS using Standard Reference Material (SRM) 3109a as a standard; sample concentration was measured by a bracketing procedure on Agilent 700X ICP mass spectrometer. We compared the performance of ID ICP-MS with those of three other reference methods using the same serum & aqueous samples. Among them, a total of 46 different serum samples were analyzed by both the aluminum internal standard ICP-MS & ID ICP-MS method in our laboratory, while 16 samples including nine serum & seven aqueous samples were tested in various laboratories using two-way ID ICP-MS, ion chromatography method along with our ID ICP-MS method.

Results: The relative expanded uncertainty of the sample concentration was 0.40% (k = 2). The range of repeatability (within-run precision), intermediate precision (between-run precision) & intra-laboratory precision were 0.12%-0.19%, 0.07%-0.09%, & 0.16%-0.17% respectively, for two serum samples with high or low concentration. SRM909bI, SRM909bII, SRM909c & GBW09152 were found to be within the certified value interval, with mean relative bias values of 0.29%, 0.02%, 0.10%, 0.19% & intra-laboratory CV of 0.18%, 0.18%, 0.11%, 0.16%, respectively. The range of recovery was 99.87%-100.37%. Methods comparison results showed ID ICP-MS method had a good comparability with three other reference methods with correlation coefficient of 0.99983, 0.9932 & 0.9796. Aqueous samples results shows it has a better performance with lower bias & imprecision due to its low interference including isobar, polyatomic ions (oxide, chloride, hydride, & argon compounds) & doubly charged ions.

Conclusion: New ID ICP-MS is a simple, precise & accurate candidate reference method for serum calcium measurement.

B-035

Effects of in vitro exposure of static magnetic field on human blood electrolyte levels

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Background: Major concerns exist regarding safety of static magnetic fields (SMF) and their effects on physiology. These are sometimes attributed to changes in cell membrane property. The authors hypothesize that any global effect on membrane physiology is likely to impair the electrolyte transport across the membrane. Here, the authors have tried to experimentally evaluate the effect of SMF on membrane physiology in vitro.

Methods: In this study, 6 ml of blood was collected in heparinised vials from 30 young (18 to 25 yrs) healthy volunteers after informed consent and institutional ethical clearance. Each sample was divided into 6 equal parts (1ml each) in 3 pairs. One aliquot from each pair was then exposed for 20 minutes to SMF strengths of 500Gauss (G). SMF was generated by a coil electromagnet between 2 soft iron cores and the control samples were shielded by placing them in an iron box. After exposure, all samples were immediately estimated for electrolytes: sodium (Na^+), potassium (K^+), ionic calcium (Ca^{++}) and chloride (Cl^-) by Combiline blood gas and electrolyte analyzer (manufactured by Eschweiler, Germany). The process was repeated for the other sample pairs with SMF exposure of 5000G and 1Tesla (1Tesla = 10000G). Paired shielded controls were used each time to eliminate the effect of the time lapse on electrolyte estimation. Results were analyzed using paired 't' test. $p<0.05$ was taken to be significant.

Results: The results are depicted in Table 1. Statistically significant changes in the ionic concentrations between cases and controls were not observed for any level of SMF exposure.

Conclusions: This indicates that SMF of 500 G, 5000 G and 1 Tesla do not result in any significant change in the membrane permeability of RBCs. This probably excludes the chances of any global effect of SMFs on cell membrane physiology.

Blood electrolyte levels at different Static Magnetic Fields strength

	500 Gauss SMF		5000 Gauss SMF		1 Tesla SMF	
Electrolytes	**Controls** Mean ±SD	**Cases** Mean ±SD	**Controls** Mean ±SD	**Cases** Mean ±SD	**Controls** Mean ±SD	**Cases** Mean ±SD
Potassium K^+ (mmol/L)	4.49 ± 0.45	4.48 ± 0.45	4.49 ± 0.39	4.51 ± 0.63	4.52 ± 0.45	4.45 ± 0.43
Sodium Na^+ (mmol/L)	143.15 ± 1.87	143.12 ± 1.83	142.65 ± 2.74	142.86 ± 2.50	142.67 ± 2.79	143.09 ± 2.41
Ionic Calcium Ca^{++} (mmol/L)	1.22 ± 0.05	1.22 ± 0.05	1.23 ± 0.06	1.23 ± 0.06	1.25 ± 0.07	1.25 ± 0.05
Chloride Cl^- (mmol/L)	110.56 ± 5.00	110.20 ± 4.64	110.19 ± 4.71	110.09 ± 4.66	110.46 ± 4.39	110.37 ± 4.83

B-036

Unstable Trends in Metabolites Predict Mortality Within 48 Hours Among Long Term Hospitalized Patients

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Background: Patients who are hospitalized for an extensive period are at risk for adverse outcomes and are likely to have a high mortality rate. These patients often rapidly deteriorate leading to death, with cause of death attributable to different factors like sepsis and end organ damage. To date, there has been limited study of end of life laboratory trends. In this study, we aim to evaluate end of life laboratory values time trends among deceased long term inpatients.

Methods: Time stamped laboratory data for deceased adult inpatients who had died in hospital from all-cause mortality between January 2014 and December 2016 was extracted. All adult deceased patients who were hospitalized for at least one week were included in the study. Time stamp data was reformatted to show time to death (in hours) and data was averaged for each reformatted time stamp. The time series of averages as well as lower and upper bounds of confidence interval were evaluated using ARIMA and Mann-Kendall trend test. Recent unstable trend was evaluated by comparing variations of the observed values from the fitted ARIMA model.

Results: Laboratory results from 110 patients were evaluated. The average length of hospitalization prior to death was 12.3 days. Significant time trends that were observed included increases in BUN, AST and ALT implying Mann-Kendall trend test showed that there is an upward trend in BUN and liver function tests indicative of end organ damage. Segmentation of the data showed that in the last two days of life the slope of the fitted curve significantly increases and Pettitt's homogeneity test shows a shift in upper bound values in the last 48 hours of life. Sodium, chloride and potassium levels are stationary over time, however, in the last 48 hours of life the metabolites become unstable with values varying from the expected value by more than one standard deviation.

Conclusion: Our results suggest that in the last 48 hours of life in chronically morbid hospitalized patients an alteration of the physiologic state of the patient occurs which manifests as subtle changes in metabolite levels especially when compared to the long-term result trends of the patient. Perhaps early detection of these changes can allow for timely interventions for the patients.

B-037

Verifying Biological Reference Intervals of venous blood gases of High endurance Athletes - Biological variation on athletes BIOVAth Study

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Background:A special physical condition can modify the reference intervals (RI) of certain biological magnitudes and could lead to misinterpretation of laboratory results. The aim of this study was to verify the biological reference intervals established in our laboratory for blood gas parameters in a high endurance athlete's population. **Methods:** 29 athletes including runners and triathletes (15 males and 14 females) aged from 18 to 53 were included. All of them were advised to not perform exercise in the previous 12 hours. Venous blood drawn was performed after a fasting overnight, between 8:00-10:00 by the same phlebotomist using syringes safePICO (Radiometer). pH, pO2, pCO2, sodium, potassium, chloride, ionized calcium, bicarbonate, lactate, base excess, anion Gap, glucose, hemoglobin, carboxyhemoglobin and methemoglobin were measured immediately after blood collection in ABL90 Flex (Radiometer). The RIs were taken from healthy Spanish subjects study and verified in our general healthy population. A statistical analysis was performed to verify the RIs in this specific group of subjects following the CLSI EP-28 A3 protocol. **Results** All results fit a normal distribution model and no outliers were found. **Conclusion:** pO2, pCO2, chloride, ionized calcium, bicarbonate, lactate, base excess and anion Gap reference intervals could not be verified in athlete's population. The values outside the IR could be explained by the increase of the metabolic activity related to physical condition. Specific Reference intervals should be estimated in these subjects in order to get a correct interpretation of laboratory testing results.

Results: *(-) Below RI; (+) Above RI

Analyte	Units	RI	% Outside Limits	p-Value	Verified
pH	mmHg	7.33-7.43	7	0.659	Yes
pO2	mmHg	30-50	78 (-)	<0.0001	No
pCO2	mmHg	38-50	64 (+)	<0.0001	No
Sodium	mEq/L	136-146	0	0.108	Yes
Potassium	mEq/L	3.5-5.0	4	0.905	Yes
Chloride	mEq/L	98-106	42 (+)	<0.0001	No
Ionized Calcium	mg/dL	1.0-1.2	36(+)	<0.0001	No
Bicarbonate	mg/dL	23-27	81 (+)	<0.0001	No
Lactate	mg/dL	0.5-1.6	17 (+)	0.0011	No
Base Excess Female, Male	-	(-3.4-1.4), (-2.7-2.5)	67, 79 (+)	<0.0001	No
Anion Gap	-	8-16	28 (-)	<0.0001	No
Glucose	mg/dL	70-105	0	0.1075	Yes
Hemoglobine Females, Males	mg/dL	(12.0-16.0),(13.5-17.5)	0	0.429, 0.476	Yes
Methemoglobine	mg/dL	0.0-1.5	0	0.102	Yes

B-038

Abbott Alinity c Sigma Metrics and Precision Profiles for Na, Cl, and K

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Introduction: Assay performance is dependent on the accuracy and precision of a given method. These attributes can be combined into a sigma metric, providing a simple value for laboratorians to use in evaluating test methods. In addition to sigma metrics, precision profile charts can be used to visually assess the precision performance of a product across a concentration range. Sigma metrics were determined for 3 assays – Sodium, Chloride and Potassium – tested on the Alinity c-series. Additionally, precision profile charts were created for each assay to compare the precision performance of the assays tested using the Alinity c-series and the ARCHITECT *c* system.

Methods: A sigma value was estimated for each assay and was plotted on a method decision chart. The sigma value was calculated using the equation: *sigma = (%TEa - |%bias|) / %CV*, where the CLIA TEa value was used as the total allowable error. A precision study was conducted at Abbott on each assay using the Alinity c-series per CLSI EP05-A2 where assay controls and panels were tested in replicates of 2-3 during 2 runs each day for 20 days, and the data were used to calculate a within-laboratory %CV. To estimate the %bias, >100 serum samples with concentrations spanning the assay's measuring interval were tested in duplicate at Abbott on the Alinity c-series and ARCHITECT *c*8000 systems. The mean concentration of the Alinity c-series results were regressed versus the mean ARCHITECT *c*8000 results and a weighted Deming regression model was fit. Using the regression model, the %bias was estimated at a medical decision point. A precision profile chart was created by plotting the within-laboratory %CV values versus the mean concentration values for both the Alinity c-series and the ARCHITECT *c*8000 system, where the ARCHITECT *c* system within-laboratory %CV and mean concentration values were obtained from the assay package inserts.

Results: The method decision chart showed that Sodium had at least 4 sigma performance and Chloride and Potassium had at least 5 sigma performance at or

near the medical decision point. The precision profile charts of the within-laboratory %CV results for the Alinity c-series overlaid with the ARCHITECT *c* system showed similar performance for each assay.

Conclusion: Sigma metrics, method decision charts, and precision profile charts can be valuable tools for evaluating and comparing product performance by providing a comprehensive understanding of expected assay performance. Chloride and Potassium had sigma values greater than 5, and Sodium had a sigma value greater than 4. The precision performance on the Alinity c-series and ARCHITECT *c* systems was comparable for the three assays. Laboratorians can use these tools as aids in choosing high-quality products, further contributing to the delivery of excellent quality healthcare for patients.

B-039

Glucose Assay Performance on Abbott's next-generation immunochemistry analyzer (Alinity c)

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Objective: To evaluate the analytical performance of the Glucose assay for measurement in human serum/plasma, urine and cerebrospinal fluid (CSF) on Alinity c, clinical chemistry analyzer using photometric technology. The Alinity c instrument is a high throughput instrument for up to 900 tests per hour. The sample is dispensed into a cuvette followed by reagent. The contents are mixed and incubated allowing for the reaction to occur. Absorbance readings of the sample are taken at regular intervals throughout the process at a primary and a secondary wavelength. Data reduction generates a calculated absorbance based on the reaction mode of the assay (end point) and measures the calculated absorbance using a calibration curve to generate a result.

Methods: Key performance testing including tube type, precision, linearity, sample dilution and method comparison were assessed per CLSI protocols. The assay measuring interval was defined by the range which acceptable performance for bias, imprecision and linearity was met. Impact of common interferences was assessed at low and high analyte concentrations. Sample dilution studies were performed to assess performance between the Alinity c and ARCHITECT c systems. Reference interval verification was performed using healthy subjects.

Results: Total imprecision, linearity, and defined measuring intervals are shown for the Glucose assay in the table below. Results versus an on-market comparator assay demonstrated a slope 0.99 - 1.00 and r = 1.00. The assay was not affected by endogenous or exogenous interferents.

Assay	Total %CV	Linearity	Measuring Interval
Glucose Serum	≤ 5	0 - 828 mgl/dL	5 - 800 mgl/dL
Glucose Urine	≤ 6	0 - 843 mgl/dL	1 - 800 mgl/dL
Glucose CSF	≤ 5	0 - 843 mgl/dL	1 - 800 mgl/dL

Conclusion: The Alinity Glucose assay demonstrated excellent precision, linearity, dilution and correlation with an on-market comparator assay. The Glucose assay also showed minimal interference from endogenous serum interferents (hemolysis, lipemia, bilirubin), exogenous urine interferents, and exogenous drug interferents.

B-040

Validating Lipaemic Interference on Roche Cobas 501 for common analytes

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Background: Lipaemic interference is the second most common pre-analytical artefact after hemolysis encountered by clinical laboratories. Lipaemia affects the reliability of results through spectral interference, particularly for methods which employ spectrometric absorbances at lower wavelengths [such as aspartate aminotransferase (AST), alanine aminotransferase (ALT) and albumin], or methods which create volume displacement (eg indirect potentiometry such as sodium and potassium). Manufacturers have incorporated serum indices in automated biochemistry analyzers to determine lipaemia interference. Individual laboratories should validate these cut-off values and implement a workflow to manage lipaemic specimens.

Objective: We aim to validate the manufacturer's threshold for common analytes on the Cobas c501 analyser (Roche Diagnostics, Basel, Switzerland). We also aim to determine the effectiveness of high speed centrifugation for lipaemic specimens.

Methods: Fifteen levels of lipaemia were obtained by spiking varying amount of SMOFlipid (Fresenius Kabi, Germany) to pooled patient serum. For each of the 15 levels and baseline pooled serum, sodium, potassium, alanine aminotransferase, aspartate aminotransferase, and albumin were analysed on Cobas c501 analyser (Roche Diagnostics) in triplicates. Lipaemic index (L-index), a measure of lipid turbidity, was obtained via spectrometry on the c501 analyser. Means and coefficients of variation were determined for each level. Controls for each level of lipaemia were produced by spiking deionized water and were analyzed in triplicates. To assess the effectiveness of high speed centrifugation in removing lipaemia, 5 levels of lipaemic samples underwent high speed centrifugation at 21000G for 60 minutes. With the lipid faction removed, the aqueous phase was analysed in duplicates and the mean obtained. The results were compared to the baseline pooled serum sample.
Results: Our results were largely in agreement with the manufacturer's inserts. At up to an L-index of 1079, sodium showed good recovery of 97.2% (difference of 4 mmol/L from baseline, 139 mmol/L vs baseline 143 mmol/L) and potassium had good recovery of 97.4% (difference of 0.1 mmol/L from baseline, 3.8 mmol/L vs baseline 3.9 mmol/L). AST and ALT had recovery of 87.2% and 81.6% respectively at an L-index of 158, consistent with the manufacturer's claim of interference threshold at L-index of 150. Albumin had a recovery ratio of 95.1% at an L-index of 626, consistent with manufacturer's claim of L-index threshold at 550. Upon high-speed centrifugation, L-index dropped from 426.5, 823.5, 1212.5, 1551.5, 1952 to 19.5, 24, 29.5, 35.5 and 41.5 respectively. The 5 levels of analytes that underwent high speed centrifugation showed good recovery (97%-107%) compared to baseline pooled serum values. Prior to centrifugation, recovery were poor from 17% to 111%, with worse results for AST and ALT. **Conclusion:** Our study shows that lipaemic thresholds for the common biochemical analytes of sodium, potassium, aspartate aminotransferase, alanine aminotransferase and albumin on the Roche c501 analyser follow manufacturer's claims. For laboratories that do not have an ultracentrifuge in view of space and financial constraint, high speed centrifuge at 60 min 21 000G facilitates the removal of lipids.

B-041

Dilute and shoot FI-MS-MS method for quantifying Glucocholic acid in bile using standard addition

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Background

Bile acids not only aid in digestion of dietary fat and cholesterol homeostasis but also play crucial role in pathological conditions of liver, gall bladder and small intestine including cancer. Hence quantitation of bile acids in various fluid compartments might be useful in detecting cancer at early stages. Though most methods reported quantify bile acids in serum, plasma and feces, very few quantify bile acids in bile. In our current work, we chose Glycocholic acid (GCA) as a model bile acid molecule to develop a simple and fast flow-injection MS/MS quantification method. In order to ensure minimize matrix effect, the sample has been diluted and quantified using a standard addition-internal standard technique instead of using a traditional internal standard-calibration curve.

Methods

Briefly each bile sample was first diluted by 4000 times with methanol and standard solutions are added into the aliquots of diluted bile along with internal standard. A 10 µL of resulted sample was directly flow-injected without any chromatographic separation into the ESI source of a triple-quadrupole mass spectrometer using 90% methanol at 0.3 mL/min for 2.5 minutes. Detection was carried out in negative MRM mode with the transitions, 464.1 ® 74 and 401.2 ® 249.1 for GCA and internal standard respectively. Linearity was achieved in the range of 12.5 to 200 ng/mL. The method was also validated for LLOQ, matrix effect, accuracy, inter and intra-day precision.

Results

Linearity, calibration and LLOQ: The standard addition curve constructed from the calibrators demonstrated a correlation coefficient of 0.99. The method was found to be linear in the range of 12.5-200 ng/mL and the %CV for the LLOQ was less than 15%.

Accuracy and precision: Accuracy, Intra and inter-day precision were determined using three QCs. The % relative error (% RE) of intra and inter assays was 7.38-14.88 and -12.03-14.80 respectively. The % relative standard deviation (% RSD) of intra and inter-assays ranged from 4.00-11.60.

Matrix effect: The matrix effects determined by comparing the peak area ratios of GCA and IS in diluted bile and solvent. The mean matrix effect ranged from 87.35 to 94.78 and % RSD was 4.05-9.97which were within the limits.

Conclusion

In conclusion, a greatly simplified MS/MS method has been developed and validated for the quantification of a model bile acid, GCA in bile. With the advantages of high

throughput, and low cost, the method is especially beneficial in a clinical laboratory setting. To the best of our knowledge, this is the first flow injection method that takes advantage of standard addition-internal standard strategy. The method has been validated according to FDA guidelines. This method can also be modified to facilitate individual or simultaneous quantification of other bile acids in bile.

B-042

Accuracy of glucose measurements by two popular blood gas analyzers as assessed by error grid, ISO and FDA criteria

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Objective: We used retrospective comparison of central laboratory (CL) glucose results to evaluate the glucose accuracy of two point of care blood gas systems, the GEM 4000 and the Radiometer ABL 800, housed in, or just outside intensive care units (ICU) in two university hospitals.

Materials and Methods: A laboratory data repository provided arterial glucoses generated by two GEM 4000s on ICU patients in 2012-2013 at Calgary's Foothills University Hospital and glucoses produced by the central laboratory (CL) Roche Cobas 8000-C702 modules. Another repository provided arterial glucoses produced by two Radiometer ABL 800 systems in 2012-2013 on University of Alberta Hospital ICU patients as well as glucose results produced by the CL Beckman DxC. Point of care and CL glucoses were compared if the interval between their analyses was under 30 minutes. The agreements between the CL and the point of care glucoses were assessed with the 2000 Parkes Error Grid, the 2014 Klonoff Surveillance Error Grid, the 2013 ISO 15197 limits and the 2014 FDA draft guidance limits.

Results: The Table summarizes our findings. There are many more GEM than Radiometer CL comparisons. The Radiometer and GEM usual and hypoglycemic mean glucoses are roughly equivalent. The Radiometer demonstrates a positive bias compared to the CL glucose. There is little difference in the accuracy assessments with the Parkes error grid and surveillance error grid showing very limited outlier distributions and both demonstrating acceptable ISO 15197 agreement, but demonstrating unacceptable FDA performance.

Conclusions: The use of this retrospective approach probably cannot adequately assess the FDA's 10% or 7 mg/dL accuracy requirements as glycolysis in the CL specimen will invalidate the assessment. Delayed analysis and resultant glycolysis of the CL glucoses at the Radiometer site may explain the positive Radiometer glucose bias.

	Radiometer	GEM
Total	2786	15217
Bias (mean) mg/dL	5.1 (145)	-0.27 (153)
hypoglycemic (N)	43	396
hypoglycemic bias	-4.1 (65)	-9 (64)
Parke's Error Grid Analysis % Risk Zones E, D, C, B, A	0; 0; 0; 2; 98	0; 0; 0; 0.5; 99.5
Surveillance Error Grid Analysis % Risk Zones H, G, F, E,	0; 0; 0; 0; 0.1; 0.5; 1.77; 97.76	0; 0; 0; 0.1; 0.1; 0.3; 1.3; 98
ISO 2013		
>100 mg/dL (within +/- 15%)	2511 (98.1%)	12347 (96.22%)
<100 mg/dL (within +/- 15mg/dL)	275 (95.3%)	2870 (95.1%)
FDA		
>73 mg/dL (within +/- 10%)	2743 (93.7%)*	14821 (91.2%)*
<73 mg/dL (within +/- 7 mg/dL)	43 (69.8%)* *<95	396 (70.2%)* *<95

B-043

Analysis of clinical phenotype of of compound heterozygotes of Hb NewYork and β-thalassemia

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Background: Hb New York has been noted to be a relatively common variant in Southern China. A few cases of double heterozygosity of β-thalassemia and Hb New York had been mentioned, while the spectrum of its clinical manifestations was reported consistent withβ-thalassemia trait. But cases in this study showed different conditions.

Methods: Peripheral blood samples from 2 patients with double heterozygosity of Hb NewYork and β-thalassemia and 10 Hb New York heterozygous cases were collected. The investigation of deafness heredity was made in a family by the consent of the family members. RBC analysis, serum bilirubin detection and hemoglobin electrophoresis were performed.Genotypes of α and β-globin were also analyzed.

Results: The father of the proband 1 and the 10 sporadic cases were Hb NewYork carriers.All of them were asymptomatic and had normal hematological parameters except for an abnormal hemoglobin band detected on hemoglobin electrophoresis. The mother and brother of the proband 1 were β-thalassemia mutation CD41/42 alone, the hemoglobins of them were 109g/L and 118g/L, respectively. Mean corpuscular volume of red cell was smaller than that of normal sample and the results of serum bilirubin detection were in the normal reference ranges. The proband 1 who maintained a stable hemoglobin level at 8 g/L was a compound heterozygote for Hb NewYork and β-thalassemia mutation CD41/42, characterized by low pigment-small-cell anemia. Proband 2 was a compound heterozygote for Hb NewYork and β-thalassemia mutation IVSII-654, whose hemoglobin was 143 g/L and mean corpuscular volume of red cells was smaller . Both of heterozygotes had different levels of hemolysis, and the results of blood bilirubin detection were 37.8μmol/L and 81.2μmol/L, respectively, which were out of normal reference ranges. Results of hemoglobin electrophoresis showed that Hb A2, Hb F increased and Hb A were not detected.Abnormal hemoglobin bands Hb NewYork were also detected.

Conclusion: Carriers of Hb NewYork alone are asymptomatic. but double heterozygosity of Hb New York and β0 codons 41/42 has clinical symptoms such as anemia and hemolysis, which is more serious than that of CD41/42 alone. Double heterozygosity of Hb New York and β0 IVSII-654 also has symptom of hemolysis.Therefore,couples with one carrying Hb NewYork and another carrying a β-thatassemia mutation need to be notified that it would be a problem.

B-044

Evaluation of Nova Biomedical Clot Catchers for Analysis of Blood Gas Samples on the Radiometer ABL90

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Background: The Radiometer ABL90 (Radiometer Medical ApS, Brønshøj, Denmark) blood gas analyzer can be used to analyze neonatal and other low volume blood gas samples (0.5mL in 3.0mL blood gas syringe (Smiths Medical, Keene, NH)). Shortly after implementation, we began to experience a high number of calibration error flags, consumable replacements, and extended downtime. Representatives from Radiometer suggested that silicone, micro-clots or other substances in low volume blood gas specimens could cause damage to internal components and recommended use of a clot catcher before sample analysis to reduce instrument errors and downtime.

Methods: The number of calibration and analyzer errors, consumable replacements, and analyzer downtime were recorded for 3 months using our standard low volume blood gas collection protocol. For three months we trialed the use of Nova Biomedical Stat Profile Critical Care Express syringe clot catchers (Nova Biomedical, Waltham MA) for all heparinized whole blood specimens analyzed on the ABL90. To ensure a clean and optimally-operating analyzer before beginning the clot catcher trial, preventative maintenance was performed, new tubing was installed, and fresh consumables were loaded. We then compared the number of calibration and analyzer errors, consumable replacements, and analyzer downtime in the three months after implementing clot catchers to the three months prior to the use of clot catchers.

Results: Calibration errors decreased 23% (n= 26 pre-clot catcher versus n= 20 post-clot catcher). Sensor cassette maintenance interruptions, indicating that the analyzer cannot perform calibration, were eliminated with the use of clot catchers (n= 21 pre-clot catcher versus n= 0 post-clot catcher). The number of sensor cassettes and solution packs required during the pre- and post-clot catcher periods decreased 50% and 35%, respectively (16 cassettes and 17 packs pre-clot catcher versus 8 cassettes and 11 packs post-clot catcher). Lastly, analyzer downtime was significantly reduced by 92% (416 hours pre-clot catcher versus 32 hours post-clot catcher).

Conclusion: The use of clot catchers for blood gas analysis on the Radiometer ABL90 greatly reduced the number of error codes, consumable replacements, and downtime. Future studies are planned using clot catchers for additional sample types prone to micro-clot and sample debris issues such as cord blood and pleural fluid.

B-045

Validation of spinal fluid lactate measurements and effect of HIL interferences using the Abbott ARCHITECT plasma lactic acid assay

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Background: Differentiation between viral and bacterial causes of meningitis is critical because aseptic meningitis is usually less severe and resolves on its own, while bacterial meningitis can be life threatening and requires immediate medical attention. Lactate measurements on spinal fluid (SF) specimens can be a key marker with elevations above 3.0 mmol/L being suggestive of bacterial meningitis. However, the Abbott ARCHITECT® assay is cleared for use with plasma but not SF specimens. **Objectives:** To validate the analytical performance of the ARCHITECT Lactic Acid assay (#9P18) on SF specimens, and to expand the limited information on the effects of common interferences due to hemolysis, icterus, and lipemia (HIL) on the performance of this assay in plasma specimens. **Methods:** A new ARCHITECT lactic acid reagent was released in June 2016 to replace the previous assay (#9D89). The old and new reagents were compared using 60 SF specimens. Imprecision of the new assay was determined using two levels of Bio-Rad Liquichek™ Spinal Fluid Quality Control measured in duplicate, two times per day for 11 days (n = 44). Linearity was assessed by mixing high and low patient SF specimens. Accuracy and dilution recovery were evaluated by spiking with sodium lactate. The effects of HIL interference on lactate quantitation were studied on plasma specimens at 1.0 or 4.0 mmol/L lactate by spiking with red cell lysate, unconjugated or conjugated bilirubin, or Intralipid® (triglycerides). Data were processed using EP Evaluator® Release 7. **Results:** The two assays correlated well over a range of lactate concentrations from 0.82 to 5.94 mmol/L, with a slight positive bias for the new reagent (slope = 1.03; intercept = -0.03; R^2 = 0.997; mean bias = +0.02 mmol/L). Total imprecision at 2.03 and 3.99 mmol/L lactate was 1.0% and 0.9% CV, respectively. Linearity was confirmed from 0.7 to 8.8 mmol/L lactate, and dilution recovery was 93 to 110%. Accuracy ranged from 95 to 99.8% recovery at 1.0, 3.0, and 7.0 mmol/L lactate. However, automatic on-board dilution above the analytical measurement range (13.3 mmol/L) resulted in 90% recovery at 16.0 mmol/L. Significant positive interference (>10% error) from hemoglobin occurred at 1.2 and 4.6 g/L for the 1.0 mmol/L and 4.0 mmol/L lactate specimens, respectively. At the corresponding lactate levels, conjugated bilirubin showed significant negative interference at 69 and 232 µmol/L, while unconjugated bilirubin did not reveal a significant negative bias until concentrations were 177 and 360 µmol/L, respectively. Triglycerides up to 47 mmol/L did not significantly interfere at 4.0 mmol/L lactate, but showed a positive bias above 44 mmol/L at 1.0 mmol/L lactate. **Conclusion:** The new Abbott ARCHITECT Lactic Acid assay correlates well to the predecessor using SF specimens. The assay meets performance goals for precision, linearity, and dilution recovery in SF specimens, but is susceptible to moderate levels of hemolysis and icterus in plasma specimens. Overall, these data support the ARCHITECT Lactic Acid assay for the testing of lactate in spinal fluid for clinical purposes.

B-046

Comparison of Relative Frequency, Magnitude and Etiology of Zero/Negative Anion Gaps of two Popular Blood Gas Analyzers

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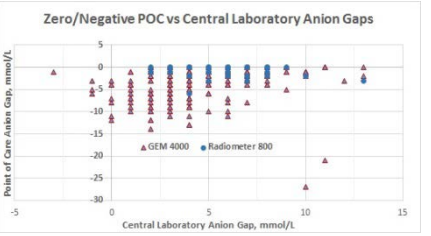
Background: Negative anion gaps occur infrequently and are often attributed to laboratory error. Probably the most common cause of negative anion gaps is random error affecting the measurement of sodium, chloride, and/or bicarbonate generating pseudohyponatremia, pseudohyperchloremia, pseudohyperbicarbonatemia, or a combination of these measurement errors. As zero/negative anion gaps can indicate significant altered pathophysiology, it is important that they be investigated. We used data mining to correlate zero/negative anion gaps discovered by point of care blood gas analysis to concurrent electrolyte measurements performed in the central laboratory.

Methods: A laboratory data repository provided arterial blood gas, electrolyte and metabolite results generated by two GEM 4000s on ICU patients in 2012-2013 at Calgary's Foothills University Hospital as well as electrolyte results produced by the Roche Cobas 8000-C702 modules. Another repository provided similar results generated by two Radiometer ABL 800 systems on ICU patients in 2012-2013 at University of Alberta Hospital as well as electrolyte results produced by the Beckman DxC. Point of care and central laboratory electrolytes were correlated If the interval between their testing was under 30 minutes.

Results: The Figure shows the distribution of the zero/negative anion gaps compared to the central laboratory. Of 7586 GEM gaps, 348 were zero/negative with the average Na, Cl, HCO3 deviating by -1.5, +2.5 and +3.9 mmol/L, respectively. Of the 2985 Radiometer gaps, 73 were low with the Na, Cl, HCO3 deviating by -1.6, +3.5, and +1.2 mmol/L, respectively. The relative incidence of zero/negative gaps is higher for the GEM compared to the Radiometer ($p<0.001$)

Conclusion: The GEM 4000 tends to produce larger and more artefactual zero and negative gaps than the Radiometer with these gaps being associated with positive shifts in HCO3.



B-047

Increased disialotransferrin evident with chronic alcohol consumption

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Background: Single biomarkers for alcohol abuse screening provide insufficient sensitivity and specificity. Multiple analytes including carbohydrate deficient transferrin (CDT), GGT, and AST: ALT ratio are needed to avoid misinterpretation. CDT is an abnormal transferrin glycoform known to arise following heavy alcohol consumption (> 60 g of ethanol per day for at least two weeks). Tetrasialotransferrin is the predominant fraction in healthy people, and the increased presence of tri-, di-, mono- or asialotransferrin alludes to abnormal glycan metabolism. Typically, di- and asialotransferrin are influenced by heavy alcohol consumption, whereas tri- and monosialotransferrin appear to be unaffected by heavy alcohol use. %CDT is the percentage of altered transferrin relative to total transferrin and can be measured by immunoassays, although the specific isoform being measured remains unclear. High performance liquid chromatography (HPLC) is a more specific method and allows for quantification of each transferrin glycoform. The purpose of this study was to compare CDT immunoassay and HPLC measurements to determine which transferrin glycoform has the greatest influence on the CDT immunoassay results. Furthermore, HPLC analysis was performed on patient samples with measured ethanol concentrations to determine the effect of acute elevations in ethanol on transferrin glycoform profiles.

Design and Methods: 21 apparently healthy patient samples submitted for alcohol abuse screening were analyzed for CDT and transferrin by particle-enhanced immunonephelometric and immunonephelometric assay, respectively, on a Siemens BN ProSpec (Siemens Healthcare Limited). %CDT was calculated as [CDT (mg/L)/ Transferrin (g/L)]/10. GGT, ALT, AST were analyzed on the Roche Modular (Roche Diagnostics). Transferrin glycoform profiles were analyzed by HPLC on an Agilent 1200 using an anion exchange column and UV-Vis detector (GE Healthcare). Prior to HPLC analysis, patient samples were iron-saturated with ferric nitrilotriacetic acid (FeNTA) and lipoproteins precipitated. Additionally, 12 patient samples with elevated ethanol concentrations were analyzed by HPLC to determine whether acute elevations in ethanol concentrations affected transferrin glycoform profiles.

Results: %disialotransferrin fraction on HPLC analysis correlated highly with %CDT (R^2 = 0.9829), whereas %trisialotransferrin fraction demonstrated poor correlation with %CDT (R^2 = 0.1064). Only 2 and 4 of 21 patient samples had detectable mono- or asialotransferrin, respectively. Overall, this suggests that the CDT immunoassay detects disialotransferrin. A high concordance of abnormal results was observed between %disialotransferrin fraction on HPLC and %CDT. Of 12 patients with %CDT above the normal reference range (%CDT ≤ 2.5%), 11 also had %disialotransferrin above the normal reference range (%disialotransferrin < 1.7%). No significant correlation was evident between %disialotransferrin fraction and GGT or AST:ALT ratio ($R^2 \leq 0.001$ and $R^2 \leq 0.002$, respectively). HPLC analysis of patient samples with elevated ethanol concentrations demonstrated poor correlation between %disialotransferrin and ethanol concentration (R^2 = 0.08), suggesting that acute heavy alcohol consumption does not induce rapid changes to transferrin glycoform profiles.

Conclusion: The CDT immunoassay appears to detect disialotransferrin, and a significant increase in %disialotransferrin on HPLC is observed in patients suspected of chronic alcohol abuse. The lack of correlation between ethanol concentration and %disialotransferrin suggests that changes in transferrin glycoform profile are observed in chronic and not acute alcohol abusers.

B-048

Evaluation of Candidate Serum/Artificial Serum Low Level Creatinine Reference Materials by Routine Clinical Assays in an Interlaboratory Study

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Background: The National Institute of Standards and Technology (NIST) provides a variety of Standard Reference Materials® (SRMs) intended for use as accuracy controls in the analysis of clinical samples. While these materials are typically composed of pooled donor samples, NIST has begun to investigate the use of artificial matrices as bases or diluents for the preparation of a new generation of reference materials. NIST currently sells SRM 967a Creatinine in Frozen Human Serum, which provides two levels of creatinine in serum at adult normal and high levels to support clinical measurements for assessment of kidney disease. Pediatric ranges for serum creatinine are significantly lower than the adult normal range. Therefore, the current SRM 967a does not support the accurate measurement of creatinine in the range necessary for measuring serum creatinine and screening for kidney disease in the pediatric population, which is a concern that has been voiced in recent years by the National Kidney Disease Education Program (NKDEP) of the National Institute of Diabetes and Digestive and Kidney Diseases-National Institutes of Health. As it is not feasible to obtain large volumes of pediatric serum, NIST has begun to investigate the use of artificial serum matrices for a next-generation material with a target value of 4 µg/g (0.4 mg/dL) creatinine.**Methods:** NIST obtained SeraFlx BIOMATRIX and SeraFlx LCMSMS artificial serum from Cerilliant. In addition, a pre-market SigMatrix Ultra Serum Diluent was provided by MilliporeSigma. Based on previous studies at NIST, all these artificial serum matrices performed satisfactorily when analyzed by isotope-dilution liquid chromatography mass spectrometry (ID-LC-MS). To determine if these materials would be fit-for-purpose in routine clinical creatinine assays, NIST organized a interlaboratory study with manufacturers and clinical laboratories. NIST prepared six candidate materials with combinations of the artificial and normal human serum or pure creatinine. Creatinine values were determined by a NIST ID-LC-MS Reference Measurement Procedure (RMP) and ranged from 2.1 µg/g (0.22 mg/dL) to 5.1 µg/g (0.52 mg/dL). Candidate materials and SRM 967a were shipped to ten laboratories and analyzed in triplicate for creatinine using a total of eleven Jaffe-based and twelve enzymatic-based assays.**Results:**For SRM 967a Level 2, all assays reported the certified value [(3.877 ± 0.082) mg/dL]. However, several Jaffe and enzymatic values were outside the certified range [(0.847 ± 0.018) mg/dL] for SRM 967a Level 1. Candidate mixtures containing either SeraFlx BIOMATRIX or SeraFlx LCMSMS resulted in errors for several Jaffe and enzymatic assays, possibly due to turbidity caused by undissolved components, and displayed a wide range of % bias to the NIST RMP value (-163 %, +78 %). The narrowest range of % bias was observed in the material containing normal serum diluted with SigMatrix Ultra (-13 %, +32 %). **Conclusion:** Additional feedback from stakeholders regarding the results of the study will be required to determine if any of these materials are fit-for-purpose with routine methods or if specific materials are required for Jaffe versus enzymatic methods to improve measurements of creatinine in low level serum samples.