Asparaginase-induced pseudohyponatremia, a case-driven working strategy in pediatric hemato-oncologic patients

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Objective

Validating a patient friendly working strategy for reliable sodium determination in high lipemic samples

Methods & Material

Sodium and total protein (TP) were analyzed on the Cobas 8000 (Roche Diagnostics, Switzerland) in venous plasma. Sodium in arterial or venous whole blood was determined on the ABL90 Flex (Radiometer, Denmark). We evaluated 4 strategies in a pediatric patient with asparaginase-induced pseudohyponatremia,verified the impact of TP on sodium (n=2274) and tested the interchangeability (n=40) of methods (direct vs indirect ISE) and sample types (arterial, venous, mixed up routine venous blood).

Results

Sodium measured with the indirect ISE, before and after ultracentrifugation, differed significantly from the direct ISE and calculated sodium ($P < 0.05$) from those of the direct ISE and the calculated sodium (Table 1). With 1500 mg/dL as triglyceride threshold, significant difference between direct and indirect ISE was found ($P < 0.05$). TP influenced Na when TP >83 mg/mL, with 22% of biases exceeding the criterion (EKE d% = 3.4%), which is 7-times higher than the group of TP 65-83 mg/L (Table 2). The interchangeability study did not reveal any significant differences between the three groups of sample types and analysers. Passing-Bablok curves and Bland-Altman test showed comparability (Figure 1). Making it possible to re-use Li-heparin tubes after routine testing for accurate sodium determination with direct ISE in cases of hypertriglyceridemia.

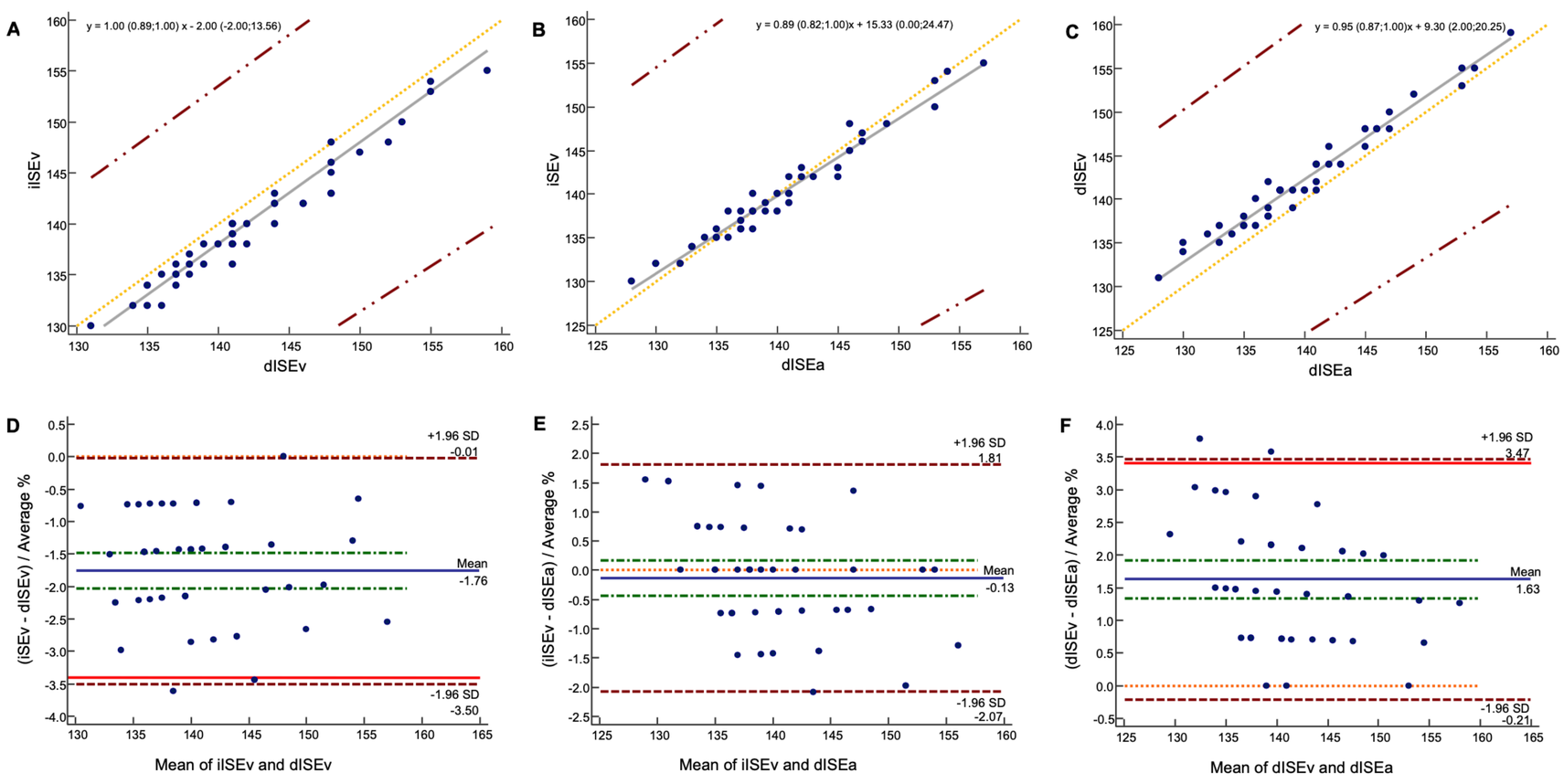
Table 1. Summary of the test results over 8 days.

Na-iISEv, sodium by indirect ISE; Na-UC, sodium after ultracentrifugation by indirect ISE; Na-dISEv, Li-heparine sample by direct ISE; Na-dISE, sodium by direct ISE; Na-cal, calculated sodium; L-index Before-UC, Lipemic index before ultracentrifugation; L-index After-UC, Lipemic index after ultracentrifugation; NA, not available.

Sample / Day	Na-iISEv (mmol/L)	Na-UC (mmol/L)	Na-dISEv (mmol/L)	Na-dISE (mmol/L)	Na-cal (mmol/L)	Triglycerides (mg/dL)	L-Index Before-UC	L-Index After-UC	Lipase (U/L)
Ref. int.	136-145	136-145	137-145	137-145	-	48-219	-	-	<31
Day 1	124	125	NA	NA	129	2041	307	181	22
Day 2	130	NA	133	133	134	1859	232	NA	24
	130	132	133	133	135	1960	234	139	NA
Day 3	128	132	133	133	136	3286	490	257	NA
Day 4	129	130	133	133	136	2741	394	226	20
Day 5	130	132	133	NA	135	2076	242	188	16
Day 6	130	130	133	133	134	1587	226	158	13
Day 7	132	130	132	132	134	861	83	51	16
Day 8	133	132	133	132	134	602	101	83	22

Table 2. Results of the impact of non-soluble components on sodium determination by ISE. ([a]$P < 0.0001$)

Group	TP (g/L)	N	Range TP (g/L)	Mean Bias% ± 95 CI	Number of bias > 3.4% (%)
A	<65	761	31 – 64	-0.19 ± 0.06	0.74
B	65-83	1486	65 – 83	-1.26 ± 0.08	3.41
C	>83	18	84 – 102	-2.53 ± 0.43	22.22[a]



Our strategy can reduce the sampling volume by 1 mL, from 3.6 to 2.6 mL for each sampling. Which has an important impact on patients who need daily sampling. In this pediatric case, 7 mL of blood would have been saved during follow-up, which is a significant amount of blood. Moreover, pediatric patients treated for leukemia are often anemic and could potentially benefit from such sampling strategies.

Figure 1. Passing–Bablok and Bland–Altman plots for the interchangeability (n = 45) between methods for sodium: A/D) Venous indirect ISE (iISEv) vs. venous direct ISE (dISEv), B/E) venous indirect ISE (iISEv) vs. arterial direct ISE (dISEa) and C/F) venous direct ISE (dISEv) vs. arterial direct ISE (dISEa).

Yellow dotted line, y = x; grey line, Passing–Bablok curve; alternating dot-tick brown line, 95% confidence interval; orange dotted line, bias equal to zero; blue line, mean; brown tick-line, limits of agreement; alternating dot-tick green line, confidence interval of the mean; red line, bias acceptance criterion of +/–3.4%.

Conclusions

Indirect ISE suffered from high triglycerides, without lipemic indexes exceeding insert cutoffs. Direct ISE was insensitive to hypertriglyceridemia. Direct ISE results on whole blood, after mixing up, and direct ISE results on blood gas tubes were statistically comparable. We propose the consecutive use of only one Li-heparin venous sample for both analyzers. Samples can follow the regular workflow and a reflex-analysis will be performed on the ABL Flex on the same tube. Preventing re-sampling in patients. Resulting in less patient burden and stress which is beneficial for patient care. In future cases of hypertriglyceridemia, a triglyceride threshold of 1500 mg/dL will be used for reliable sodium determination, until confirmation of a more specific L-index threshold for sodium.

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