Calculated osmolality is underestimating osmolality changes in children with diabetic ketoacidosis: an observational study

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Introduction: In diabetic ketoacidosis (DKA), serum osmolality is elevated due to hyperosmolar dehydration. In clinical practice, calculated serum osmolality using the formula Osm_{calc} = (*2x Sodium)* + *glucose* is used. Point of care laboratory analyzers provide only calculated serum osmolality. However, it is known that measured and calculated serum osmolality can differ. Studies have shown, that a marked early and fast decrease in serum osmolality increases the risk of cerebral edema as a complication of DKA in children with type 1 diabetes (T1D). We aimed to investigate the temporal course difference between measured and calculated serum osmolality during rehydration therapy in children with T1D and DKA.

Methods: Data used originate from an observational multi-center study including pediatric patients with T1D admitted for DKA and aged 1-18 years [1]. Serum osmolality was analyzed in laboratory using the freezing point depression method (Osm_{meas}) and was calculated (Osm_{calc}) from the blood gas analysis. Serial serum osmolality measurements (measured and calculated) and blood gases were used at up to 14 time points from the start of rehydration therapy to 72 hours post rehydration start. Clinical parameters such as age, severity of DKA (mild = pH<7.3, moderate = pH<7.2, or severe pH<7.1) and Glasgow Coma Scale (GCS) were documented. Osm_{meas} and Osm_{calc} were summarized by mean ± standard deviation for each time point. The mean difference ($\Delta Osm_{meas} - Osm_{calc}$) was evaluated by repeated measures ANOVA, 95% confidence intervals were calculated for each time point.

Results: Data from 28 children with T1D (20 newly diagnosed) and DKA (mild: n=3, moderate: n=12, severe: n=13) were included in the study. Median [IQ range] age was 11.5 years [8, 14], GCS was 15 points [15, 15], no patient had GCS <12 or suffered from cerebral edema. 223 paired serum measured and calculated osmolality measurements were obtained (median: 8 per participants). At a mean glucose level of 28 (10.5) mmol/L at the beginning of the rehydration therapy mean Osm_{meas} (±SD) was 318.5 mOsm/kg (±15.4) vs. Osm_{calc} 299 mOsm/kg (±10.8), (repeated measures mean: Δ=21.3 [95%CI: 17.8-24.7], P<0.001), while the magnitude of difference varied over time (P<0.001). Mean differences were Δ=14.3 [10.6; 18.1] mOsm/kg at 6 hours, Δ=7.0 [4.4; 9.6] mOsm/kg at 12 hours and Δ=5.6 [2.9-8.2] mOsm/kg at 24h after the start of rehydration and insulin therapy.

Conclusions: This is the first data set available on sequential measured and calculated osmolality levels in a hyperosmolal state such as DKA in children and adolescents. Laboratory measured osmolality was significantly higher than calculated osmolality, this difference was most pronounced during the first 12 hours after the start of rehydration therapy. It indicates that serum osmolality is underestimated using calculated osmolality. This discrepancy should be considered when treating DKA in view of individual risk for cerebral edema.

[1] Burckhardt MA et al. *Copeptin kinetics and its relationship to osmolality during rehydration for diabetic ketoacidosis in children*. J Clin Endocrinol Metab. 2020 Nov 1;105(11):dgaa568. doi: 10.1210/clinem/dgaa568.