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Original Article

Evaluation of the effects of glucose on osmolal gap using freezing point depression and vapor pressure methods

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Abstract The measurement of serum osmolality, and the calculation of osmolal gap (OG) from a calculated osmolality are widely used in clinical and emergency medicine. In this study, the possible effects of blood glucose on OG were investigated by freezing point depression and vapor pressure methods. The concentrations of sodium, glucose, blood urea nitrogen and osmolalities of 2640 samples were measured. There were two methods for calculating serum osmolality: freezing point depression method (n = 2399) and vapor pressure method (n = 241). The OG was positively associated with glucose in glucose 110–450 mg/dL ($r = 0.191$, $p < 0.001$) and glucose > 450 mg/dL ($r = 0.372$, $p < 0.001$), but not in glucose < 110 mg/dL ($r = 0.017$, $p = 0.711$) in freezing point depression method. However, OG had no correlation with glucose regardless of glucose level in vapor pressure method. In freezing point depression method, compared with the groups of glucose <110 and 110–450 mg/dL, the group with glucose >450 mg/dL had higher OG ($p < 0.001$) and higher prevalence of OG > 10 mOsm/Kg H_2O ($p < 0.001$). Our study demonstrated that OG is impacted by

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increasing blood glucose concentration using freezing point depression method, special attention should be made to blood glucose concentrations when using freezing point depression method to determine OG.

Introduction

Osmolality is the total concentration exerted by soluble materials in the blood. It is generally influenced by 3 major species including: sodium (Na), Glucose (Glu), and blood urea nitrogen (BUN) [1]. Normal osmolality is of about 275–295 mOsm/kg H_2O, where osmolality of greater than 300 mOsm/kg H_2O is indicative of concentrated blood osmoles. The possible cause of this increase in osmolality can include: dehydration, high sodium, high blood sugar, alcohol, methanol poisoning, and uremia [2]. The clinical determination of osmolality is mainly used for diagnostic and assessments for diseases, such as for diabetes patients in the emergency room [3]. The determination of osmolality can be utilized for emergency patients to assess low blood sodium, dehydration, and kidney functions.

The difference between measured osmolality and theoretically calculated osmolality is termed osmolal gap (OG) (OG = measured osmolality − calculated osmolality). The osmolality is calculated as: calculated osmolality = 2*Na + Glu/18 + BUN/2.8 [1]. The OG has specific meanings for diagnosis, treatment, and prognosis for the clinical evaluation of unmeasurable osmolalities. The calculated value is generally 10 mOsm/kg H_2O less than the measure value, resulting in an OG of 10 mOsm/kg H_2O [4–7]. A OG value greater than 10 mOsm/kg is a critical clinical value for indications of (1) assessment of serum water content in hyponatremia with hyperlipidemia or hyperglycemia; and (2) the assessment of ingestion of substances such as ethanol, methanol, and acetone [8].

Currently, there is no literature that had suggested the correlation between OG and Glu. There are two common methods of determining osmolality: (1) freezing point depression method and (2) vapor pressure method. This study utilizes both of these aforementioned methods for determining the effect of Glu on OG.

Subjects and methods

Study patients and design

This study was conducted at a medical center and a regional hospital in southern Taiwan, and enrolled 2640 patients from January 2011 to December 2016. The medical orders and results that occurred within 6 years were obtain from the clinical database and retrospectively analyzed in this study. Samples with alcohols were excluded from this study. The study protocol was approved by the Institutional Review Board of Kaohsiung Medical University Hospital, and all participants provided written informed consent to participate in this study. The methods were carried out in accordance with the approved guidelines.

Collection of demographic and laboratory data

Data including age, and sex were recorded from the patients' medical records or interviews. Serum osmolality, GLU, BUN, creatinine and Na were analyzed on the same blood specimen. Osmolality was measured by freezing point depression method with Advance 3250 (Advanced Instrument, USA) and vapor pressure method with APRO® Vapor Pressure Osmometer (Wascor, EliTech Group, USA). The testing GLU and BUN reagents were prepared with Unicel® DxC 800 Synchron® Clinical System and SYNCHRON® SYSTEMS AQUA CAL 1, 2 (Beckman Coulter Inc, USA). The Sodium concentrations in blood were quantified by Unicel® DxC 800 Synchron® Clinical System (Beckman Coulter Inc, USA). The value of estimated glomerular filtration rate (eGFR) was calculated using the 4-variable equation in the Modification of Diet in Renal Disease (MDRD) study [9].

Statistical analysis

All statistical analyses were performed using SPSS software for Windows version 19.0 (SPSS Inc. Chicago, USA). Data were expressed as percentages, means ± standard deviations, and means ± standard error of the mean for OG. The differences between groups were checked by Chi-square test for categorical variables, or by independent t-test for continuous variables. The relationship between two continuous variables was assessed by a bivariate correlation method (Pearson's correlation). Multiple comparisons among the study groups were performed by one-way analysis of variance (ANOVA) followed by post hoc test adjusted with a Bonferroni correction. A p value of less than 0.05 was considered to indicate statistical significance.

Results

A total of 2640 serum samples were included. There were 2399 OG samples using freezing point depression method and 241 samples using vapor pressure method, respectively. The mean age was 65.1 ± 21.1 years. Table 1 shows the comparison of clinical characteristics among the study groups using freezing point depression method and vapor pressure method.

Comparison of glucose, BUN and Na in patients with OG≦ and >10 mOsm/Kg H_2O using different methods

Table 2 showed the comparison of glucose, BUN and Na in patients with OG ≦ and >10 mOsm/Kg H_2O using different methods. In freezing point depression method, compared

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