Development of Equation for Calculated Osmolarity in the Thai Elderly Urban Emergency Department Patients and its Accuracy

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Abstract

Background: Older people are more susceptible to dehydration owing to their physiological changes and down-regulated thirst response. In the literature, serum osmolarity remains the gold standard for diagnosing water-loss dehydration. This study aimed to develop an equation specifically for calculating osmolarity in older Thai adults. Furthermore, our study compared the accuracy of the proposed equation with that of previously published equations.

Methods: This study was a secondary analysis of a prospective cohort study. We enrolled all the patients aged ≥65 years who visited our emergency department (ED) during the period from May 15, 2017, to July 31, 2017. We used linear regression to develop a new calculated osmolarity equation from the patients' laboratory data compared with the measured serum osmolarity. In a receiver-operating characteristic (ROC) plot, the new equation was compared with other 5 equations in terms of its ability to diagnose dehydration (calculated osmolarity > 300 mOsm/kg). The Bland-Altman method was used to assess the mean difference (MD) with each equation.

Results: A total of 322 participants were included in the study. The new equation originated from our older patients' data was 1.75 × (Na + K) + 0.9 × Glucose + Urea + 25.7, all in mmol/L. This equation had the highest ROC-area under the curve (AUC) of 0.81 among all the equations. The MD between the calculated and measured osmolarity values was 0.49 mOsm/L (95% confidence interval [CI], −0.40 to 1.38 mOsm/L). Equations 1, 2, 3, 4, and 5 showed ROC-AUC of 0.73, 0.78, 0.75, 0.80, and 0.81, respectively. The MDs (95% CI) were 6.18 (5.13–7.23), −4.19 (−5.15 to −3.23), −5.38 (−6.37 to −4.39), −5.31 (−6.20 to −4.41), and −6.89 (−7.8 to −5.98), respectively.

Conclusion: We developed a new equation with good performance in calculating osmolarity. However, further validation and ability to predict dehydration of this equation should be assessed.

Keywords: osmolarity, equation, elderly, dehydration

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การสร้างสมการเพื่อคำนวณค่าออสโมลาริตีในผู้ป่วยสูงอายุไทยของแผนกเวชศาสตร์ฉุกเฉินในโรงพยาบาลเขตเมืองและความแม่นยำของสมการ

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บทคัดย่อ

บทนำ: ผู้สูงอายุนั้นเป็นกลุ่มเสี่ยงต่อภาวะขาดน้ำเนื่องจากมีการเปลี่ยนแปลงทางสรีรวิทยาและการปรับลดลงของขบวนการตอบสนองการกระหายน้ำ จากวรรณกรรมก่อนหน้านี้มีการใช้ค่าออสโมลงริตีในเลือดเป็นเกณฑ์การวินิจฉัยภาวะขาดน้ำในผู้สูงอายุ การศึกษานี้จึงมีวัตถุประสงค์เพื่อสร้างสมการที่ใช้คำนวณค่าออสโมลาริตีเฉพาะเจาะจงกับผู้สูงอายุชาวไทยและเปรียบเทียบความแม่นยำกับสมการก่อนหน้า

วิธีดำเนินการวิจัย: การศึกษานี้เป็นการวิเคราะห์ข้อมูลจากการศึกษาตามแผนแบบไปข้างหน้า ที่ศึกษาในผู้ป่วยแผนกเวชศาสตร์ฉุกเฉินอายุ ≥65 ปี ช่วงวันที่ 15 พฤษภาคม ถึง 31 กรกฎาคม 2560 โดยนำมาวิเคราะห์พหุโลจิสติกถดถอยเพื่อหาตัวแปรในการสร้างสมการ จากนั้นทดสอบความแม่นยำในกราฟเส้นโค้งโดยเปรียบเทียบกับ 5 สมการก่อนหน้าที่มีความแม่นยำสูง และใช้กราฟแบลนด์อัลต์แมนเพื่อประเมินค่าความแตกต่างกันของค่าเฉลี่ย

ผลการวิจัย: จากข้อมูลผู้ป่วย 322 ราย นำมาซึ่งการสร้างสมการคือ 1.75 × (Na + K) + 0.9 × Glucose + Urea + 25.7 (หน่วย mmol/L) และพบว่ามีค่าพื้นที่ใต้เส้นโค้งเท่ากับ 0.81 เป็นค่าที่สูงที่สุดในสมการทั้งหมดที่นำมาทดสอบ ความแตกต่างกันของค่าเฉลี่ยระหว่างการคำนวณและค่าที่วัดได้จากเลือดเท่ากับ 0.49 (95% CI, −0.40 to 1.38) ในขณะที่สมการที่ 1 2 3 4 และ 5 มีค่าพื้นที่ใต้เส้นโค้งเท่ากับ 0.73 0.78 0.75 0.80 และ 0.81 ตามลำดับ ความแตกต่างกันของค่าเฉลี่ยเท่ากับ 6.18 (5.13–7.23), −4.19 (−5.15 to −3.23), −5.38 (−6.37 to −4.39), −5.31 (−6.20 to −4.41), และ −6.89 (−7.8 to −5.98) ตามลำดับ

สรุป: จากการสร้างสมการเพื่อคำนวณค่าออสโมลาริตีในผู้ป่วยสูงอายุไทยของแผนกเวชศาสตร์ฉุกเฉินพบว่ามีความแม่นยำที่ดี ทั้งนี้ควรทำการทดสอบกับกลุ่มตัวอย่างอื่นๆ และทดสอบความสามารถในการวินิจฉัยภาวะขาดน้ำต่อไปในอนาคต

คำสำคัญ: ออสโมลาริตี, สมการ, ผู้สูงอายุ, ภาวะขาดน้ำ

วันที่รับบทความ: 7 เมษายน 2564 **วันแก้ไขบทความ:** 26 พฤษภาคม 2564 **วันตอบรับบทความ:** 28 พฤษภาคม 2564

Background

The physiological regulation of water balance in the elderly changes over time. During advanced ages, the human body encounters a reduction in water proportion from 60%–70% to 50%[1]. Normally, thirst response, which prevents our bodies from dehydration, reacts if it reaches the osmolality threshold of the cellular osmoreceptor[2]. However, previous studies found that older healthy adults had a higher level of plasma osmolality than younger adults. Moreover, reduction in renal function, including the ability to concentrate urine and water reabsorption, and water reserve in soft tissues contribute to risk of dehydration in the elderly[3-5].

Water-loss dehydration or hypertonic dehydration (HD) causes numerous clinical impacts on older adults such as increased risks of falling, fracture, bedsore, kidney stone, kidney failure, stroke, and myocardial infarction[6-9]. Globally, different countries have examined the prevalence of HD in older people. It ranges from 20% in community dwellers to 37% in hospitalized older patients[10-13].

The reference standard for water-loss dehydration is the direct measurement of serum osmolality, as this parameter is controlled by the regulation of the body and any changes that would affect body biochemistry. In a Cochrane review of water-loss dehydration cases in older people, the cutoff measured osmolality value, referred to as >300 mOsm/kg, is defined as current dehydration. Any measurement between 295 and 300 indicates an impending dehydration and between 275 and <295 indicates euhydration[14].

Calculated osmolarity is an effective substitution method for predicting dehydration. Hooper et al analyzed the diagnostic accuracy of different equations validated in elderly cohort studies. The aim of their study was to assess which osmolarity equation yielded the best performance in accurately predicting screening dehydration[15]. The result revealed that some equations showed reasonable agreement with the measured serum osmolality; consequently, the reported areas under the curve-receiver-operating characteristic (AUC-ROC) were between 0.74 and 0.82. However, the equations were developed from the database of healthy subjects from all age groups and not specifically for Asian older adults. In Thailand, many health care facilities were not capable of the measurement of serum osmolarity. Hence, it is beneficial to explore that which osmolarity equation is best suitable for Thai older patients. In this study, we aimed to develop an equation for calculated osmolarity for older Thai patients in the emergency department (ED) and compare its accuracy with those of 5 previously published equations.

Methods

Study design and setting

This was a secondary analysis of a prospective cross-sectional study conducted in the ED of an urban university hospital in Bangkok, Thailand. The study included patients aged ≥65 years who presented to the ED between May 2017 and July 2017 and enrolled in the study by using convenience sampling. Patients who were too unwell and whose participation in the study may delay medical treatment, such as patients assessed by medical staff as critically ill or needing any immediate lifesaving procedure, patients transferred from another hospital, patients who received any prehospital intravenous fluid, and patients previously diagnosed as having metastatic cancer were excluded. Details of the study were described elsewhere[16]. Briefly, 370 participants were recruited in the study. After the enrollment process, blood samples were collected and sent for analysis of osmolality, electrolytes, blood urea nitrogen, creatinine, and glucose. Osmolality was measured with a freezing point depression technique using Fiske Micro-Osmometer Model 210, provided by the department of clinical pathology and central laboratory of our hospital. Our primary study was approved by the institutional review board of the Faculty of Medicine Vajira Hospital, Navamindradhiraj University.

Osmolarity equations

In 2015, Hooper et al assessed the diagnostic accuracy for current dehydration of 39 equations, of which 36 were from Fazekas et al and 3 were commonly used equations from MDCalc, Wikipedia, and Joint British Diabetes Societies[15,17]. The study was also validated in 5 data sets from different cohorts that included only participants aged ≥65 years who were healthy or frail, free-living or requiring residential care, hospitalized or receiving medical care, and had or had no cirrhosis and diabetes. They extracted the most useful equations where for ≥3 of 5 cohorts, the mean difference (MD) ranged from −1 to +1, and the p-value was not statistically significant (≥0.01). The result showed that 5 equations fulfilled the criteria, which are presented in Table 1.

Statistical analyses

All the analyses were conducted using the Stata 13.0 software (StataCorp LP, College Station, TX, USA). Descriptive data are presented as mean with standard deviation (SD) for continuous variables, median with interquartile range (IQR, 25th–75th percentile) for time variables, and frequencies for categorical variables. A multiple linear regression analysis (backward stepwise method) was used to develop a new equation by determining the best coefficient of each variable to predict serum osmolality. The variables used in the regression were sodium (Na), potassium (K), glucose, and urea (blood urea nitrogen [BUN]) levels. The extreme values, based on Hooper et al[15], were excluded from the statistical model. A p-value of <0.05 was considered statistically significant. Assessing the fit of the regression model was done using F-test, F 0.05 (3,38) = 2.999 (p-value = 0.038) R-squared = 0.6029.

The Bland-Altman plot was used to evaluate each equation by comparison with the directly measured osmolality and tested for agreement between the measured and calculated osmolarity values. A paired *t* test was performed to compare between the calculated and measured osmolality values.

ROC plots were used to compare the ability of each of the 5 equations to diagnose current dehydration (serum/plasma osmolality > 300 mOsm/kg). A chi-square test was used to compare the AUC between the new equation and other equations.

Table 1:
Summary of osmolarity equations

Equation	mmol/L	AUC
Eq1	2.1 × Na	0.74
Eq2	2 × Na+ + 0.9 × glucose + 0.93 × 0.5 × urea + 8	0.81
Eq3	1.36 × Na+ + 1.6 × glucose + 0.45 × urea + 91.75	0.80
Eq4	1.86 (Na+K) + 1.15 x Glucose + Urea + 14	0.82
Eq5	1.09 × 1.86 × Na+ + glucose + urea	0.82

Abbreviations: Eq, equation; Na, sodium; K, potassium; AUC, area under the ROC curve.

Results

Participants' characteristics

Of the 370 patients in the data set, 48 were excluded from the analysis because of their extreme osmolality values (serum osmolality, >340 mOsm/kg; potassium, >8 mmol/L; sodium, <120 or >160 mmol/L; blood glucose, >300 mg/dL; and BUN, >70 mg/dL). A total 322 patients were included in the study. All the laboratory parameters were collected to form a new equation. The patients' baseline characteristics are described in Table 3. Their mean age was 77.5 years. Of the patients, 64% were female. A quarter of the patients were concomitantly diagnosed as having myocardial infarction and moderate to severe renal failure.

Development of the new equation

A multiple linear regression analysis was performed to determine the relationship between the variables. We found only 4 significant variables, namely sodium, potassium, urea, and blood glucose levels (all converted in mmol/L), and their coefficients were 1.75, 1.69, 1.04, and 0.87, respectively as shown in Table 2. Moreover, a constant of 25.7 was also derived from the model. Finally, we adjusted the coefficients of sodium and potassium to simplify the equation as shown below:

$$1.75 \times (Na + K) + 0.9 \times Glucose + Urea + 25.7$$

Statistical comparison

The MD between each equation and the measured serum osmolarity was calculated. Table 4 shows that the new equation has a MD of 0.49 (95% CI, −0.40 to 1.38; p = 0.279). Similarly, Equations 1, 2, 3, and 4 had MDs of 6.18 (95% CI, 5.13–7.23; p < 0.001), −4.19 (95% CI, −5.15 to 3.23; p < 0.001), −5.38 (95% CI, −6.37 to −4.39; p < 0.001), and −5.31 (95% CI, −6.20 to −4.41; p < 0.001), respectively. By contrast, Equation 5 had the widest MD −6.89 (95% CI, −7.80 to −5.98; p < 0.001). In Figure 1, the Bland and Altman plot shows the agreement between the MD of the measured osmolality and new equation. The solid line represents a level of 0.49 with the limit of agreement ranging from −15.72 to 16.70.

The diagnostic data of the ROC analyses for all the equations are shown in Table 5 and Figure 2. The new equation had the largest AUC of 0.81 (95% CI, 0.74–0.87), which was also the AUC of Equation 5 (95% CI, 0.74–0.87; p = 0.645). The AUC of Equations 4 and 2 were slightly lower at 0.8 (95% CI, 0.73–0.87; p = 0.088) and 0.78 (95% CI, 0.71–0.85; p = 0.031), respectively. Equation 3 had an AUC of 0.75 (95% CI, 0.68–0.83; p < 0.001), and Equation 1 had the lowest AUC of 0.73 (95% CI, 0.66–0.80; p < 0.001).

Table 2:
Result from multiple linear regression analysis

Variables	Coefficients	95% Confident interval	p-value
Blood sugar (BS)	0.87	0.55-1.20	0.000
Sodium (Na)	1.75	1.58-1.93	0.000
Potassium (K)	1.69	0.20-3.18	0.026
Urea	1.04	0.83-1.26	0.000
Constant	25.7	0.24-51.22	0.048

Table 3:

Baseline characteristics (n=322)

Variables		
Age (years)		77.54 ± 7.76
Gender		
Female	206	(64.0)
Education (years)		
0-6	226	(70.2)
7-12	56	(17.4)
≥13	40	(12.4)
Comorbidities		
Myocardial infarction	91	(28.3)
Congestive heart failure	35	(10.9)
Peripheral vascular disease	14	(4.3)
Cerebrovascular disease	55	(17.1)
Dementia	22	(6.8)
Chronic pulmonary disease	23	(7.1)
Ulcer disease	20	(6.2)
Mild liver disease	4	(1.2)
Hemiplegia	20	(6.2)
Moderate or severe renal disease	77	(23.9)
Diabetes with end organ damage	63	(19.6)
Any tumor	34	(10.6)
Leukemia	2	(0.6)
Lymphoma	5	(1.6)
Moderate or severe liver disease	4	(1.2)
AIDS	2	(0.6)
Charlson Comorbidity Score	5	(4-7)
Body Weight (kg)		58.53±12.01
BMI		23.51±4.74
Laboratory		
Serum osmolality (mmol/kg)		289.4±12.85
BUN (mg/dL)		22.14±12.07
Cr (mg/dL)		1.80±8.70
BS (mg/dL)		134.66±50.55
Na (mmol/L)		137.87±5.31
Na > 145, n (%)		22 (4.04)
K (mmol/L)		4.17±0.61
K > 5, n (%)		8.39 (27)
CL (mmol/L)		101.32±7.87
HCO_3 (mmol/L)		25.85±4.31
eGFR		58.82±25.23

Data are presented as n (%), mean ± SD, or median (interquartile range).

Table 4:
Results of the statistical evaluation of equation for calculated osmolarity

Equation	Calculated osmolarity		Mean difference (95%CI)		p-value*
	Mean ± SD	Range			
Measured osmolality	289.40 ± 12.85	245 - 330	-	-	-
New Equation	288.91 ± 9.90	252 - 318	0.49	(-0.40 to 1.38)	0.279
Eq1	283.22 ± 10.53	245 - 306	6.18	(5.13 to 7.23)	< 0.001
Eq2	293.59 ± 10.51	254 - 315	-4.19	(-5.15 to -3.23)	< 0.001
Eq3	294.78 ± 7.99	265 - 318	-5.38	(-6.37 to -4.39)	< 0.001
Eq4	294.71 ± 10.51	255 - 325	-5.31	(-6.20 to -4.41)	< 0.001
Eq5	296.29 ± 11.3	255 - 327	-6.89	(-7.80 to -5.98)	< 0.001

*t-test for comparison between calculated and measured osmolality.

Table 5:
Results of the statistical evaluation of equations for predicting dehydration

Equations	AUC	(95%CI)	p-value*
New Equation	0.81	(0.74 - 0.87)	
Eq1	0.73	(0.66 - 0.80)	< 0.001
Eq2	0.78	(0.71 - 0.85)	0.031
Eq3	0.75	(0.68 - 0.83)	< 0.001
Eq4	0.80	(0.73 - 0.87)	0.088
Eq5	0.81	(0.74 - 0.87)	0.645

* Chi-square test comparison AUC between new equation and other equation.

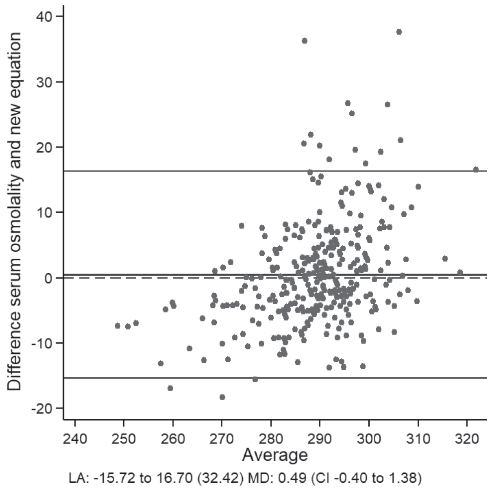

Figure 1: Bland and Altman plot of measured and calculated osmolarity

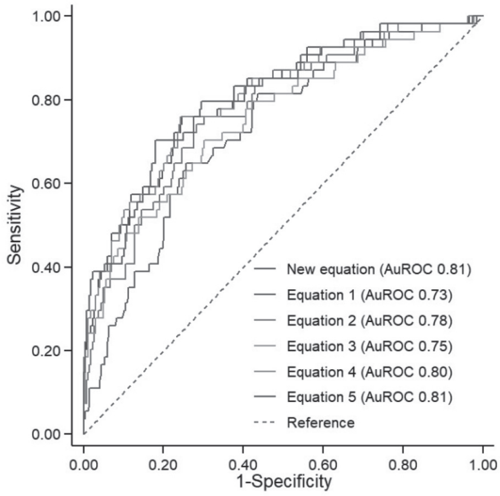

Figure 2: Receiving operating characteristic (ROC) plots comparing each equation

Discussion

Dehydration in older adults has been known as a leading cause of hospital admissions, contributing to increased risk of death and worsening functional status[8,18-19]. This study sought to develop an equation for predicting HD in older patients with acute illness. Hooper et al chose 39 equations from all published data on commonly measured laboratory biochemical parameters such as sodium, potassium, glucose, and urea levels[15]. Our enrolled patients also had the values of all the above-mentioned parameters; moreover, the coefficients of the new equation derived from multiple linear regression were similar to those of the previous Equation 5.

When we focused on MDs, the new equation had the narrowest number. This is because of validating using the same data from which the equation was derived from. Although we could still observe that even if we had minimally modified the coefficients of sodium and glucose, the MD was simply 0.49. Among the equations, Equations 2–5 showed negative MD values despite the positive value of Equation 1.

In the previous study, Equation 4 showed a narrower MD, between −1 and +1; however, this was not observed in our study because the data sets used to validate Equations 1–5 were different. Among the data sets, that from the Dietary Strategies for Healthy Ageing in Europe was the largest, and the proportion of participants with sodium levels > 145 mmol/L was <1%, while that in our study was 4.04%[20]. Sodium and potassium are key elements in all the equations; especially hypernatremia correlates with increased plasma osmolality when fluid intakes are restricted[21]. Consequently, any changes in these minerals would contribute to the elevation of the calculated osmolarity, especially when tested in a sample with a higher proportion of hypernatremia cases.

Our enrolled patients had some significant differences in baseline characteristics as compared with those in the reference study. As mentioned earlier, our study included not only patients with higher laboratory values such as sodium and potassium levels but also a larger number of patients with poor renal function (estimated glomerular filtration rate < 30). Nonetheless, we could not conclude that these factors could impact the changes in hydration, as the studied population demonstrated a disparity in demographics.

The ability of the new equation to diagnose current dehydration was comparable with those of Equations 4 and 5. A possible interpretation of this similarity is that Equation 5 was consistently useful and precisely accurate in predicting dehydration in the elderly in a previous report[15].

Several limitations should be considered when interpreting the results of this study, as external validation was lacking. Validating our results in other populations would add value to the new equation. The resuscitative patients were excluded from the enrollment because the consent process may delay their treatment. Therefore, selection bias of the participants might be considered. In addition, this was a single-center study and may not be representative of other Asian ED centers.

Conclusions

Our newly developed equation based on the data of Thai elderly patients who visited the ED, $1.75 \times (Na + K) + 0.9 \times Glucose + Urea + 25.7$ showed good performance in calculating osmolarity. However, further external validation and ability to predict dehydration of this equation is needed.

Ethics approval

This study was conducted with the approval of the institutional review board of the Faculty of Medicine Vajira Hospital, Navamindradhiraj University (COA 038/2564).

Disclosure

The authors declare that they have no competing interests.

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