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The Correlation between Urine Specific Gravity and Urine Osmolality in Patients with Hyponatremia

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Abstract

Range of urine osmolality can usually be predicted by multiplying the last two digits of urine sp.gr. by a factor of 30 and 40 (conventional formula). The objective of this study is to evaluate the accuracy of conventional formula in the prediction of urine osmolality in patients with hyponatremia. A prospective study examining hospitalized patients with hyponatremia. Urine samples are concomitantly measured for sp.gr. (strip test) and osmolality (freezing point technique).The predicted urine osmolality is calculated by the conventional formula. Values of the predicted and actual urine osmolality are compared. The results show that 82 patients are enrolled. Mean serum Na^+ is 119.38 ± 7.82 mMol/l. Causes of hyponatremia include “Hypovolemic Hyponatremia (Gr 1; n=25), “Diuretic induce Hyponatremia” (Gr 2; n=27), “Low solute Intake” (Gr 3; n=3), “SIADH” (Gr 4; n=25), “Hypervolemic Hyponatremia” (Gr 5; n=2). Mean urine sp.gr. is 1014 ± 0.004. Mean actual urine osmolality is 347.99 ± 138.19. The conventional formula can accurately predict urine osmolality in 11.5%, 22%, 0%, 0 %, 12.5% and 0% for Gr 1-5 respectively.

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For patients with hypovolemic and euvolemic hyponatremia, mean actual urine osmolality is 20-33 times higher than the mean value of the last two digits of urine sp.gr. In conclusion; Urine sp.gr. has a linear relationship with measured urine osmolality in patients with hyponatremia. However, the accuracy of conventional formula to predict urine osmolality from urine sp.gr. is not good. A multiplying factor of 20-33 is better than 30-40 in predicting urine osmolality of most patients with hyponatremia.

Keywords: hyponatremia; urine osmolality; urine specific gravity; syndrome of inappropriate ADH; volume status.

1. Introduction

Antidiuretic Hormone (ADH, arginine vasopressin) secretion results in a concentrated uine. The latter is usually measured by the value of urine osmolality or urine specific gravity at the bedside. Patients who have hypovolemia and intact ADH secretion, the value of urine osmolality will increase and may be as high as 1200 mOsm/kg. In contrast, patients with normal volume status will have suppressed ADH secretion and dilute urine. The value of urine osmolality in the latter setting will be as low as 50 mOsm/Kg. For bedside evaluation, urine specific gravity (sp.gr.) can be used as an initial tool to assess the renal concentrating ability and diluting capacity. However, urine osmolality is a more precise test. These two tests are measured by different rationale. In principle, value of urine osmolality increase with the number of dissolved particles per unit of water in the urine. However, urine specific gravity is a measure of the concentration of solutes in the urine and is impacted by both the number and size of particles being dissolved in the urine. In clinical practice, it is estimated that the increase of urine specific gravity by 0.001 will lead to increase of urine osmolality by 30-40 mOsm/kg.(1-3). Hence physician can predict the value of urine osmolality by a formula shown below.

Predicted urine osmolality = (specific gravity -1) x (30,000-40,000) (equation 1)

The limitation to the use of the sp.gr. is that the value of urine specific gravity will be much increased in the presence of radio contrast agents, (4) glucose, protein and mannitol. It is estimated that the increase of each 270 mg/dl of glucose or 330 mg/dl of protein will lead to a spurious increase of urine specific gravity by 0.001; hence, the presence of these solutes in the urine can lead to a higher value of urine specific gravity than the amount of dissolved particles being measured. Urine osmolality is usually measured by freezing point depression technique. This is operated in the laboratory setting and cannot be done at bed side. However, test for urine specific gravity is a simple test. Urine specific gravity can be measured by refractometer or by strip test. Value of urine specific gravity obtained by the strip test is the measurement of amount of polyacid that will be presence in according to the urinary ionic concentration.(5) It is therefore possible that urine with a high concentration of non-ionic solutes (such as glucose or urea or some types of radiographic contrast agents) will yield a result that will be spuriously lower than that measured by refractometer. Previous studies have demonstrated a good correlation of the value of urine specific gravity obtained by both methods. (5, 6). In the clinical setting where the large solutes mentioned above are not presence in the urine, value of urine specific gravity can be initially used to determine the urinary concentrating and diluting capacity. Previous study has shown that urine specific gravity is not an ideal predictor of kidney concentrating ability in hypertensive patients (7). For a differential diagnosis of patients with hyponatremia, a physician will require a value of urine osmolality. However, urine sp. gr. can be easily measured at the initial evaluation. To our knowledge, information regarding the correlation between urine sp. gr. and urine osmolality in patients with hyponatremia are limited. It is not clearly known whether the physician can predict value of urine osmolality by the conventional formula in the setting of hyponatremia. Our study has two main objectives. The first objective is to determine the correlation between urine specific gravity and urine osmolality in patients with hyponatremia. The second objective is to determine the accuracy of urine specific gravity to predict urine osmolality from the conventional formula. The formula is shown equation 1.

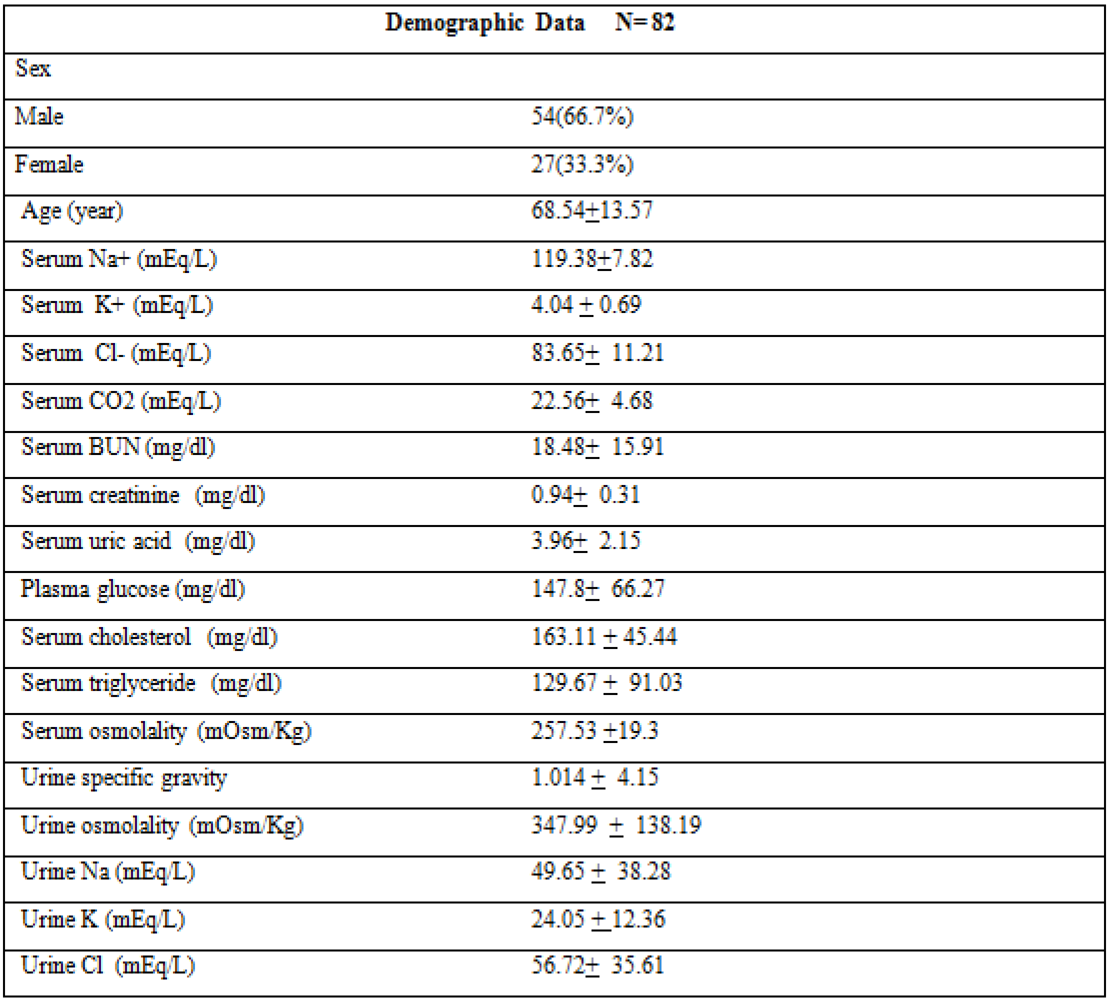
2. Research Method

This is a single center prospective study. Enrolled subjects are adult patients who are admitted within the investigating hospital with any causes and have significant hyponatremia (serum Na < 130 meq/l and serum osmolality < 280 mOsm/Kg) during a seven months study period. Patients will be excluded from the study if they have received radio contrast media or mannitol at the time of study. Patients will also be excluded if they have glycosuria, or nephrotic range proteinuria or a serum creatinine value more than 2.0 mg/dl. The urine specific gravity is measured by urine strip test (Comber Test® M) operated by automated machine (MIDITRON) ®. The urine and serum osmolality are measured by freezing point depression technique. Patients were evaluated for important demographic data include age, sex, medical background, use of diuretic. The blood test included serum osmolality, blood urea nitrogen, serum creatinine, uric acid, glucose, cholesterol, and triglyceride. Serum cortisol and thyroid function test are tested in indicated patients. The urine will be examined for routine urinalysis, osmolality, specific gravity (strip test), and sodium. Patients will be classified according to the volume status specifically “Hypovolemia”, “Hypervolemia” and “Euvolemia” according to the study definition. Hypervolemia is defined by the presence of at least one targeted finding. These include pitting edema, engorged neck vein (with a jugular venous pressure more than 5 cms), presence of S3 heart sound gallop, presence of pulmonary congestion, and presence of ascites. Hypovolemia is defined by the presence of at least one targeted findings. These include hypotensive state (BP less than 90/70 mm Hg with signs of poor tissue perfusion), orthostatic hypotensive state (BP less than 100/70 with a decline of systolic blood pressure more than 20 mm Hg upon upright position), and a flat jugular venous pressure (less than 3 cms). Euvolemia is defined by the clinical settings when there are no criteria of hypervolemia or hypovolemia as is described above. All patients are investigated for urine and serum osmolality. Serum electrolytes, cholesterol and Triglyceride are measured simultaneously. The urine sodium is also tested in all patients. Then the patients will be classified according to the volume status and investigation in to five groups. Group 1 is “Hypovolemic Hyponatremia”. This is defined by the presence of hypovolemia and hyponatremia. Group 2 is “Hypervolemic Hyponatremia”. This is defined by the presence of hypervolemia and hyponatremia. Group 3 is “Diuretic induced Hyponatremia”. This is defined by the finding of recent diuretic intake and hyponatremia. The fourth group is “Syndrome of Inappropriate ADH secretion (SIADH)”. This is defined by the presence of euvolemic hyponatremia and a value of urine osmolality that is not maximally diluted (UOsm > 100 mOsm/Kg). The patients who have hypocortisolism and hypothyroidism will be included in this group. The fifth group is “Low solute intake”. This is defined by a clinical setting when hyponatremia occurred in conjunction with a total urinary osmolar clearance per day less than 600 mOsm per day. The demographic data are shown as mean and standard deviation as appropriate. Correlation between urine specific gravity and osmolality is calculated by using linear regression analysis. Value of the correlation coefficient is expressed by r and adjusted R^2. The study is approved by the “Ethics Committees” of the investigating hospital.

3. Results and analysis

A total of 82 patients were enrolled. Fifty four (65.85%) were male and twenty eight (34.15%) were female. Patients’ mean age was 68.54± 13.57 years. At the time of hyponatremia, mean serum Na^+ was 119.38 ± 7.82 meq/l. Mean serum osmolality was 257.53± 19.3 mOsm/Kg. Mean urine osmolality was 347.99 ± 138.19 mOsm/Kg. Mean urine specific gravity was 1.014 ± 0.004. The demographic information was shown in Table 1.

Table 1: Baseline characteristic and the val of important laboratory investigation at the time of hyponatremia.



Demographic Data N=82	
Sex	
Male	54(66.7%)
Female	27(33.3%)
Age (year)	68.54±13.57
Serum Na+ (mEq/L)	119.38±7.82
Serum K+ (mEq/L)	4.04 ± 0.69
Serum Cl- (mEq/L)	83.65± 11.21
Serum CO2 (mEq/L)	22.56± 4.68
Serum BUN (mg/dl)	18.48± 15.91
Serum creatinine (mg/dl)	0.94± 0.31
Serum uric acid (mg/dl)	3.96± 2.15
Plasma glucose (mg/dl)	147.8± 66.27
Serum cholesterol (mg/dl)	163.11 ± 45.44
Serum triglyceride (mg/dl)	129.67 ± 91.03
Serum osmolality (mOsm/Kg)	257.53 ±19.3
Urine specific gravity	1.014 ± 4.15
Urine osmolality (mOsm/Kg)	347.99 ± 138.19
Urine Na (mEq/L)	49.65 ± 38.28
Urine K (mEq/L)	24.05 ±12.36
Urine Cl (mEq/L)	56.72± 35.61

Table 2 shows that the patients were then classified to five diagnosis groups. They are “Hypovolemic Hyponatremia” (n=25), “Hypervolemic Hyponatremia” (n=2), “Diuretic induce Hyponatremia” (n=27), “SIADH” (n=25) and “Low Solute Intake” (n=3).

Table 2: Baseline characteristic and results of investigation of all five diagnosis groups.

	Hypovolemic hyponatremia	Diuretic	Low solute intake	SIADH	Hypervolemic hyponatremia
Age	64.48 ± 17.03	69.85±11.35	66.33 ± 15.82	71.12± 12.59	51 ± 14.14
Serum osmolality (mOsm/Kg)	249.82 ± 58.4	249.16± 22.08	248.67± 11.26	258.63± 15.35	271 ± 21.2
Urine osmolality (mOsm/Kg)	361.16± 125.57	365.3± 136.56	95.67 ± 6.6	365.64 ± 131.99	330.5±123.74
Urine Specific gravity	1.018 ± 0.004	1.011 ± 5.22	1.008 ± 0.002	1.014 ± 0.004	1.015
Serum Na+ (mEq/L)	121.84 ± 5.24	116.41 ±10.03	111 ± 4.58	121.44 ± 6.3	122.5 ± 3.54
Urine Na+ (mEq/L)	35.73 ± 33.78	66.52 ± 46.58	31 ± 13.08	51.3 ± 28.78	13.5± 0.71
Blood urea nitrogen (mg/dl)	21.68± 16.9	16.44 ± 10.84	6.33 ± 2.52	15.5± 9.1	15 ± 9.9
Serum creatinine (mg/dl)	1.1 ± 0.36	1.07 ± 0.65	0.6 ± 0.17	0.95 ± 0.64	1 ± 0.14
Serum uric acid (mg/dl)	4.85± 2.37	4.12± 1.97	2.17± 0.72	2.93 ± 1.55	3.8 ± 3.25
Total =82	25	27	3	25	2

Patients with “Hypervolemic Hyponatremia” have the lowest mean age. Patients with SIADH have the highest mean age. The value of serum osmolality is not different among the five groups. However, patients with low solute intake have the lowest value of urine osmolality, urine specific gravity and urine Na+ when compare with the other four groups.

The value of urine specific gravity is then used to predict the value of urine osmolality for each group. By the conventional formula, the last two digit of the urine specific gravity is multiply by a value of 30-40. The result was then compared with the measured urine osmolality and defines whether the actual value was within the range of the predicted value. The accuracy of conventional formula was calculated by the following formula.

$$\text{accuracy} = \frac{A}{B} \times 100 \qquad \text{(equation 2)}$$

A = number of patients who have the actual urine osmolality within the range of predicted urine osmolality (calculated from the conventional formula)

B = number of all patients

The accuracy of conventional formula to predict urine osmolality for patients in each group was calculated by equation 2. The results show that the accuracy for patients with “Hypervolemic Hyponatremia” and “Low solute Intake” was very low (0%). The accuracy of conventional formula was 12.5 % for “SIADH”, 11.5% for “Hypovolemic Hyponatremia” and 22.2% for “Diuretic induce Hyponatremia”.

However, the value of urine specific gravity was found to be linearly correlated with the value of actual urine osmolality. Linear regression analysis shows that the calculated regression coefficient (r) was 0.25. and the adjusted $R^2 = 0.05$ (p value= 0.023).

From the results above, a multiplying factor to predict the value of urine osmolality from the urine specific gravity was calculated by equation 3.

$$\text{Multiplying factor} = \frac{\text{measure urine osmolality}}{\text{last two digits of urine sp.gr.}} \qquad \text{(equation 3)}$$

Calculation from equation 3 showed that the mean value of multiplying factor for all patients was 22.6. Subgroup analysis found that the value of multiplying factor for “Hypovolemic Hyponatremia” was 20, for “Hypervolemic Hyponatremia” was 22, for “Diuretic induce Hyponatremia was 33, for “SIADH” was 26 and for “Low solute Intake” was 12 respectively.

4. Discussion

In clinical practice, measurement of urine osmolality will be useful in several aspects of hyponatremia· (8) (9).

For euvolemic hyponatremia, the value of urine osmolality less than 100 mOsm/Kg is suggestive of primary polydipsia. As this study do not include patient with primary polydipsia, we do not have patient with a value of urine osmolality less than 100 mOsm/Kg.

Nowadays, use of urine strip test to measure urine specific gravity is widely practiced. A good correlation between urine specific gravity measured by the strip test in comparison with spectrometry are shown (6, 10). Previous studies have also demonstrated a good correlation between urine specific gravity and osmolality as a marker of kidney concentrating ability in both adult and pediatric population. (6) (11, 12). In contrast, correlation between urine specific gravity and osmolality as a marker of kidney concentrating ability in hypertensive patient with dehydration is not so good. (7). The result from our study should therefore be useful in the initial evaluation of patients with hyponatremia. We have shown that there is a linear correlation between the value of urine specific gravity and osmolality in patients with hyponatremia. However, the value of regression coefficient is not very high ($r= 0.25$, adjusted $R^2 = 0.05$). This reflects that there can be a wide range of variation of the actual value of urine osmolality if predict from a single value of urine specific gravity. For example, a value of urine specific gravity of 1.005 can be associated with a value of measured urine osmolality range from 90 - 500 mOsm/Kg (data not shown).

The accuracy of the conventional formula for the prediction of urine osmolality in our studied patients range from 0-22.2%. In order to improve the accuracy, we have investigated for a new multiplying factor. This ranged between 12-33. However, the number of patients with “Low solute Intake” and “Hypervolemic Hyponatremia” is low (n =3 and 2 respectively). Hence, the value of multiplying factor range between 20-33 in most cases. This leads to a view that, for patients with hypovolemic and euvolemic hyponatremia, it is better to predict the value of urine osmolality from the last two digits of urine specific gravity multiply by 20-33 (see results) and not by 30-40 as is suggested by the conventional formula.

When taking in to account the results of medical history and physical examination, the value of urine osmolality is very useful to manage “hyponatremia” according to the three types of volume status being found. First, for euvolemic hyponatremia, a value of urine osmolality higher than 300 mOsm/Kg is suggestive of the presence of ADH activity. However, a value of urine osmolality ranges between 100-300 mOsm/Kg raises a difficult issue. Physicians can make initial further management while wait for the result of actual urine osmolality. The latter will help to differentiate between “SIADH” and “low solute intake”. Second, for hypovolemic hyponatremia, the presence of ADH activity is an appropriate response. Hence, a value of urine osmolality higher than 100 and usually more than 300 mOsm/Kg is expected. Further result of actual urine osmolality will be required. A value of UOsm > 350 mOsm/Kg suggests that the patient with hypovolemia do not have diabetes insipidus. Third, for hypervolemic hyponatremia, a value of urine osmolality higher than 350 mOsm/Kg suggests that the patient have effective circulating volume depletion rather than water intoxication. Physicians can make an initial prediction of the urine osmolality. However, the value of actual urine osmolality is essentially required for the differentiation between effective circulating volume depletion and water intoxication.

Our study has some limitation. First, we have included only patients with hyponatremia who were admitted within the hospital. Our results then may not be applicable with patients with mild degree of hyponatremia who are treated in the out- patient clinic. Second, we have not included many patients with hypervolemic hyponatremia. However, euvolemic and hypovolemic hyponatremia are much more common than hypervolemic hyponatremia and we feel that our results might be applicable to most but not all patients with hyponatremia.

5. Conclusion

The value of urine osmolality is important information for the approach to patients with hyponatremia. Urine specific gravity is an initial bedside finding that can lead to a prediction of urine osmolality. The conventional formula has a low accuracy in the prediction of measured urine osmolality. For euvolemic and hypovolemic hyponatremia, it is better to predict the value of urine osmolality of patients by multiplying the last two digit of urine specific gravity by a factor of 20-33.

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