Diagnostic Performance of Afternoon Urine Osmolality to Assess Optimal Hydration Status in an Adult Healthy Population

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ABSTRAK

Latar belakang: *hidrasi optimal merupakan hidrasi yang dianggap cukup untuk menggantikan kehilangan cairan, menjamin produksi urin adekuat untuk mengurangi risiko urolitiasis dan penurunan fungsi ginjal, serta mencegah keluarnya arginin vasopresin (AVP). Osmolalitas urin 24 jam diketahui dapat mengukur status hidrasi seseorang, namun dirasakan memberatkan karena kemungkinan urin tercecer dan membatasi aktivitas kerja. Penelitian ini bertujuan mengetahui peranan pemeriksaan osmolalitas urin sewaktu sore hari untuk menilai status hidrasi optimal.* ***Metode:*** *studi potong lintang dilakukan pada karyawan sehat berusia 18-59 tahun di lingkungan FKUI/RSUPN Cipto Mangunkusumo, memakai metode consecutive sampling. Dilakukan analisis kurva ROC untuk mendapatkan titik potong dan akurasi osmolalitas urin sore hari dalam menilai status hidrasi optimal.* ***Hasil:*** *antara bulan Agustus-September 2016 terkumpul 120 subjek (73,8% perempuan, median usia 32 tahun) yang memenuhi kriteria penelitian dengan median osmolalitas urin 24 jam 463,5 (95% IK, 136-1427) mOsm/kg H_2O dan median osmolalitas urin sore hari 513 (95% IK, 73-1267) mOsm/kg H_2O. Pada analisis didapatkan korelasi sedang ($r=0,59$; $p<0,001$) antara osmolalitas urin sore hari dengan osmolalitas urin 24 jam. Dengan kurva ROC didapatkan nilai AUC 0,792 (95% IK, 0,708-0,875) dengan titik potong 528 mOsm/kg H_2O. Dalam menentukan hidrasi optimal, osmolalitas urin sore hari memiliki sensitivitas sebesar 0,7 (95% IK, 0,585-0,795) dan spesifisitas 0,76 (95% IK, 0,626-0,857) serta Likelihood Ratio (LR) (+) 2,917 (95% IK, 1,74-4,889) dan LR (-) 0,395 (95% IK, 0,267-0,583).* ***Kesimpulan:*** *osmolalitas urin sore hari dapat menjadi indikator dalam menilai status hidrasi optimal pada populasi sehat dengan titik potong 528 mOsm/kg H2O serta sensitivitas 0,7 dan spesifisitas 0,76.*

Kata kunci: *osmolalitas urin sore hari, hidrasi optimal.*

ABSTRACT

Background: *optimal hydration represents adequate total daily fluid intake to compensate for daily water losses, ensure adequate urine output to reduce the risk of urolithiasis and renal function decline, and also avoid the production of arginine vasopressin (AVP). Twenty-four-hour urine osmolality has been used to assess hydration status, but it is challenging because of the possibility of spilling urine and limitation of daily activities. This study is aimed to determine the performance of the afternoon urine osmolality to assess the optimal hydration* *status compared with 24-hour urine osmolality.* ***Methods:*** *a cross sectional study was conducted on healthy employees aged 18-59 years at Universitas Indonesia Medical Faculty/Cipto Mangunkusumo Hospital, with consecutive sampling method. The ROC curve was analyzed to obtain the optimal cut off point and the accuracy of the afternoon urine osmolality in assessing the optimal hydration status.* ***Results:*** *between August-September 2016 there were 120 subjects (73.8% female, median age 32 years) who met the study criteria with a median 24-hour urine osmolality 463.5 (95% CI, 136-1427) mOsm/kg H_2O and median afternoon urine osmolality 513 (95% CI, 73-1267). We found moderate correlation (r=0.59; p<0.001) between afternoon urine osmolality and a 24-hour urine osmolality. Using ROC curve, the AUC value was 0.792 (95% CI, 0.708-0.875) with the cut off 528 mOsm/kg H_2O. To assess the optimal hydration status, the afternoon urine osmolality had the sensitivity of 0.7 (95% CI, 0.585-0.795) and the specificity of 0.76 (95% CI, 0.626-0.857), Likelihood Ratio (LR) (+) 2.917 (95% CI, 1.74-4.889) and LR (-) 0.395 (95% CI, 0.267-0.583).* ***Conclusion:*** *afternoon urine osmolality can be used as a diagnostic tool to assess the optimal hydration status in healthy population with cut off 528 mOsm/kg H_2O, sensitivity of 0.7, and specificity of 0.76.*

Keywords: *afternoon urine osmolality, optimal hydration.*

INTRODUCTION

Hydration is a dynamic balance between water intake and loss preserved in narrow range through behavioral and physiological response.[1] Our body needs 2-2.5 L of water per day which can be obtained from food and beverage.[2] However, we still cannot declare a good hydration even when the amount of water was achieved. Perrier's[3] study in 2015 shows that 24-hour urine osmolality ≤500 mOsm/kg H_2O could be an indicator of optimal hydration. In this term, optimal hydration means hydration that represents adequate total daily fluid intake to compensate for daily water losses, ensuring urinary output, and avoiding production of arginine vasopressin (AVP).[3] It has been proven that 24-hour urine osmolality has several weaknesses, including the possibility of spilling urine, limitation of daily activities, and error in sampling so there is a lack amount of urine in 30% of population.[2]

As an alternative method, we consider to substitute 24-hour urine osmolality with spot urine by the following evidence. Kavouras's[4] study showed that morning urine has a correlation with hydration status. The result was contradictive with Lee and Chan's[5] study which observed desmopressin administration in children. They show that there is no difference of morning urine osmolality between two groups. Moreover, a systematic review in 2012 which analyzed 9 studies found that night urine osmolality had stronger correlation with 24-hour urine osmolality than random spot urine [0.76 (0.60–0.86) and 0.35 (0.12–0.47), consecutively].[6]

Another study from Mann and Gerber[7] showed that afternoon urine sodium concentration has the strongest correlation with adjusted 24-hour urine sodium concentration (r=0.86, p<0.001). Perrier's[8] study also shows that urine osmolality values obtained from late afternoon collection were the most likely to agree with 24-hour value, with 87% of values falling within 50 mOsm/kgH_2O of corresponding 24-hour value. This study also showed that morning urine was still affected by AVP from intrinsic mechanism, so it cannot represent 24-hour condition.[8]

Based on these arguments, we can assume that the best time for spot urine collection is in the afternoon. The aim of this study was to prove that afternoon urine osmolality can be used as the indicator to assess optimal hydration status. By comparing it with 24-hour urine osmolality as the gold standard, we expect this study can measure the performance of afternoon urine osmolality to assess optimal hydration status easily.

METHODS

This was a diagnostic study with a cross-sectional design was conducted from August to September 2016 at Universitas Indonesia Medical Faculty/Cipto Mangunkusumo Hospital. We performed consecutive sampling on 18-59 years old subjects. Subject with chronic illnesses such as diabetes mellitus, diabetes insipidus, hypertension, autoimmune, malignancy, urolithiasis, cerebro-cardiovascular diseases, chronic liver disease, impaired renal function (eGFR<60 ml/min/1.73m^2), and abnormality in urinalysis were excluded. This study had obtained ethical approval from Ethical Committee on Health Research, Faculty of Medicine, Universitas Indonesia Number 397/UN2.F1/ETIK/2016 and written informed consent was obtained from each subject.

We then proceeded to do history taking of identity and past medical history, vital signs examination (blood pressure, heart rate, breathing frequency, weight, and height), and also laboratory examination (plasma creatinine and urinalysis). Then subjects were asked to collect their afternoon (5-7 pm) and 24-hour urine. Hydration was considered optimal when the value of 24-hour urine osmolality is ≤500 mOsm/kg H_2O.

The calculation and analysis of this study used SPSS software for windows version 24.0. Correlation analysis of afternoon and 24-hour urine osmolality was done by Spearman test. We also analyzed area under the curve (AUC) value to determine performance of urine osmolality and optimal cut off point. Sensitivity and specificity analysis were also calculated to determine accuracy of afternoon urine osmolality to assess optimal hydration status.

RESULTS

Total of 120 subjects participated in this study with the recruitment algorithm as shown in **Figure 1** and the characteristics shown in **Table 1**.

The median of 24-hour urine osmolality was 463.5 mOsm/kg H_2O (95% CI, 136-1427) and afternoon urine osmolality was 513.5 mOsm/kg H_2O (95% CI, 73-1267), with moderate correlation ($r=0.594$, $p<0.001$) (**Figure 2**). There were 70 (58.3%) subjects who were optimally hydrated (with 24-hour urine osmolality ≤500 mOsm/kg H_2O).

Moreover, from ROC analysis (**Figure 3**) our study showed significant value ($p<0.001$) with AUC 0.792 (95% CI, 0.708 – 0.875). The optimal cut-off of afternoon urine osmolality to predict optimal hydration status was 528 mOsm/kg H_2O with sensitivity of 0.7 (95% CI, 0.585-0.795) and specificity 0.76 (95% CI, 0.626-0.857). This study also found positive predictive value (PPV) 0.803 (95% CI, 0.687-0.884) and negative predictive value (NPV) 0.644 (95%

Table 1. Subjects' characteristics

Characteristics	Value
Age (year), median (range)	32 (19-57)
Sex, female, n (%)	91 (75.83)
Systolic blood pressure (mmHg), mean (SD)	118.36 (13.475)
Diastolic blood pressure (mmHg), mean (SD)	76.95 (8.767)
Heart rate (beats/minute), mean (SD)	80.52 (10.854)
Weight (kg), median (range)	59.8 (38.6-93.3)
Height (cm), median (range)	158 (145-177)
Body mass index (kg/m^2), mean (SD)	24.184 (4.196)
Estimated glomerular filtration rate (mL/min/1.73m^2), median (range)	117.5 (65-146)
Urine volume (cc), median (range)	1600 (520-8440)

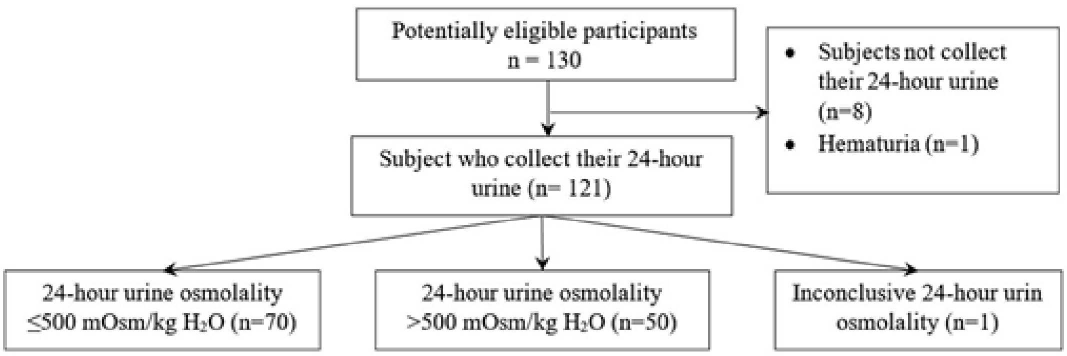

Figure 1. Subject flowchart

CI, 0.517-0.754). Furthermore, the LR (+) 2.917 (95% CI, 1.74-4.889) and LR (-) 0.395 (95% CI, 0.267-0.583).

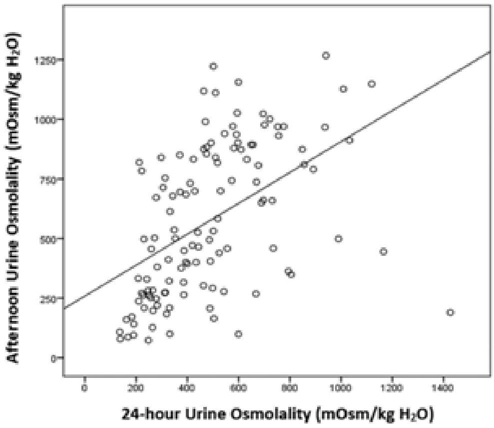

Figure 2. The correlation between 24-hour urine osmolality and afternoon urine osmolality

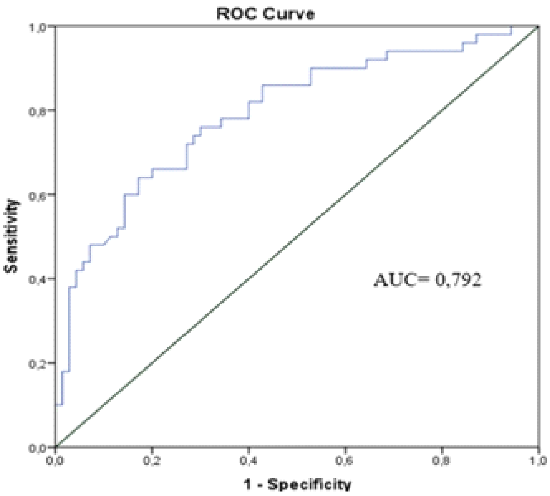

Figure 3. The AUC curve of afternoon urine osmolality

Table 2. Afternoon urine osmolality performance analysis

Afternoon urine osmolality	Twenty four-hour urine osmolality		Total
	≤500 mOsm/kg H_2O	>500 mOsm/kg H_2O	
≤528 mOsm/kg H_2O	49	12	61
>528 mOsm/kg H_2O	21	38	59
Total	70	50	120

DISCUSSION

Yeh, et al.[9] found that age, sex, race, body mass index (BMI), blood pressure, total of water consumption, plasma osmolality, alcohol, chronic illness, albuminuria, and diuretics drug affect the value of urine osmolality. Since we only include healthy subjects to our study, the confounding factors would not influence both plasma nor urine osmolality values. Our study found the median of 24-hour urine osmolality was 463.5 mOsm/kg H_2O. This result was different from a study in the USA which found that the mean 24-hour urine osmolality is 648 mOsm/kg H_2O.[9] Another study from Anyabolu, et al.[10] in Nigeria reported low 24-hour urine osmolality value (160 mOsm/kg H_2O). This differences happened because of intercultural variation which affect drinking habits (e.g. consumption of water, beer, wine) and food. Moreover, water consumption increases with higher sodium and protein intake.[11]

Our study found moderate correlation (r=0.594, p<0.001) between afternoon and 24-hour urine osmolality. Perrier's[12] study showed that urine parameters including osmolality, color, specific gravity, volume, and solute concentrations in 24-hour urine had strong correlation with total fluid intake. Other study showed hydration parameters from urine had better accuracy than plasma to assess hydration status. The study also showed significant difference in urine parameters between high drinkers and low drinkers, while their plasma osmolality were similar.[13] However, the challenges to collect 24-hour urine sample had become the weakness of the study.

In addition, another study from Perrier showed afternoon (during 4-8pm) urine osmolality most reflects 24-hour urine osmolality with 87% of total values 50 mOsm/kg H_2O from 24-hour urine osmolality.[8] Perrier's study supports our result which obtained moderate correlation (59.4%) between the two variables. This result can be explained by review from Truedel, et al.[14] which observed circadian effect of AVP excitation and found the highest level of AVP in the night to prevent water loss during sleeping time. This process produces low volume and high concentration of first morning urine.

Claybough JR, et al.[15] also support this study by finding the significant relation between urine osmolality and higher AVP in night.

From our study, the prevalence of subjects who were optimally hydrated was 58.3% using European Food Safety Authority (EFSA)'s cut off point (24-hour urine osmolality <500 mOsm/kg H2O). Previous studies found wide variation of prevalence for good hydration between countries. Study in Nigeria shows good hydration status in 10.3% of general population (cut off 300-750 mOsm/kg H_2O of 24-hour urine osmolality).[10] In contrast, the study in the US found that the prevalence of good hydration was 88.8% (cut off 450-840 mOsm/kg H_2O of 24-hour urine osmolality).[9] This variation is due to multiple factors including total water intake, race, diuretic consumption, weather, sodium intake, etc. However, these differences may be caused by various 24-hour urine osmolality cut off that were used in their studies.

Our study discovered that AUC value of afternoon urine osmolality was 0.792 (95% CI, 0.708-0.875). On the other hand, the AUC value of previous study which compares 24-hour urine osmolality with adequate fluid intake according to EFSA standard was 0.893.[3] Other study showed AUC value of 24-hour urine osmolality was 0.80 in assessing hydration status.[16] Hooper L, et al.[17] in his paper mentioned the AUC value of 24-hour urine osmolality to determine dehydration status in elderly was 0.56. In the same study, Hooper[17] found lower AUC (0.58) when using specific gravity from dipstick urine; (0.51) when using urine color variable; and (0.54) when using urine volume. From the study, we can assume that urine osmolality still gives the best result comparing to other urine parameters in assessing dehydration status, especially in elderly.

Another of Perrier's[3] study found that the optimal cut off for 24-hour urine osmolality in assessing optimal hydration status was 544 mOsm/kg H_2O. Perrier applied EFSA recommendation as minimum standard of total fluid intake. The study also obtained 525 mOsm/kg H_2O as the optimal cut off to prevent formation of kidney stones in female with >1850 mL water intake each day.[3] The reference of the amount of water intake that is used in Perrier's study was published before in 2004 by Curhan, et al.[18] Meanwhile, the optimal cut off for 24-hour urine osmolality to prevent recurrent kidney stone formation was 488 mOsm/kg H_2O.[3] In general, the cut off values found in Perrier's study was not very different from EFSA recommendation who suggests urine osmolality value to be less than 500 mOsm/kg H_2O. Our study also found similar optimum cut off with EFSA recommendation and Perrier's study. The afternoon osmolality cut off value to assess optimal hydration status found in our study was 528 mOsm/kg H_2O. The similarity can be explained by moderate correlation between the two variables, that have been mentioned earlier.

Sensitivity and specificity of afternoon urine osmolality to assess optimal hydration status in our study was 0.7 and 0.76, consecutively. Previous study which compared 24-hour urine osmolality with total fluid intake based on EFSA recommendation found that the sensitivity was 0.86 and specificity was 0.83. From our study, we obtained PPV 0.803 (95% CI, 0.687-0.884) and NPV 0.644 (95% CI, 0.517-0.754) with LR (+) 2.917 (95% CI, 1.74-4.889) and LR (-) 0.395 (95% CI, 0.267-0.583). Our study also found post-test probability (+) value 0.8 and post-test probability (-) value 0.35. By implementing this values, physicians can increase their confidence approximately 21.7% to determine optimal hydration status using afternoon urine osmolality. While, if someone have afternoon urine osmolality >528 mOsm/kg H_2O, it means they still have a chance of about 35% to be optimally hydrated.

This study can be applied to patients with normal kidney function and in any conditions that do not influence urine osmolality value. For example, physicians can assess optimal hydration status using our cut off value in patients with vomitus, diarrhea, dengue fever, or other cases which affect hydration. There are conditions in which this study cannot be applied due to their effects on urine osmolality, such as (1) diabetes insipidus, where AVP secretion is too low so urine osmolality will tend to decrease; (2) in elderly (>60 years old) where production of AVP is increased due to hypertrophy of hypothalamus resulting in increased urine osmolality.

This is the first study which reported afternoon urine osmolality as a diagnostic tool to determine optimal hydration status. This study also obtained a cut off value, so we can calculate the accuration of afternoon urine osmolality (sensitivity, specificity, and LR) to assess optimal hydration status. We can use afternoon urine osmolality value to replace 24-hour urine osmolality considering its effectiveness. However, this study has limitation that it can only be applied in healthy people. Moreover, because this was a diagnostic study, we categorized two hydration status, based on the cut off value (528 mOsm/kg H_2O), the optimal and the non-optimal ones. These categories impact the interpretation of hydration status which could be contradicting to what we found on physical examination. As an example, two patients with afternoon urine osmolality of 530 mOsm/kg H_2O and 900 mOsm/kg H_2O which based on this study, both will be diagnosed as non-optimal hydration may have different hydration status (good hydration and hypo-hydration) clinically.

CONCLUSION

Afternoon urine osmolality has moderate correlation with 24-hour urine osmolality with correlation coefficient of 0.594. Optimal hydration status can be predicted from afternoon urine osmolality with AUC value 0.792 and optimum cut off ≤528 mOsm/kgH2O (sensitivity 0.7 and specificity 0.76) in assessing optimal hydration status.

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