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Osmotic diuresis in chronic kidney disease: its significance and clinical utility

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Abstract

Introduction The kidneys contribute to maintain plasma osmolality in normal range by achieving the adequate daily osmolar urine excretion (DOUE). An equation has been described for estimating the expected daily urine volume necessary to excrete the osmolar load required to keep serum osmolality in normal range. According to this equation, a difference between real and expected daily osmolar diuresis (DOD) can be obtained, being normally this difference value zero (± 500 cc). However, a positive DOD difference signifies a reduced urine concentration capability, while a negative DOD difference signifies a reduced urine dilution capability. Therefore, we decided to originally investigate how DOUE, and DOD difference are modified through the different stages of CKD.

Materials and methods 61 patients suffering from CKD (stages I–V) secondary to glomerulopathies were studied. Creatinine clearance (CrCl), DOUE, and difference between real and expected DOD were obtained from each patient. Besides, correlation (Spearman) between CrCl and DOUE, and between CrCl and real–expected DOD difference were also obtained.

Results Spearman correlation between CrCl and DOUE was positive and significant (Spearman's $\rho = 0.63$, $p < 0.0001$). In addition, CKD patients who were not able to achieve the minimal DOUE required (600 mOsm/day) were mostly those with CrCl < 40 mL/min. Spearman correlation between CrCl and real–expected DOD difference was negative and significant (Spearman's $\rho = -0.4$, $p < 0.0013$). Additionally, abnormal DOD difference (> 500 cc) was found in CKD patients with CrCl < 80 mL/min/1.73 m^2.

Conclusion Daily osmolar urine excretion, and difference between real and expected daily osmolar diuresis are simple and significant clinical parameter which can be useful to easily evaluate urine concentration–dilution capability (tubular function) in CKD patients.

Keywords Osmolar diuresis · Osmolar excretion · Chronic kidney disease

Introduction

One of the main renal functions consists of contributing to maintaining body homeostasis, which includes keeping plasma osmolality in normal range. The kidneys achieve this objective by excreting the required amount of water and osmoles in urine, an amount which depends on the oral intake and metabolic activity of the organism [1].

In this sense, it is known that for an individual who has normal renal function and is on a western diet, the daily osmolar urinary excretion (DOUE) is usually between 600 and 900 mOsm/day. Even more, an equation has already been described for estimating the expected daily urine volume necessary to excrete the osmolar load required to keep serum osmolality in normal range. This volume is known as *daily osmolar diuresis* (DOD).

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The *daily osmolar diuresis* (DOD) equation is based on two data: daily urine osmolar excretion (DOUE) and daily urine osmolar concentration (DOUC). This mentioned equation is as follows [2]:

DOD = DOUE/DOUC.

For instance:

- DOUE = 900 mOsm/day
- DOUC = 400 mOsm/L.

Thus, DOD = 900 mOsm/day/400 mOsm/L = 2250 mL/day.

Therefore, according to this equation, a difference between real DOD and theoretical (expected) DOD can be obtained, and it should normally be zero (± 500 cc). However, a real DOD higher than expected (positive difference) could signify a reduced urine concentration capability; while a real DOD lower than expected (negative difference) could signify a reduced urine dilution capability [3].

This renal concentration–dilution capability mainly depends on its tubular function, which is usually altered at early stages of chronic kidney disease (CKD), and it can be evaluated by calculating the patient's real DOD, and comparing it with the expected DOD [1]. Consequently, the periodical evaluation of DOD and its real–expected difference in CKD patients could be useful to early detect progression in early stages of chronic nephropathy.

Therefore, we decided to originally investigate how DOUE, and the difference between real and expected DOD are modified through the different stages of CKD (from stage I to stage V).

Material and methods

Sixty-one patients (40 male) suffering from CKD secondary to glomerulopathies at different CKD stages (from stage I to stage V) periodically assisted in Clinica de la Costa of Barranquilla, Colombia, were studied. This studied population had an average age of 68 years old (range 30–92), and among their main causes of CKD were nephroangiosclerosis, diabetes mellitus nephropathy, Ig A nephropathy, and lupus glomerulonephritis. Blood and 24-h urine samples were obtained from each volunteer to measure their creatinine clearance (CrCl) and DUOE. In addition, the difference between 24-h real and expected DOD from each patient was calculated.

Finally, correlation (Spearman) between measured CrCl and DUOE, as well as between CrCl and real–expected DOD difference, was also obtained. Patients who had DOD difference above 500 cc (positive or negative) were considered to have abnormal DOD difference.

This study was approved by the Institutional Bioethical Committee, and informed consent was obtained from all the participants included in the study.

Results

Regarding the Spearman correlation between CrCl and DOUE, a positive and significant correlation was documented between these two variables (Spearman's $\rho = 0.63$, $p < 0.0001$) (Fig. 1). In addition, it is worth pointing out that CKD patients who were not able to achieve the minimal DOUE required (600 mOsm/day) were mostly those patients who had a CrCl below 40 mL/min (Fig. 2).

The correlation between CrCl and real–expected DOD difference (real DOD − expected DOD) was negative and significant between these two variables (Spearman's

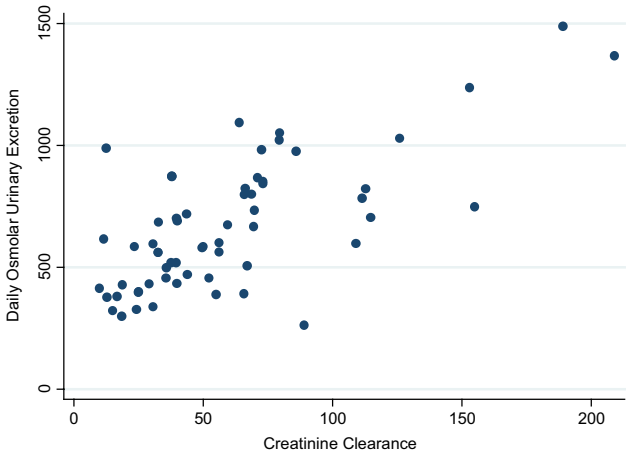

Fig. 1 Correlation between daily osmolar urine excretion (mOsm/day) and creatinine clearance (mL/min/1.73 m^2)

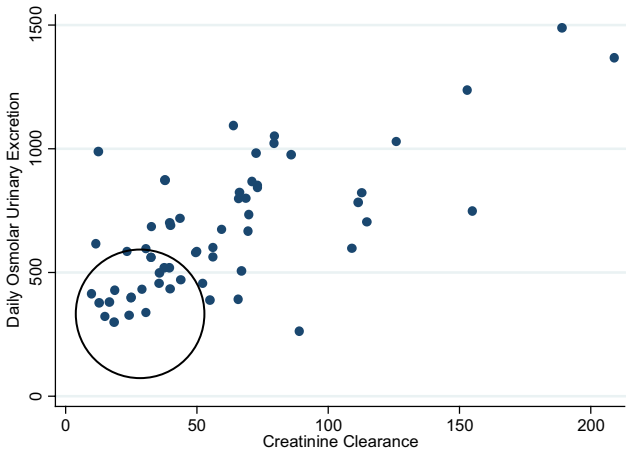

Fig. 2 Chronic kidney disease patients with daily urine osmolar excretion (DUOE) below 600 mOsm/day

$\rho = -0.4$, $p < 0.0013$) (Fig. 3). Additionally, it is worth pointing out that an abnormal DOD difference (> 500 cc, positive or negative), which means a concentration–dilution incapability, was documented in those CKD patients who showed a CrCl < 80 mL/min/1.73 m^2, being the DOD difference even worst (> 1000 cc, positive or negative) in those CKD patients who showed a CrCl < 40 mL/min/1.73 m^2 (Fig. 4).

Finally, only 34% of the studied patients showed the expected DOD value, while 17% showed a significant positive DOD difference (altered urine concentration capability), and 49% showed a significant negative DOD difference (altered urine dilution capability).

Discussion

In this study, there were patients of different CKD stages (Table 1), and it was documented that there was a positive and significant correlation between CrCl and DOUE ($\rho = 0.6$, $p < 0.0001$), being this excretion insufficient (< 600 mOsm/day) in patients who had a CrCl below 40 mL/min (stage III-b CKD) (Fig. 2).

This finding is very interesting since a glomerular filtration rate (GFR) below 40 mL/min was the threshold from which several studies had documented mortality was increased in CKD patients [4–6]. Perhaps, this inadequate osmol retention would be related with the uremic toxins retention implicated in the increased cardiovascular risk of these patients.

Besides, it was also documented that there was a negative significant correlation between CrCl and DOD difference ($\rho = -0.4$, $p < 0.0013$). In this sense, an abnormal DOD difference, which means an absolute difference (negative or positive) higher than 500 cc between the real and the expected DOD, represents an altered tubular function

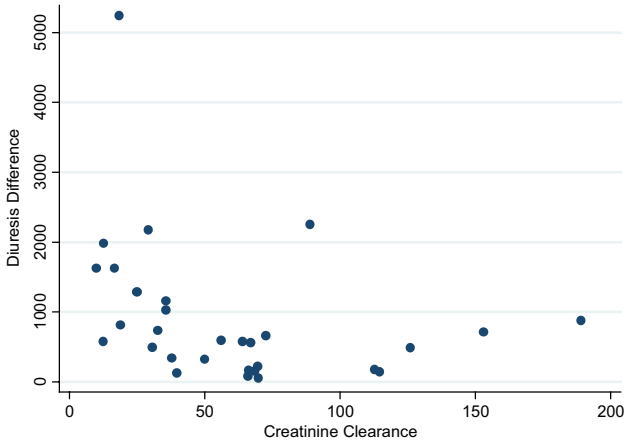

Fig. 3 Correlation between daily osmolar diuresis (DOD) difference (mL/day) and creatinine clearance (mL/min/1.73 m^2)

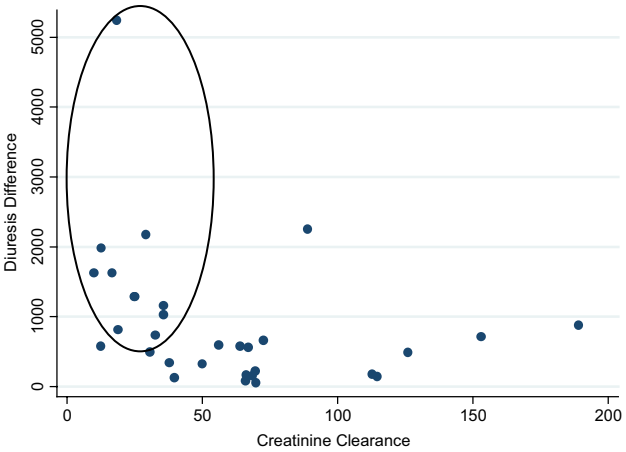

Fig. 4 Chronic kidney disease patients with abnormal daily osmolar diuresis (DOD) difference (above 500 cc)

either in urine concentration incapability (difference above + 500 cc) or urine dilution incapability (difference below − 500 cc). This finding is very interesting since it was also documented in this study that DOD difference started to be abnormal from CrCl below 80 mL/min/1.73 m^2 (stage II CKD). This phenomenon could be explained since the concentration–dilution capability is usually altered before beginning GFR reduction in CKD patients [1]. In addition, this abnormal DOD difference was worse (volume difference above 1000 cc) in those CKD patients who had CrCl below 40 mL/min/1.73 m^2 (stage III-b CKD), a GFR level at which, as it was mentioned above, general mortality is increased in this group (Fig. 4) [4–6]. Since DOD has recently been proposed as a useful diagnostic parameter in clinical nephrology, and it is currently proposed that tubular function should be periodically evaluated in CKD patients, DOD difference, which can detect early concentration–dilution incapability (tubular dysfunction), could be used for that purpose [3].

Even though, CKD prognosis is currently determined mainly by obtaining the patient's GFR value and his/her albuminuria–proteinuria levels, it should be taken into account that renal physiology is represented not only by GFR but also by tubule–interstitial function. In addition, the crucial role that tubular function has in the excretion of

Table 1 Chronic kidney disease (CKD) stages: patients' distribution

CKD stages	Percentage (%)
Stage I	15
Stage II	20
Stage III-a	11
Stage III-b	28
Stage IV	18
Stage V	8

several "uremic toxins" which are not excreted by GFR, as well as the renal prognosis value that tubule–interstitial damage has, is currently recognized. Therefore, it makes sense that DOD evaluation could be incorporated to periodic CKD evaluation, as an additional variable for evaluating the renal tubular capability in CKD patients [7].

Of course, new prospective clinical studies should be performed to further evaluate the clinical usefulness of this parameter, and its prognostic implications in CKD.

Conclusion

Daily osmolar urine excretion, and difference between real and expected daily osmolar diuresis are simple and significant clinical parameter which can be useful to easily evaluate urine concentration–dilution capability (tubular function) in CKD patients.

Compliance with ethical standards

Conflict of interest All the authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from the patient.

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