Doctor, how much should I drink?

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There is little information in chronic kidney disease (CKD) management guidelines on the potential benefits of a proper hydration to prevent renal damage. Despite the lack of any concluding evidence, experimental and population studies suggest that the liquid intake amount may be a non-established risk factor for CKD. Adverse renal effects caused by insufficient hydration can be mediated by the increase in vasopressin. In this sense, a generous water intake to remove at least the osmotic load may preserve the renal function in CKD patients that are still able to generate high urine volume.

The following theoretical analysis endeavours to provide a reasonable argument that answers the abovementioned question: doctor, how much should I drink? A standard diet generates approximately 650mOsm solutes, which are excreted through the kidney. If we assume that the maximum urine concentration is 1200mOsm/kg, at least 500ml of urine would be needed to eliminate the solute load. When a patient suffers advanced renal damage, the urine concentration ability is lost and isosthenuric urine is produced (250-300mOsm/kg). If the obligatory urine output is obtained by dividing the daily osmolar excretion by the maximum urine osmolality, at least 2l of diuresis would be required to eliminate a normal solute load. This is achieved with a liquid intake of between 2.5 and 3.5l per day, depending on extrarenal fluid losses.

Despite the ability to produce a high diuresis until the later stages of CKD, this recommendation must be managed with the upmost caution and it has to be personalised. It cannot be applied to patients who suffer from cardiorenal diseases or have risk of hydrosaline retention. Additionally, forced intakes can exceed the kidney dilution capacity and induce hyponatraemia. Thus serum and urine levels must be monitored in order to prevent hyponatraemia and dehydration, the latter being frequent in summer months and the elderly who are the majority of patients who suffer from advanced chronic kidney disease (ACKD).

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HYDRATION AND VOLUME OF URINE

In our daily clinical practice we have to answer questions that worry our patients and verify the level of adherence to our recommendations. ACKD management guidelines, with KDIGO (Kidney Disease Improving Global Outcomes) as a point of reference[1], lack in information for some of these questions. They exhaustively analyse proteinuria («top» predictor for the progression of renal damage), controversial calculation equations of the Glomerular filtration rate (GF), the importance of controlling blood pressure and the use of heart and renal protective measures, among others. However, the optimum handling of these patients requires the assessment of other factors such as the volume of urine, electrolytes, nitrogen…, which are of great use in our daily practice.

Many patients frequently ask: «Doctor, how much should I drink? I urinate a lot and if I drink more, I'll urinate more. Is that bad? ». These questions must have convincing answers. KDIGO[1] guidelines do not establish recommendations for water intake and diuresis in ACKD patients. The electronic document UPTODATE speaks of diuresis, but only gives warnings on the risk of retaining hydrosaline, in the complications section (http://www.uptodate.com/home: *Overview of the management of chronic kidney disease in adults*), especially if there is history of congestive heart failure and systolic dysfunction. This is logical, but if we apply it to all patients, we would be giving the idea that liquid intakes should be restricted, and this recommendation may have unwanted consequences.

In spite of the lack of information on this subject, medical literature provides beneficial data on the proper liquid intake required to prevent renal damage[2-4], and other contradictory[5]. Two excellent reviews [6, 7] have recently been published on the mechanisms of how a low liquid intake may have adverse effects on the kidney and the urinary tract in four scenarios of the illness: urolithiasis, urine infections, bladder cancer and

CKD. Below, we will analyse the possible adverse effects of liquid intake on the progression of CKD.

HYDRATION AND SOLUTE LOAD IN HEALTHY ADULTS

The classical message of «drink at least 8 glasses of water a day»[8] is well-known although there is only clear evidence that a forced liquid intake benefits patients with nephrolithiasis[9,10].

The kidney needs water to filter and excrete waste products from the blood[9,11,12]. A standard diet generates approximately 650mOsm* solutes, which must be excreted through the kidney[13]. This renal solute load (RSL) comes from food intakes and can be estimated using the following equation: RSL = Na + Cl + K + P + (N/28). Na, K, Cl and P are expressed in mmol and N, in mg. This equation assumes that all proteins are converted in the urea and all minerals from foods are eliminated through the kidney. The urine Osm can be calculated using this formula: Urine Osm = RSL (mOsm/day) / (water intake – extrarenal water losses in l/day)[13].

A healthy kidney can modify the urine osmolality (Osm) between approximately 40-1200 mOsm/kg of water[12,13] and the urine volume will vary depending on the amount of osmols required to excrete. In this normal situation, the urine Osm is two to three times more than the plasma, therefore the daily average diuresis in healthy adults is 1.2-2.0l[7,14]. Thus, the obligatory urine volume obtained by dividing the daily osmolar excretion (mOsm/day) by the maximum urine osmolality (mOsm/kg H_2O), is approximately 500ml of urine in its highest concentration.

This information provides us with reasonable grounds to estimate the minimum diuresis necessary to eliminate solute loads in ACKD.

*__Osmolality__ (mOsm/kg of water) or __osmolarity__ (mOsm/l of solution) differ in the units they are expressed in. Although osmolality is more accurate, we can use them both indistinctively for clinical purposes; both of them express the concentration of solutes and osmols of a solution.

WATER INTAKE AMOUNTS MAY BE A NON-ESTABLISHED A RISK FACTOR FOR CHRONIC KIDNEY DISEASE

Old studies on renal physiology claimed that a high liquid intake could prevent renal damage, and even recommended a diuresis of 3l/day[15]. Afterwards, research showed that there were benefits of high liquid intakes in CKD[16,17], especially in Adult Polycystic Kidney Disease (PKD).

In more recent years, Strippoli et al.[4] divided the general population over the age of 50 in two parts, showing that people who had a high liquid intake (higher quintile: > 3,2l/day) were less at risk of developing CKD. Thus, Clark et al.[3] analysed the relation between the volume of urine and renal deterioration in 2148 patients with GF>60ml/min during a follow-up period of six years. The authors observed an inverse relation between the volume of urine and renal damage, highlighting that patients with a diuresis of >3l displayed less renal deterioration.

The study by Peraza et al.[18] is very interesting; they studied the population that is exposed to insufficient and prolonged hydration, concluding that these people suffered subclinical acute renal damage and as a consequence, were more susceptible of suffering CKD. This manuscript and long-winded review in an accompanying editorial[19] warned us that «global warming», resulting from climate change may be a risk factor for CKD, especially in populations which are exposed to hard-working conditions in warm climates.

The possible association between renal damage and hydration in CKD patients was studied by Hebert et al.[5] using MDRD[20] data for the group with GF 25-55ml/min/1.73m^2. The results were the opposite to the previous ones, that is to say, a greater diuresis and lesser urine Osm, quick progression of CKD, in patients with and without PKD. These results have been questioned as it was not an object of study and could be a consequence of the quick deterioration of patients. PKD patients with higher water intakes obtained the best results.

THE ANTIDIURETIC HORMONE IS AT FAULT

Data from medical literature note that adverse renal effects caused by insufficient hydration may be measured by an increase in vasopressin or an antidiuretic hormone (ADH)[2,21]. ADH induces vasoconstriction of efferent arterioles, glomerular hyperfiltration and redistribution of renal flow; it increases the tubular reabsoprtion of Na[22] and stimulates renin synthesis by activating V2[2] receptors[23]. On a glomerular level, there is a direct effect on mesangial proliferation[24]. This leads to events which finally produce tubule-interstitial damage and nephrosclerosis[2,12,25]. The reduction of endogenous ADH levels with high liquid intake decreases blood pressure and proteinuria and may possibly benefit the kidney functions[25,26]. In PKD patients there have been adverse effects of ADH[2,27-29], showing that the increase in water intake prolongs the growth of cysts in animals, by means of the direct suppression of ADH[2,27-29].

DOCTOR, HOW MUCH SHOULD I DRINK? SUGGESTIONS FOR CLINICAL PRACTISE

The information we obtained was from population and experimental research and the fact that there is no

strong evidence that recommends forced liquid intakes (however there isn't any evidence on restricting liquid intakes) in CKD patients. However, this theoretical analysis endeavours to provide a reasonable argument to answer the question of this article: doctor, how much should I drink?

As we already mentioned, 600mOsm per day is required to maintain homeostasis and to excrete the obligatory solute load through the kidney. We also know that advanced renal damage produces a loss in the urine concentration capacity and between 250 y 300mOsm/l of isosthenuric urine on average[7,14,] the latter being verified with a number of patients from our consultation. We observed that these values are on a very narrow interquartile range (Table 1). Thus, CKD with a reduced renal active mass must excrete more water to eliminate solutes obtained from your diet. As we mentioned previously, if the obligatory urine volume is obtained by dividing the daily osmolar excretion (mOsm/day) by the maximum urine osmolality (mOsm/kg H_2O)[7,14], a diuresis of 2l would be the minimum requirement to excrete normal solute loads. This is achieved with a liquid intake of between 2,5 and 3,5l a day, depending on extrarenal losses. We generally estimate that 20% of the liquid intake comes from solid foods and the remaining 80% from water and other liquids[13].

In this sense, «drink when you are thirsty » may not be enough, especially in illnesses in elderly patients[30] and during summer month. The benefits of a higher liquid intake may be the key to delaying the progression of CKD[6,7]. In fact, another classic symptom that was noted is the increase in serum creatinine during warm periods of the year and in events that lead to dehydration (fever, diarrhoea, vomiting...), although the patients recovered after an appropriate liquid intake. In these events we must advise the patient to reduce or suspend the use of diuretics, rennin-angiotensin blockers as a preventive measure of a possible irreversible acute deterioration of the kidney function.

We must take a lot of care as these previous concepts cannot be applied to patients who have cardiorenal[31] syndrome symptoms. Forced water intake in patients with a precarious cardiac function (systolic dysfunction or even server diastolic dysfunction) and a history of congestive cardiac insufficiency, will lead to the risk of hydrosaline and hyponatraemia retention, especially when the urine Na is low as it indicates that the compensating neurohormonal mechanisms are at a maximum.

Our ACKD consultation monitors urinary parameters and we ask our patients to measure their urine output for 24 hours once or twice a month, with the aim to learn more about the amount they bring for their regular analysis. Thus, we have the urine volume of the patients in perspective so we can provide accurate recommendations and verify frequent comments like: «Doctor, the day that I urinate less when I have to urinate for an analysis ». Table 1 displays the values of diuresis, urine Osm, urine Na and serum in 94patients in our ACKD consultation in stages 4 and 5 (64±14 years, 78% men, 48% diabetics, 71% received loop diuretics); patients with a GF under 30ml/min are recommended to drink enough water to reach a urine volume of more than 2 l, except if they explicitly told not to do so. Thus, we can verify that a high urine volume is a characteristic of CKD until advanced stages (only 25% of patients had a diuresis of under 2l). The Osm shows that the urine is clearly isosthenuric, as described in the past and the urine Na is maintained at a higher level than previous recommendations.

The values of serum Na have shown a low risk of hyponatraemia in spite of stimulating a liquid intake and reducing Na in diets. Only 4 patients displayed Na figures below 130mEq/l without presenting any symptoms. However, this tells us that some patients find it more difficult to dilute urine, when there is forced liquid intake. Given that it is difficult to detect this situation a priori, we must be aware of this possibility and correct it early.

Conflicts of interest

The author states the following conflicts of interest:

He receives payment on some occasions for speeches and on subjects which are not compiled herein.

Table 1. Urinary parameters in 94 patients with an advanced chronic kidney disease in the4th and 5th stages at our consultation.

	Diuresis	Urine Osm	Serum Sodium	Urine Sodium
	m L/ 24h	mOsm/ Kg water	mEq/ L	mEq/ 24 h
Median	2740	296	139	139
CI Range	1940-3510	246-349	137-141	104-193

IQ: interquartile; Osm: osmolality.

KEY CONCEPTS

Complementary measure for patients with precarious renal function that are still able of producing high volumes of urine:

1. ACKD Patients with a high volume of urine is maintained until advanced stages of the illness.

2. Higher water intakes than the necessary amounts to eliminate osmotic loads may help to preserve the renal function. A diuresis of between 2-3l per day, or even more is a reasonable and appropriate proposal. This measure has more positive results in patients with PKD.

3. This recommendation must be applied with caution and be individualised:

   3.1. It cannot be applied to patients with cardiorenal syndrome, with high risks of hydro-saline retentions or congestive cardiac insufficiency.

   3.2. Forced liquid intake can surpass the renal diluting capacity and induce hyponatraemia.

4. Complementary control measures (to prevent aforementioned adverse effects):
   4.1. Regular measurement of the urine output during 24 hours by the patient and weight control.
   4.2. Systematic monitoring of urinary osmolality and sodium in the blood and urine in consultations.

5. Take measures to prevent dehydration in summer months and in elderly patients which are the main patients who suffer from ACKD.

6. Doctors must insist on the self-control of medication, reducing and stopping diuretics and renal-angiotensin- aldosterone blockers when there is a risk of dehydration.

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