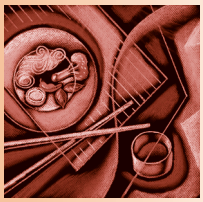

Effects of Water Consumption on Kidney Function and Excretion

Ivan Tack, MD, PhD

Water homeostasis depends on fluid intake and maintenance of body water balance by adjustment of renal excretion under the control of arginine vasopressin hormone. The human kidney manages more efficiently fluid excess than fluid deficit. As a result, no overhydration is observed in healthy individuals drinking a large amount of fluid, whereas a mild hydration deficit is not uncommon in small-fluid-volume (SFV) drinkers. Small-fluid-volume intake does not alter renal function but is associated with an increased risk of renal lithiasis and urinary tract infection. In that case, increasing fluid intake prevents recurrence. The benefit of increasing fluid intake in healthy SFV drinkers had never been studied until now. Two recent studies from Danone Research indicate that increasing water intake in such people leads to a significant decrease of the risk of renal stone disease (assessed by measuring Tiselius' crystallization risk index). Because renal lithiasis and urinary tract infection prevalence are quite high in western countries, this preliminary observation supports the interest of an approach based on primary prevention using voluntary increase in water-based fluid consumption in SFV drinkers. Complementary studies are required to determine other clinical impacts of SFV intake and to evaluate the benefits of increasing fluid intake. Nutr Today. 2010;45(6S):S37–S40

Some 380 million years ago, during the Devonian period, prehistoric animals progressively started to leave a water environment to colonize the ground. Biologists believe that primitive kidneys, initially devoted to excrete excess water and save electrolytes, evolved to excrete metabolic wastes and electrolytes in a small volume of water, allowing these organisms to save water.

The human kidney plays a critical role in water homeostasis. Every day, plasma ultrafiltration produces 150 L of filtrate (ie, 100 mL/min) via approximately 2 million nephrons. This primary urine is almost entirely (ie, 90%) reabsorbed in parallel to electrolytes. Reabsorption of the remaining volume depends on the presence or absence of an antidiuretic hormone, arginine vasopressin (AVP). Usually, only 1% of the initial amount of filtrate is excreted, leading to a urine volume of 1.5 L/d. In humans, because usual fluid intake is above the requirement for sufficient hydration, the kidney mostly excretes excess water. However, in situations where fluid intake becomes insufficient, the kidney is able to save a noticeable amount of water by concentrating the urine.

Kidney Water Regulation: What Are the Limits?

Renal capabilities for water handling are large but unequal, if one compares conservation and elimination capabilities. Water conservation is crucial for life in a dry environment, and, as soon as total body water content decreases, neurons within hypothalamic nuclei secrete AVP; AVP is then stored in the posterior pituitary until it is released. This hormone makes the distal nephron permeable to water, allowing reabsorption of most water that appears at this site. In this case, urine concentration can reach 1200 mOsm/kg of water (ie, 4 times plasma osmolality). Assuming a daily amount of waste containing 600 mOsm, only 0.5 L of urine is required to excrete this osmotic load. In this condition, the theoretical water saving is 1.5 L/d, because of urine concentration above plasma osmolality. At maximal urine concentration, if the amount of water available to excrete urine content is insufficient, waste elimination will worsen dehydration. Finally, if the fluid deficit becomes too large, extracellular dehydration will impact renal blood flow. This decrease, if severe, may lead to the collapse of renal filtration;

the resulting anuria signifies the loss of renal homeostatic function.

By contrast, the kidneys are able to easily eliminate a large amount of fluid. An excess of fluid decreases plasma osmolality, which, in turn, inhibits AVP secretion. In the absence of AVP, the distal nephron becomes almost impermeable, allowing passive elimination of a large amount of water. Indeed, the kidney cannot excrete pure water, and the maximum daily excretion of fluid depends on the osmotic load presented to the kidneys. Because the minimal urine osmolality is 50 mOsm/kg of water, an osmotic load of 600 mOsm results in a urine volume of up to 12 L/d. When compared with plasma isotonicity, urine dilution represents a net excretion of 10 L of solute-free water. Thus, thanks to the kidney's dilution capability, drinking a volume of fluid that moderately exceeds the body's requirement is not harmful and, in healthy individuals, will not alter total body water content chronically. To summarize, the kidney manages a fluid excess more easily than a fluid deficit.

Effects of Increasing Water Intake

The most common misconception regarding renal handling of water involves the belief that drinking a large volume of fluid helps to eliminate more wastes. In fact, as initially proposed by Smith,[1] renal function is ultimately related to the glomerular filtration rate. As long as extracellular volume (which primarily depends on regulation of sodium rather than regulation of water) is sufficient to maintain renal blood flow, the amount of water made available by glomerular filtration will allow healthy renal tubular function. Only a drastic reduction of total body water is able to impair renal function in healthy kidneys. If euhydrated people consume excess fluid, renal water reabsorption decreases, and the excretion of solute-free water increases.

When fluid intake is just sufficient to maintain body water content, the protracted period of time between fluid intakes requires that the body save water by concentrating urine. Such an occurrence commonly happens when one waits to be thirsty before drinking. At that time, plasma osmolality has risen by approximately 2%, and total body water has decreased in the same proportion. In fact, at the time where thirst appears, the elevated plasma concentration of AVP stimulates nearly maximal renal concentration. Thirst also indicates that one is imperfectly hydrated (ie, 1%–2% loss of body weight); the clinical impact of chronic mild dehydration remains uncertain, but we know that the risks of renal lithiasis and urinary tract infection are increased. Women especially experience the relationship between ample fluid intake and the decreased risk of urinary tract infection. Surprisingly, this relationship is not supported by evidence-based medicine because only a few publications have studied this matter. At present, the risk of renal lithiasis (ie, stone formation) recurrence has been verified in individuals who consume a small fluid volume (SFV) each day.[2]

Renal Lithiasis and Urinary Waste

Renal stone formation mostly results from an excessive concentration of low-solubility urinary products that contain either an absolute or relative excess of "wastes." Calcium and oxalate are primarily involved in more than 75% of renal calculi in Western countries. Because most urinary wastes come from food intake, the high prevalence of renal lithiasis in industrialized countries appears to be related to the characteristics of a Western diet, which provides a large amount of protein and minerals. The metabolism of protein produces urea and increases net acid excretion through ammonium and phosphates ions. Further, protein-rich foods provide a lot of salt, leading to increased sodium chloride excretion. These nutrients account for more than 95% of the total urine osmotic content excreted each day.

Thirty years ago Robertson et al[3] were among the first to show the relationship between protein intake and renal excretion of calcium and oxalate. More recently, Tiselius[4] proposed and validated a crystallization risk index (CRI) that helps to evaluate the risk of stone recurrence in lithiasic patients. The formula is based on the product of the total amount of calcium, oxalate, citrate, and magnesium (the latter two being crystallization inhibitors) and urine volume excretion. The higher this product, the higher is the risk of crystallization and of stone formation. Using Tiselius' CRI, our group has recently shown in a sample (n = 312) of kidney stone patients from Southwestern France that (1) there was a significant correlation between body mass index, CRI, and urinary osmotic load; (2) this relationship was related to protein metabolism (estimated using urine urea excretion); (3) sodium, calcium, and oxalate excretions were significantly correlated with protein metabolism; and, by contrast, (4) no statistically significant correlative relationship existed between urine osmotic load or body mass index and urinary volume or fluid intake. This latter observation is crucial because it suggests that there is no physiological feedback between the amount of waste to excrete and the amount of fluid necessary to do it safely. As a result, the more that kidney

stone patients eat, the more the urine becomes concentrated and the greater the risk of renal lithiasis increases. The only way to adapt in this case is to intentionally and preventively increase the volume of dietary fluid.

Is Increased Fluid Intake Helpful to Healthy People?

Epidemiological studies[5] have shown that low urine volume (ie, as a result of hot climate, intense physical activity, or low water intake) is an important risk factor for kidney stone recurrence. Pak et al[6] also demonstrated, some 30 years ago, that increasing dietary water intake increases urine volume and lowers the risk of renal lithiasis recurrence. However, these observations were made in patients already exhibiting active stone disease, and this study involved treatment, not prevention. Nevertheless, in Western countries, assuming that renal lithiasis prevalence is approximately 10% of the adult population and that half of these cases reoccur, it is logical to develop a primary preventive approach as long as it is neither costly nor risky. Based on this assumption, and considering that the fluid with the lowest metabolic impact is water, it is reasonable to ask individuals who consume an SFV to increase their water consumption,[2] especially if they eat large meals. Unfortunately, no literature is available regarding the potential benefit of increasing fluid intake in such a healthy population.

Elimination Studies in Healthy Subjects

Two studies recently have been sponsored by Danone Research to evaluate the potential benefit of increasing water intake (ie, by 2 L/d) on the CRI (see above) of healthy SFV subjects. One study was performed in Spain (using the Font Vella water brand) and the other in Mexico (using the Bonafont water brand).

These experiments were designed as open, parallel, randomized studies; they were stratified by center and sex and involved 48 healthy volunteers from each country. Both sexes were equally represented, and ages ranged from 25 to 50 years (ie, the age at which people first develop lithiasis). Volunteers who were classified as consuming SFV were selected because they exhibited highly concentrated 24-hour urine samples. The intervention consisted of asking them to drink 2 L of water, above their basal ad libitum fluid intake, for 6 consecutive days. The control group was asked to eat and drink as usual. The main outcome variable was change in CRI in both the first morning urine (when urine concentration is greatest) and 24-hour urine samples.

Efficacy of the intervention was assessed by checking the 24-hour urine volume. Not surprisingly, the mean urine volume in the intervention group (ie, instructed to consume 2 L of water above the daily basal amount) significantly increased when compared with the control group, but by 1.1 L in Mexico and 1.4 L in Spain. This occurred because test participants increased their water intake but concomitantly reduced the intake of other beverages.

In the Mexican study, the CRI was initially low, test volunteers increased their average fluid consumption by 1.1 L, the CRI decreased significantly, and a very low risk of crystallization resulted. Further, in Mexico, the LFV participants spontaneously and significantly increased their fluid consumption after receiving instructions to do so. This means that people who consume LFV can be quite easily reconditioned, if they are identified and well informed. It also suggests that they were not aware of their drinking behavior.

In the Spanish study, baseline CRI was higher, suggesting that people from Mexico spontaneously exhibit a lower risk of crystallization than their European counterparts. This observation is not surprising because Tiselius' CRI initially originated from the data of Northern Europeans, who consume a protein-rich Western diet similar to those who live in Spain. Interestingly, all subjects who initially exhibited a CRI above the threshold of risk went below this threshold after increasing their water intake. Also, in the Spanish study, the 1.4-L postintervention increase in urine volume significantly decreased the CRI, regardless of the time of day that the urine sample was collected (ie, 24 hours or first morning).

Biological tolerance to the increased water intake was evaluated by measuring plasma and urine osmolality. As could have been predicted from physiological knowledge, and despite the hypotonicity of the 2 Danone water products, plasma osmolality remained unchanged. The rapid renal excretion of solute-free water dismissed any risk of excessive plasma dilution. By contrast, 24-hour urine osmolality significantly decreased (ie, approximately equal to plasma isotonicity, a typical target for the treatment of patients with a history of renal stone formation).

Contrary to the misleading belief that drinking water "cleans out the system," increasing water intake by 2 L did not significantly modify solute excretion. The urea, uric acid, creatinine, sodium, potassium, calcium, chloride, oxalate, and citrate 24-hour excretion rates remained unchanged.

Summary

The kidney is the key organ of water homeostasis. It is able to retain or eliminate water, to regulate total body water and its concentration. However, renal capacity to manage excess fluid exceeds its ability to save water during dehydration. Thus, becoming slightly dehydrated is not uncommon.

Despite many studies that have attempted to detect the early clinical impact of dehydration, it remains difficult to separate the status of "optimal hydration" from that of "slight dehydration." One can assume that not only should "drinking enough fluid" provide adequate fluid to restore or maintain total body water, it also should dilute urinary wastes enough to reduce the risk of urinary tract infection and renal lithiasis. This point appears particularly critical in (*a*) SFV drinker adults and (*b*) those who eat a large amount of proteinated food each day since the resulting increase in urine osmotic load does not produce fluid intake adjustment in the absence of dedicated renal feedback, resulting in an increased risk of stone formation.

The answer to the classic question of "how much should we drink?" still remains controversial. However, it appears that "drinking enough" means drinking a volume that eliminates urinary wastes safely; this volume is greater than the usual recommendation "to drink to avoid thirst and becoming clinically dehydrated." In fact, urine concentration may be an early and efficient measurement to assess optimal hydration, because it reflects the body's water balance. Hydration status is optimal when urine is isotonic or slightly hypotonic and tend to be negative when urine is concentrated.

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