The American Journal of the Medical Sciences
Issue: Volume 319(4), April 2000, pp 240-244
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Keywords: Electrolyte-free water clearance, Hypotonicity, Water intoxication, Hyponatremia

The Urine/Plasma Electrolyte Ratio: A Predictive Guide to Water Restriction

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[c] 5 mEq/L × (50 kg × 0.6 L/kg) = 50 mEq / 513 mEq/L of 3% saline = 292 mL, and the change in P_{Na} = [(50 kg × 0.6 L/kg × 108 mEq/L) + 150 mEq] / [(50 kg × 0.6 L/kg) + 0.292 L] = 112 mEq/L.
Submitted March 11, 1999; accepted in revised form July 13, 1999.
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Abstract

Patients with hypotonic hyponatremia are encountered commonly in the general practice of medicine. Nearly all strategies for the management of subacute or chronic hyponatremia call for some amount of water restriction. The considerations for such a prescription have not been addressed in the literature. We describe therefore a simple approach grounded in the physiology of electrolyte-free water clearance that can be used at the bedside.

A thoughtful approach to water restriction in patients with hypotonicity requires some knowledge of basic principles of fluid and electrolyte metabolism. Simply restricting water consumption to an arbitrary amount, such as 1 L per day, is seldom effective, because there is no therapeutic compensation for insensible water loss, the amount of solute in urine water, or the portion of free water in consumed fluids. Here we review one uncomplicated approach for estimating a clinical water prescription that we have found helpful.

The general principles of fluid and electrolyte balance advanced by Peters 1 and Shohl 2 emerged in this century from a larger notion of homeostasis. 3 Within this framework, body fluid compartments partition to a steady-state that depends on the balance between ingestion, distribution, and excretion of solutes and water. Excretion is principally accomplished through evaporation from alveoli and skin, or by clearance from the kidneys and gut. 4–7 Oxidation of metabolic fuel also generates about 300 mL of internal water, but the amount is almost nullified by the water volume of normal-diet stools, and neither measure appears in most rough estimates of water balance.

In addition to urine output, daily water excretion is affected by respiration and skin evaporation. 8 Patients in the hospital who are at bed rest without fever are thought to lose about 500 mL/m^2 per day of insensible water. The average 70-kg man loses about 800 mL, 4,8–10 of which 60% is insensible loss from the skin and need not be factored for pigmentation. 9 Estimates of insensible water loss should be reduced by 40% when using humidified air during respiratory therapy. Sensible perspiration during fever augments water loss, but not all of it is free water. The osmolarity of sweat is about one quarter that of plasma, due to the presence of sodium and potassium salts. 11 In the range of moderate sweating (1–1.5 L per day), a correction factor of 0.75 should be used in assessing actual free water loss and its impact on plasma sodium concentration (P_{Na}).

When body solute is in balance, water homeostasis regulates osmolarity, compartment size of body fluids, and tonicity. 12,13 Tonicity describes the volume behavior of cells in response to changes in the concentration of effective osmoles that influence transmembrane water flow. 14 Because extracellular sodium and intracellular potassium salts are the principal effective osmoles partitioning total body water, it is imperative to compare the intake of water, sodium, and potassium with their urinary losses when assessing a change in tonicity. 14–16 Other urinary solutes, such as urea, contribute to osmolarity but not to tonicity, because they do not preferentially accumulate on one side of the cell membrane compared with the other and thus do not influence transmembrane water flow or cell volume. At the bedside, one can conveniently estimate tonicity using P_{Na} as a rough measure of the net relationship between water content and effective osmoles across all body fluid spaces. 13,14

Technically speaking, a total assessment of solute and water balance in relation to intake and loss is most precise. Unfortunately, clinicians seldom can gather this information in a timely fashion to take advantage of a complete solute and water balance approach. What is usually available at the bedside is knowledge of what the patient might ingest in the future and time-sensitive information about how kidneys are handling these substances.

The ability of kidneys to modulate tonicity in the face of significant water ingestion greatly depends on urine volume, solute content, and the ability to dilute. Although urine osmolarity (U_{osm}) can be used to estimate the kidney's ability to dilute or concentrate, 1 it is an insufficient reflection of the "quantity" of urine water freed of solute. Mathematical models of osmolar clearance and free water clearance[A] developed in the latter half of this century helped to better characterize the proportions of urine solute relative to water. 17 However, not all dietary or urinary solutes are equivalent effective osmoles that influence plasma tonicity or P_{Na} concentration. This awareness eventually led to the notion of the very useful, but oft-forgotten, electrolyte-free water clearance (C^eH_2O). 15

The effective osmoles used to calculate $C^eH_2O = V \times \{1 - [(U_{Na} + U_K) / P_{Na}]\}$ are the principal sodium and potassium salts mentioned above. Although one could include plasma potassium in the denominator, its concentration can be ignored because it remains quite small relative to P_{Na}. Osmotically active anions such as chloride and bicarbonate are also ignored in both numerator and denominator to simplify the calculation.

Because it is not always practical to measure or wait for 24-hour urine volumes in making prospective decisions, C^eH_2O can be distilled further by simply focusing on the urine/plasma electrolyte (U/P) ratio: the sum of urine U_{Na} and U_K concentration from a spot collection divided by the P_{Na}. Armed with this formula, one can easily gauge free water loss in relation to tonically effective osmoles for the next liter of expected urine. 15,16,18 When the C^eH_2O is positive, electrolyte-free water is being excreted and the U/P ratio is less than 1.0 (Table 1). Significant amounts of electrolyte-free water are excreted in urine when the U/P ratio is less than 0.5. Conversely, no electrolyte-free water is excreted when the U/P ratio is equal to 1.0. For example, a patient with a U_{Na} of 70 mEq/L, a U_K of 50 mEq/L, and a P_{Na} of 120 mEq/L does not excrete any electrolyte-free water. Total urine volume or a measurement of U_{osm} simply would not predict this. For body tonicity to rise, this patient has to be both water restricted to less than insensible losses and given 240 mEq—[2 × (70 mEq/L + 50 mEq/L)]—of replacement effective osmoles (sodium and potassium salts) for each voided liter of urine.

Table 1. Approach to Raising Plasma Tonicity by Water Restriction

Urine/Plasma Electrolyte Ratio	Insensible H_2O Losses	Expected Net H_2O Loss[a]	Recommended H_2O Consumption
≥1.0	800 mL	−800 mL	0 mL
0.5–1.0	800 mL	−800 to −1300 mL	Up to 500 mL
≤0.5	800 mL	−1300 to −1800 mL	Up to 1 L

[a]These estimates are based on a U/P ratio, a simplified formulation of C^eH_2O. They also assume that urine sodium and potassium losses are replaced, that a patient has an average body surface area of 1.73 m^2 and eats a normal diet, and calculate for the period during which the next 1 L of urine is excreted.

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which the next 1 L of urine is excreted.

As the following hypothetical clinical cases illustrate, opting for a more rigorous analysis assures better assessment of variation in body tonicity. We will focus on guidelines for bedside water restriction in the management of hypotonicity. Pharmacologic approaches have recently been reviewed. [19]

Case 1: A Hypotonic Patient in the Hospital

A 72-year-old man with metastatic lung cancer presented with a moderate but persistent hyponatremia after chemotherapy. He had no symptoms related to hypotonicity. His physical examination was significant for clinical euvolemia with a P_{Na} of 119 mEq/L, serum uric acid of 2.4 mg/dL, a glucose level of 110 mg/dL, a creatinine level of 0.7 mg/dL, a P_{osm} of 248 mOsm/L H_2O, a U_{osm} of 664 mOsmol/L H_2O, U_{Na} of 100 mEq/L, U_K of 66 mEq/L, and a urine output of 900 mL/day.

The most likely diagnosis was inappropriate antidiuretic hormone secretion from malignancy. An initial oral fluid restriction of 1 L/day was prescribed as maintenance, but after 24 hours, his P_{Na} fell even further to 117 mEq/L. In retrospect, even if the patient had been fully compliant, this amount of restriction alone could not have been expected to improve his hypotonicity. His initial C^eH_2O = 0.9 L × [1 - (166 mEq/L / 119 mEq/L)] was -355 mL/day. This is a negative quantity, signifying free water retention rather than excretion. Such physiology never would have been predicted from looking only at urine volume. If one subtracts another 800 mL for daily insensible loss, his daily intake of free-water would exceed any losses by 555 mL (1000 - 800 - [-355]). Furthermore, no provision was made for replacing on-going urine losses of sodium and potassium salts and, all things being equal, this patient's P_{Na} had to fall further over the short term.

If prescription had limited his water intake to 300 mL per day, and provided that his urinary solute losses were replaced, he would have increased his net free water losses by about 1 L per week [(300 mL - (-355 mL) - 800 mL] = -145 mL × 7 days = -1015 mL. Under these conditions his P_{Na} would have slowly risen. If, on the other hand, his physicians had used CH_2O and total urine solute as a guide, the inappropriate consideration of urine urea would have predicted a water gain of 1.4 L per day.[B] This far exceeds the 355 mL water gain estimated by the C^eH_2O calculation and falsely suggests a need for more drastic measures.

Brief periods of water deprivation can be a hardship on many patients, of course. If this patient's free water intake were limited to 300 mL per day, the rate at which his tonicity might improve could be further accelerated by adding osmotic load to his dietary regimen or other pharmacologic manipulations, [19] thus permitting a further liberalization of water consumption above the severely restricted 300 mL per day.

Case 2: A Hypotonic Patient in the Office

A 65-year-old woman saw her physician for hypertension. She had a P_{Na} of 140 mEq/L, a creatinine level of 0.7 mg/dL, and no end-organ damage. She was started on hydrochlorothiazide and 2 weeks later her systolic blood pressure declined to 135 mm Hg. When she complained of headache and lethargy, a second set of electrolytes revealed a P_{Na} of 121 mEq/L.

On examination, she weighed 60 kg without orthostasis or focal neurologic signs. Additional laboratory studies revealed a P_K of 3.5 mEq/L, P_{Cl} of 86 mEq/L, P_{HCO3} of 25 mEq/L, creatinine level of 0.7 mg/dL, P_{osm} of 252 mOsm/L H_2O, a U_{Na} of 72 mEq/L, a U_K of 30 mEq/L, and a U_{osm} of 400 mOsm/L H_2O. If we assume a woman's total body water is 50% of her body weight and that she reached a new steady state of sodium balance, her water excess = present total body water - previous body water, [14] or (present weight in kg × 0.5 L/kg) × (1 - [P_{Na} / 140 mEq/L]) or 30 L × (1 - [121 mEq/L / 140 mEq/L]) = 4.1 L. This patient developed marked hyponatremia while taking a thiazide diuretic because she could not dilute her urine below 400 mOsm/L H_2O. Normal experimental subjects when

hypotonic are able to dilute their urine down to nearly 50 mOsm/L H_2O. [20]

How much water restriction should be prescribed for this woman? The C^eH_2O is typically not calculated in an ambulatory setting because daily urine volumes are unknown. If we hypothetically assume she voided 1.5 L over the previous day, her C^eH_2O = 1.5 L × [1 -(102 mEq/L / 121 mEq/L)] = 235 mL/day. If one assumes an average insensible loss of 800 mL per day, then restricting H_2O consumption to 1 L/day would not improve her tonicity. Furthermore, because we do not know her urine volume, the U/P ratio becomes especially useful for recommending the degree of initial water restriction. Water ingestion based on the approach outlined in Table 1 should be completely restricted if the spot U/P ratio for the next several liters of urine is greater than 1.0. For those patients with U/P ratios between 0.5 and 1.0, a restriction to 500 mL or less is probably sufficient. For those with U/P ratios less than 0.5, fluid should be restricted up to 1 L per day. This patient has a U/P ratio = $(U_{Na} + U_K) / P_{Na}$ = 102 mEq/L / 121 mEq/L = 0.84, which suggests the need for up to 500 mL of water restriction for the next few liters of urine—this would predict a safe and reasonable loss of 500 mL/day. In this case, of course, as the urine becomes more dilute after thiazides are discontinued, the free-water clearance will quickly rise and permit greater liberalization of water consumption provided the U/P ratio remains low. Judicious replacement of potassium salts may also accelerate the correction.

Case 3: A Hypotonic Patient with Changing Requirements for Water Restriction

A 28-year-old male schizophrenic with a long history of compulsive fluid consumption was admitted to the hospital because his home care provider no longer could cope with his behavior. His days were spent in covert search for consumable liquids, sometimes at the faucet or sometimes at the showerhead, and they often ended in a grand mal seizure. It was so preoccupying he rarely took time to eat a meal.

On physical examination he was thin (only 50 Kg) and energetic without orthostasis. He had a normal cardiovascular examination with no other known medical problems. On admission his laboratory findings included a P_{Na} of 125 mEq/L, blood urea nitrogen of 6 mg/dL, U_{osm} of 150 mOsm/L H_2O, U_{Na} of 10 mEq/L, and U_K = 32 mEq/L. An analysis of body fuel metabolism and dietary intake suggested that he was obligated to excrete only 300 mOsm/day. The maximum urine volume required to excrete this daily osmolar load can be determined by dividing osmolar load by his lowest achievable urine osmolarity (or $Uosm_{min}$). This yields 300 mOsm/day / 150 mOsm/L H_2O = 2 L/day (or 83 mL/hour). [21,22] Thus, free-water ingestion must exceed 83 mL/hour of urine plus 33 mL/hour of insensible losses before water retention would occur. His water-seeking behavior or psychogenic polydipsia easily overwhelmed his reduced electrolyte-free water clearance and resulted in symptomatic hypotonicity. [19]

One morning he was found wet on the floor of a hospital shower having cluster seizures. An emergent P_{Na} was 108 mEq/L. If we assume that total body water is 60% of body weight in a man, an excess water calculation shows that present total body water - previous body water = (50 kg × 0.6 L/kg or 30 L) × [1 - (108 mEq/L / 125 mEq/L] = 4.1 L. This suggested a short-term consumption that exceeded his electrolyte-free water clearance. Because of his desperate condition, it was decided to raise his P_{Na} by 4 to 5 mEq/L over 3 hours [19] by giving 292 mL of 3% hypertonic saline[C] with judicious prescription of furosemide to lower U_{osm} and increase C^eH_2O. This intervention raised his P_{Na} to 112 mEq/L and terminated his seizure activity.

At this time, his U_{Na} was 90 mEq/L and his U_K was 64 mEq/L—both were increased from a combination of the hypertonic saline and the effect of the furosemide. His U/P ratio for the next liter of urine was estimated to be $[(U_{Na} + U_K) / P_{Na}]$ = 154 / 112 = 1.38. Because his U/P ratio is >1.0, he is effectively retaining free water. Restricting him to the standard 1 L/day would only add to his water intoxication. Consequently, all oral fluids were withheld and the U_{Na} of 90 mEq/L and his U_K of 64 mEq/L were intravenously replaced as isotonic fluid over several hours. Six hours later, repeat urine electrolytes revealed a U_{Na} of 50 mEq/L and a U_K of 25 mEq/L with a P_{Na} of 113 mEq/L, giving him a U/P ratio of 0.66. With expected insensible losses unchanged, it would be safe at this stage to advance his water consumption to 500 mL per day and let him slowly evaporate back to a safer tonicity.

Conclusions

Several conclusions can be drawn regarding the optimal approach to restricting water consumption in the setting of hypotonicity. Our approach is based on the informal application of general principles of water metabolism.

• Real-time data regarding sodium, potassium, and water intake and loss—a picture of solute and water balance—are most optimal in sorting out the best corrective prescription. These data, however, are often unavailable, because growing numbers of patients are being managed in ambulatory settings or in hospitals with limited personnel where frequent testing is discouraged. Reasonable estimates for water restriction can be made, however, by prescribing solute and water intake and monitoring their excretion.

• Urine volume and U_{osm} are poor predictors of the amount of water that needs to be restricted.

• An improved formulation like the free water clearance does not provide the correct answer either, because it includes urea, an ineffective osmole that does not influence tonicity.

• A common error is to ignore urinary potassium and sodium losses, which can be substantial. This leads to an incorrect assessment of the level of water restriction necessary.

• The oft-forgotten C^eH_2O and the simplified U/P ratio = $(U_{Na} + U_K) / P_{Na}$ derived from it are useful tools for making effective therapeutic decisions. The clinical information required for this analysis includes a quick calculation of the U/P ratio from spot urine electrolytes and a concurrent P_{Na}, a reasonable estimate of urine volumes forward in time, and a feeling for insensible water losses. Rarely is it appropriate to uniformly restrict water intake to 1 L per day. Water restriction must be tailored to each individual patient.

Acknowledgments

We would like to thank Dr. Richard Tannen, Professor and Senior Vice-Dean for Administration, University of Pennsylvania, for critically reading and earlier version of this manuscript.

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