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Focus on Diagnosis: Urine Electrolytes

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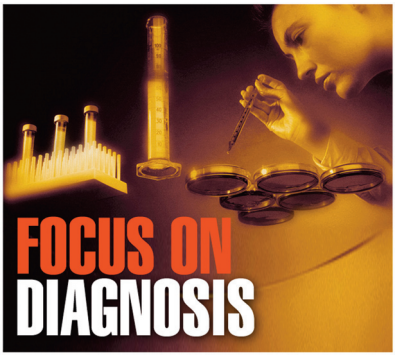

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Urine Electrolytes

J. Bryan Carmody, MD*

Introduction

Although electrolytes in the blood must be maintained within narrow limits for homeostasis, urine is the body's waste, and concentrations of urine solutes vary widely, depending on the need for the specific solute to be excreted or retained. However, in a variety of clinical situations, analysis of urine electrolytes can be very informative or even diagnostic. To maximize the usefulness of such tests (Table), the clinician must possess both a basic knowledge of renal solute handling and an understanding of the particular instances in which measurement of urine electrolytes is useful.

Frequently, clinicians are hesitant to obtain urine electrolytes due to the perceived difficulty in interpreting them in the absence of "normal" values. It is critically important to realize that urine electrolytes can only be interpreted in the context of the patient and the clinical situation. For example, a urine potassium concentration of 35 mEq/L may be appropriate for a healthy patient eating a potassium-rich diet but would indicate inappropriate renal potassium wasting in a patient whose serum potassium concentration is 2.0 mEq/L (2.0 mmol/L).

Urine Sodium Concentration

Sodium is the body's primary extracellular cation. Because water movement follows solute movement, sodium has a major physiologic role in maintaining extracellular volume, and the kidney actively varies reabsorption of sodium to maintain appropriate effective circulating volume. Therefore, the major use of the urine sodium concentration (U_{Na}) is to assess a patient's volume status. When the effective circulating volume is decreased (hypovolemia), the kidney avidly retains sodium in an effort to maintain circulating volume, and the U_{Na} is low, generally less than 20 mEq/L. Without this stimulus, sodium excretion parallels dietary intake and generally is more than 40 mEq/L. (1)

Although assessment of a patient's volume status is useful in a variety of situations, measurement of the U_{Na} is particularly useful in the evaluation of two specific states: hyponatremia and acute renal failure. Hyponatremia is caused by excessive retention of free water out of proportion to solute. In clinical practice, this state is due either to the syndrome of inappropriate antidiuretic hormone secretion (SIADH) or to the appropriate secretion of ADH that occurs in response to hypovolemia. It is important to note that the latter situation occurs not just in situations in which the total body water is decreased such as gastroenteritis or adrenal insufficiency but also in edematous states such as cirrhosis, congestive heart failure, and nephrotic syndrome. In these cases, although total body water is increased, the effective circulating volume is decreased, triggering the appropriate release of ADH. In volume-depleted hyponatremic states, the renal tubules reclaim as much sodium as possible, and the U_{Na} is low at less than 20 mEq/L. In SIADH, however, patients experience euvolemia, and sodium is excreted in the urine at the normal rate, making the urine sodium concentration greater than 40 mEq/L

Abbreviations

ATN:	acute tubular necrosis
FE_{Na}:	fractional excretion of sodium
FE_{urea}:	fractional excretion of urea
NH_4^+:	ammonium ion
RTA:	renal tubular acidosis
SIADH:	syndrome of inappropriate antidiuretic hormone secretion
TTKG:	transtubular potassium gradient
UAG:	urine anion gap
U_{Cl}:	urine chloride concentration
U_K:	urine potassium concentration
U_{Na}:	urine sodium concentration
U_{urea}:	urine urea nitrogen concentration

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Table. Common Electrolyte Measurements

Urine Electrolyte	Clinical Situation	Interpretation
U_{Na}	Hyponatremia	<20 mEq/L: Volume depletion >40 mEq/L: SIADH
	Acute renal failure	<20 mEq/L or FE_{Na} <1%*: Prerenal azotemia >40 mEq/L or FE_{Na} >2%*: ATN
U_K	Hypokalemia	TTKG <2 to 3: Nonrenal losses TTKG >2 to 3: Renal potassium wasting
	Hyperkalemia	TTKG <6 to 7: Defective potassium secretion (hypoaldosteronism or renal failure) TTKG >11: Increased potassium intake or transcellular shift
U_{Cl}	Metabolic alkalosis	<20 mEq/L: "Saline-responsive" alkalosis/volume depletion with vomiting, nasogastric suctioning >20 mEq/L: "Saline-resistant" alkalosis/renal chloride wasting with diuretic use, Bartter/Gitelman syndromes
UAG	Hyperchloremic (normal anion gap) metabolic acidosis	Positive UAG: Renal tubular acidosis Negative UAG: Gastrointestinal bicarbonate loss (diarrhea)
U_{urea}	Acute renal failure	FE_{urea} <35%: Prerenal azotemia FE_{urea} >50%: ATN

*Because immature tubules have a reduced reabsorptive capacity for sodium, the FE_{Na} is higher in younger or preterm infants.
ATN=acute tubular necrosis, FE_{Na}=fractional excretion of sodium, FE_{urea}=fractional excretion of urea, SIADH=syndrome of inappropriate antidiuretic hormone secretion, TTKG=transtubular potassium gradient, UAG=urine anion gap, U_{Cl}=urine chloride concentration, U_K=urine potassium concentration, U_{Na}=urine sodium concentration, U_{urea}=urine urea nitrogen concentration

when the patient is consuming a normal diet. (1)

For similar reasons, the U_{Na} is also valuable in the assessment of a patient who has acute renal failure. Here, the differential diagnosis typically is between prerenal azotemia and intrinsic renal failure caused by acute tubular necrosis (ATN). If the failure is prerenal, the kidney retains sodium aggressively in response to hypovolemia and the U_{Na} is low. However, in patients who have ATN, the U_{Na} is greater than 40 mEq/L due to tubular damage that impairs maximal reabsorption of sodium. (1)

In most situations, only a single random or "spot" measurement of sodium is adequate to provide diagnostic information. However, because the concentration of sodium in the urine is dependent on the amount of free water in the urine, measuring a random U_{Na} alone can be misleading in cases of impaired renal concentrating ability or excess free water in the urine. Thus, it may be preferable to calculate the fractional excretion of sodium (FE_{Na}), which is calculated as

$$FE_{Na} = (U_{Na} \times \text{plasma creatinine} / \text{plasma } Na^+ \times \text{urine creatinine}) \times 100\%$$

By expressing the percentage of the filtered sodium that is excreted, the FE_{Na} provides a measure of the sodium handling that is independent of how dilute or concentrated the urine may be. Appropriate sodium conservation (as might be seen in prerenal azotemia) results in an FE_{Na} of less than 1%; patients who have ATN have FE_{Na} measurements greater than 2%.

The FE_{Na} must be interpreted slightly differently in infants, who have diminished ability to reabsorb sodium due to their immature tubules. Thus, in term neonates, the FE_{Na} is less than 3% in a volume-depleted state, (2) and in critically ill preterm infants, FE_{Na} less than 4% indicates maximal sodium retention. (3)

Calculating the FE_{Na} requires simultaneous measurement of blood and urine sodium and creatinine. In younger children who are unable to void on command, the most practical means of obtaining samples is to place a urine collection bag, then draw blood for chemistries immediately after the child voids.

Urine Potassium Concentration

The kidney has an extraordinary ability to vary potassium excretion, depending on dietary intake and the serum potassium concentration. The major value of the urine potassium concentration (U_K) is in cases of hypo- or hyperkalemia to determine whether the kidney is responding appropriately to these stimuli. Although spot measurements of U_K may be helpful, urinary potassium handling is assessed best by calculating the transtubular potassium gradient (TTKG).

$$TTKG = (U_K)/(\text{plasma } K^+) \times (\text{plasma osmolarity})/(\text{urine osmolarity})$$

For patients eating normal diets, the TTKG typically is 8 to 9. However, when hypokalemia occurs due to gastrointestinal losses or inadequate potassium intake, the kidney should

conserve potassium and the TTKG falls to less than 3. Higher values in the face of hypokalemia indicate renal potassium wasting. (4)

Conversely, in patients who develop hyperkalemia (especially chronic hyperkalemia), a TTKG less than 7 indicates defective potassium secretion because the appropriate renal response would be to maximize potassium excretion. Because potassium excretion depends on the presence of aldosterone and adequate fluid and solute delivery to the site of aldosterone activity in the distal tubule, this finding suggests hypoaldosteronism or renal failure. (5)

Urine Chloride Concentration

The major use of the urine chloride concentration (U_{Cl}) is in the evaluation of a metabolic alkalosis. Typically, sodium and chloride are reabsorbed together throughout the nephron. Accordingly, the U_{Na} and U_{Cl} are usually approximately equal. However, in some cases of metabolic alkalosis, the kidney's need to excrete bicarbonate may require sodium to be excreted with bicarbonate, making the U_{Cl} low (typically <20 mEq/L). This response occurs with vomiting or nasogastric suction or following hypercapnia. Classically, such situations were known as "saline-responsive" metabolic alkaloses because the administration of saline and repletion of chloride would correct the alkalosis.

Alternately, metabolic alkalosis can be caused by a primary inability to reabsorb chloride, forcing sodium to be reabsorbed with another anion such as bicarbonate. In such cases, which include genetic defects of chloride reabsorption such as Bartter or Gitelman syndromes as well as diuretic use or abuse, the U_{Cl} is elevated (>20 mEq/L). Here, the alkalosis is "saline-resistant," and administration of chloride will have minimal impact on the alkalosis because the administered chloride will be lost in the urine. (1) For more complicated reasons, profound hypokalemia also leads to impaired chloride transport and can cause metabolic alkalosis. (6)

Urine Anion Gap

The value of the urine anion gap (UAG) stems from the understanding that the total number of cations in the urine must necessarily equal the number of excreted anions. Calculating the UAG can provide information about urine composition without directly measuring every possible solute. The UAG is calculated by subtracting the commonly measured anions from the commonly measured cations in urine:

$$UAG = U_{Na} + U_K - U_{Cl}$$

Unlike the serum anion gap, which is always positive, the UAG can be positive or negative, depending on the presence of excess unmeasured cations or anions in the urine. Knowing that the gap is positive (indicating the presence of excess anions) or negative (indicating the presence of excess cations) is clinically sufficient and more important than the magnitude of the gap.

The UAG is most useful in the evaluation of a normal anion gap (hyperchloremic) metabolic acidosis. In this situation, the clinician must distinguish between gastrointestinal losses of bicarbonate (such as diarrhea) and renal tubular acidosis (RTA).

In metabolic acidosis, the appropriate renal response is to excrete acid to return the serum pH to normal. Thus, with diarrhea or other gastrointestinal losses of bicarbonate, the UAG is negative (Fig. 1), indicating the excess cations in the urine due to the excretion of protons, which are typically excreted as ammonium ion (NH_4^+).

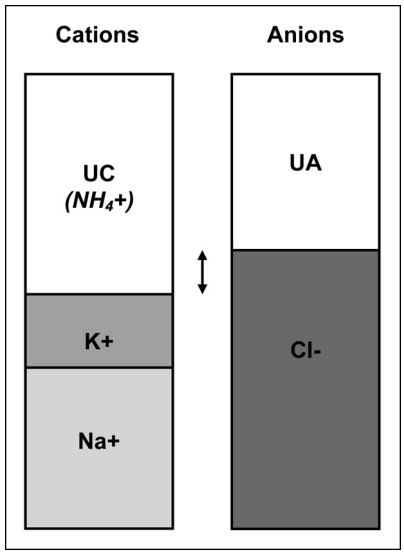

Figure 1. A graphic illustration of the principle underlying the urine anion gap. UC=unmeasured cations, UA=unmeasured anions. Because the total cationic charge must necessarily equal the total anionic charge, a change in the size of one "compartment" must be accompanied by a corresponding change in another compartment. In the situation depicted, the anion gap is negative because the number of unmeasured cations exceeds the number of unmeasured anions (the area indicated by the arrow). Because the major unmeasured cation is ammonium, this indicates an appropriate renal response to metabolic acidosis.

In contrast, the various RTAs are characterized as an impaired ability to excrete acid. The UAG, thus, is positive (Fig. 2), indicating an inability to secrete NH_4^+ and impaired renal response to acidosis. Further history and diagnostic testing are required to distinguish among the three types of RTA. (7)

Urine Urea Nitrogen

As described previously, measurement of the U_{Na} is an excellent indicator of a patient's volume status.

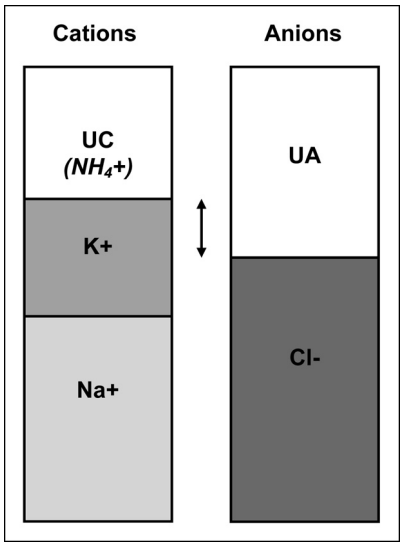

Figure 2. A graphic illustration of a positive urine anion gap, with the number of unmeasured cations exceeding the number of unmeasured anions. When this situation occurs in the context of metabolic acidosis, it is consistent with renal tubular acidosis, indicating an impaired ability to excrete protons in the urine as ammonium.

However, in cases of acute diuretic use, drug-induced natriuresis may make the measurement of the U_{Na} unreliable. In such cases, measurement of the urine urea nitrogen concentration (U_{urea}) and calculation of the fractional excretion of urea (FE_{urea}) (analogous to the calculation of the FE_{Na}) can provide similar information in the evaluation of acute renal failure.

In low-flow states, the kidney retains urea due to the need to reabsorb sodium maximally (leading to the out-of-proportion rise of blood urea nitrogen to serum creatinine that occurs in prerenal azotemia). Thus, if the kidney senses decreased effective circulating volume, the FE_{urea} is less than 35%; in cases of ATN, the FE_{urea} exceeds 50%. (8)

Conclusion

Urine electrolytes can be analyzed cheaply and quickly on standard laboratory equipment, and because there is no requirement that the urine be completely sterile, samples can be obtained painlessly, even from infants, by using a urine collection bag.

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