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New concepts for bringing urine biochemistry back to clinical practice in the intensive care unit

Novos conceitos trazendo de volta a bioquímica urinária à prática clínica na unidade de terapia intensiva

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INTRODUCTION

In the last few years, great attention has been given to the composition of the fluids that are administered to critically ill patients.[1,2] In particular, the amount of Na^+ and Cl^- is of paramount relevance because these two electrolytes are major determinants of the strong ion difference (SID) in the blood, which is the most important variable in the regulation of metabolic acid-base homeostasis, according to the quantitative physicochemical approach.[3,4] The concern about fluid electrolyte composition is justifiable because iatrogenic, low-SID acidosis may be the result of administration of high volumes of unbalanced solutions, such as normal saline.[2] In an attempt to minimize this problem, certain balanced solutions were developed, with the advantage of being more neutral in terms of acid-base equilibrium.[1]

It is known, however, that many other variables have a direct influence on the final concentrations of these electrolytes in the blood. One of these variables is certainly the concentrations of these same electrolytes in the urine, the main fluid responsible for the excretion of Na^+ and Cl^-.[5] Unfortunately, the attention given to urinary electrolyte composition in daily practice is far from ideal. The aim of this commentary is to present why we think that urine biochemistry evaluation must be part of daily practice in the intensive care unit (ICU).

Beyond fluid balance in acute kidney injury: focus on Na^+ and Cl^- overload

In an overly simplistic view, intensivists are usually worried about the amount of fluids given to their patients and concomitant fluid elimination, of which urine output is generally the most relevant for the fluid balance calculation. The rationale is that fluid balance is a synonym of volume balance. Volume overload is one of the major concerns in established acute kidney injury (AKI), and it seems to be of prognostic relevance.[6] However, fluid balance and its importance in AKI prognosis are matters not only of volume overload but also of Na^+ and Cl^- overload. If much attention is now being given to the electrolyte composition of the fluids that enter patients, why is the same attention not being given to the electrolyte composition of the fluids that leave patients? In practical terms, 2 liters of normal saline does not have the same physiological impact as 2 liters of lactated Ringer's solution or 5% dextrose. Hence, 2 liters of urine with high [Na^+] and [Cl^-] is not the same as 2 liters of urine with low concentrations of these electrolytes. We must not interpret these

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situations merely as 2 liters of fluids entering and leaving the patient. Equally important, the urinary SID is a major determinant of acid-base homeostasis,[5,7-9] so acid-base understanding and management must include both urine volume and urinary electrolyte composition.

Avid Na^+-retaining state: early and remaining sign of acute kidney injury

Daily assessment of urine biochemistry, even in spot samples, has led us to observe that urine output and urinary [Na^+] and [Cl^-] usually change in the same direction, decreasing together, at least in the early stages of AKI development. This phenomenon has already been experimentally demonstrated.[10] We recently suggested that AKI development is characterized by decreases in both urinary [Na^+] and [Cl^-], which may occur before significant decreases in urine output or increases in serum creatinine.[11] Persistent AKI, usually interpreted as structural AKI, is most often characterized by a persistent incapacity to excrete Na^+ and Cl^-. This incapacity is the result of a combination of low filtration and avid reabsorption (the old "pre-renal" AKI), which continue until the advanced stages of AKI.[11] Hence, patients with AKI have an early risk of Na^+ and Cl^- overload. Our group has also suggested that during AKI recovery, certain patients recover urine output well before Na^+ excretion recovery,[12] i.e., the urinary volume is adequate, but there is still a compromised natriuretic capacity. This phenomenon has led to the concept of "unbalanced urine", which occurs when the problem is not only in the total amount of diuresis but also in its electrolyte composition. A theoretically adequate urine output with low/decreasing [Na^+] and [Cl^-], especially in the context of fluid resuscitation (high Na^+ and Cl^- input), may be a sign of "unbalanced urine" and a certain degree of renal impairment. Natriuretic capacity seems to be related to the degree of a systemic inflammatory response.[10,12] We have also observed that the ability to excrete large concentrations of Na^+ in urine, defined here as concentrations above its equivalent in the blood, is a nearly exclusive characteristic of patients with normal or improving renal function.[13]

It is noteworthy that Na^+ and Cl^- overload is not always obvious based solely in their serum concentrations. Na^+ overload may be present with hypernatremia, hyponatremia or even normonatremia. Thus, urine must be evaluated in terms of not only quantity but also "quality" (composition),[14] in the same way that we evaluate the fluids that are being infused.

Diuretic treatment and natriuretic efficiency

Urinary electrolyte measurement also has great potential for the efficient monitoring of diuretic treatment. It is common practice to evaluate only the urinary volume after diuretic administration and the repercussions in serum electrolyte concentrations. There is a gap in this protocol, which relates to determining to what extent negative Na^+ and Cl^- balances are being reached, in addition to assessing negative volume balance. This information is very relevant when treating, for example, edema formation. An insufficient natriuretic response to diuretics may predict worsening renal function.[15]

In conclusion, AKI in the ICU is most often an avid Na^+- and Cl^--retaining state. Additional studies are necessary to optimize the information that we can obtain from urine, which may be very useful for proper AKI diagnosis and management. Na^+ and Cl^- overload may be as important as volume overload in AKI prognosis. A new focus on urine biochemistry will most likely make it again useful in daily ICU practice.

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