

COMMENTARY

Breaking old and new paradigms regarding urinary sodium in acute kidney injury diagnosis and management

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Abstract

Urinary sodium (NaU) is one of the oldest parameters used in the evaluation of azotemia and oliguria. Over the past years, however, it has progressively been considered as obsolete and useless, especially in sepsis. It is common sense that NaU frequently does not correlate well with global renal blood flow. If intra-renal microcirculatory changes are more important in acute kidney injury (AKI) than changes in global renal blood flow, we speculate that decreases in NaU may be viewed as a possible marker of microcirculatory impairment in the kidneys. Recent findings by our group (some not yet published) in which sodium retentive capacity is preserved until advanced stages of AKI and the observation of decreases in NaU preceding increases in creatinine bring us to conclude that the new paradigm of abolishing NaU consideration from daily approaches to managing patients at risk for AKI must be reevaluated.

Introduction

For decades, urinary sodium (NaU) was used to define the presence of structural damage to the kidneys in the setting of oliguria or azotemia [1,2]. The preserved capacity of the tubules to retain sodium was the physiological basis to interpret low levels of NaU as a functional response to a low renal perfusion state: so-called 'pre-renal' azotemia. The loss of this capacity by the kidneys was considered a marker of 'acute tubular necrosis' (ATN). In the past, levels of NaU below 20 mEq/L were considered markers of pre-renal impairment and above 40 mEq/L as markers of intrinsic renal disease [2].

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Recently, 'pre-renal' and 'ATN' paradigms have been frequently criticized [3,4]: first, because many cases classified as ATN lack this finding in histopathological studies [5]; and, second, because increasing knowledge of acute kidney injury (AKI) revealed a dissociation between renal hemodynamics and NaU, especially in sepsis [6]. Therefore, these old paradigms gave place to a new paradigm: that NaU is useless as a tool in AKI management [7]. The aim of this commentary is to question if this new paradigm should be sustained.

The emergence of the new paradigm

In 2006, a systematic review [8] revealed that NaU values were widely variable within and between studies with no consistent values to distinguish normal kidney function, pre-renal azotemia and ATN. A contemporaneous experimental study inducing hyperdynamic sepsis revealed progressively lower levels of NaU [6]. It was hypothesized that the sodium retentive state was due to loss of glomerular filtration pressure. In fact, progressive decreases in NaU were accompanied by decreases in creatinine clearance. The authors concluded that NaU was not a reliable marker of renal perfusion (breaking the old 'pre-renal' paradigm). Since then, a new paradigm has emerged: NaU must not be used as a diagnostic tool in AKI [7].

Reasons why the new paradigm is misleading

Dissociation between macrohemodynamics and microhemodynamics in sepsis is common. This phenomenon is the possible explanation for apparently paradoxical increases in the sublingual tissue partial pressure of carbon dioxide ($P_{sl}CO_2$; a marker of microcirculatory stagnation) in parallel with increasing cardiac output during sepsis [9]. Hence, a similar phenomenon could explain the paradox between an increased renal blood flow and low NaU levels. Glomerular perfusion pressure, not total renal blood flow, is the main determinant for NaU levels. In inflammatory states, low glomerular perfusion pressure may occur in the presence of increased renal blood flow, with activation of sodium-retaining

mechanisms. Although tubular injury is an early event in AKI [10], most studies still found low fractional excretion of sodium levels in this context [11,12]. We may conclude that too much injury is needed to impair the global tubular capacity to retain sodium. Recent unpublished results by our group also suggest that sodium retention is progressively more intense with increases in AKI severity except in very advanced stages (AKI Network stage 3); we hypothesize that extensive tubular injury jeopardized sodium reabsorption. In our findings, such progressive decreases in NaU began earlier than increases in creatinine, as described in a case report [13].

Reasons why many previous NaU studies are flawed

Most studies regarding NaU in AKI have three main limitations. First, NaU is measured only once instead of sequentially; as previously demonstrated [6,14], NaU responds fast to acute hemodynamic alterations so that relative alterations in it may be more relevant than an isolated NaU value. It is important to remember that NaU has a very large physiological range that depends on numerous variables. Of these, the most likely responsible for an abrupt decrease in NaU value is a decrease in glomerular filtration rate. Second, NaU is still treated as a categorical variable [15]; the dynamism of NaU is lost if NaU is viewed as '<20 mEq/L' or '>40 mEq/L'. This view is overly simplistic and unreliable. Third, NaU is usually assessed only in the presence of oliguria or azotemia. In a recent article [16], we suggested that urinary electrolyte measurement may alert for the presence of AKI development before increases in creatinine or oliguria. In that study, patients who developed AKI in the first 4 days after admittance to the ICU had significantly lower NaU values at admission.

Microcirculation: a possible bridge between renal blood flow and NaU

Low NaU values in AKI can be a sign of microcirculatory impairment in the kidneys. We have observed many critically ill patients with very low NaU levels on the day that renal replacement therapy was initiated. This is not surprising in the context of multiple organ failure, which may be caused by systemic microcirculatory failure. From this perspective, the lower the NaU, the greater the microcirculatory stress. On the other hand, high NaU values are more difficult to interpret. There is no well established normal range for NaU. In a study including 10 healthy volunteers, the mean NaU was 104 ± 48 mEq/L [17]. We have also found median NaU values above 100 mEq/L at ICU admission in patients who did not develop AKI during the study period [16]. However, high NaU values can be found in patients with AKI receiving diuretics or in advanced AKI stages.

Conclusion

As for many other monitoring parameters in critical care medicine, the first step in defining NaU utility in daily practice is to understand properly what it is saying to us and in which contexts. New paradigms regarding this subject should be carefully reevaluated.

Abbreviations

AKI, acute kidney injury; ATN, acute tubular necrosis; NaU, urinary sodium.

Competing interests

The author declares that he has no competing interests.

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Published: 4 February 2013

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doi:10.1186/cc11926

Cite this article as: Maciel AT: Breaking old and new paradigms regarding urinary sodium in acute kidney injury diagnosis and management. *Critical Care* 2013, **17**:115.