

Sequential Serum Phosphate and Urinary Biochemical Changes in Postoperative Systemic Inflammatory Response Syndrome: Potential Additional Diagnostic Tools in Acute Kidney Injury

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Abstract

Systemic inflammatory response syndrome (SIRS) is frequent after major surgery and may lead to multiple organ failure. Many classical parameters such as leukocytes and platelets count, lactate and c-reactive protein are measured sequentially during SIRS in order to quantify the severity of the inflammatory/metabolic stress. Blood urea nitrogen and creatinine are usually assessed to evaluate renal function since acute kidney injury (AKI) is a frequent complication of SIRS. The aim of this case report is to describe sequential serum phosphate and sodium and potassium measurement in urine in parallel with AKI development and recovery. The aim is to suggest that these parameters may help in AKI monitoring in the context of SIRS.

Keywords: Acute kidney injury; Critical illness; Surgery; Systemic inflammatory response syndrome; Urine biochemistry

Introduction

Surgical procedures are a well-known trigger of the Systemic Inflammatory Response Syndrome (SIRS), which may be a threat to normal homeostasis and lead to multiple organ failure. Severe SIRS is usually followed by Acute Kidney Injury (AKI), among other manifestations of organ dysfunction. AKI in the context of SIRS seems to be multifactorial and not merely a result of renal hypoperfusion and ischemia [1]. Most studies regarding urine biochemistry in SIRS were made experimentally, studies in septic animals [2-4]. It has been demonstrated that, during endotoxemia, AKI may develop in parallel with an increased renal blood flow [2,3]. In addition, sequential urinary sodium (NaU) assessment has shown that septic AKI is an avid-sodium retaining state [2]. A recent prospective study in humans [5] has also suggested that AKI development is marked by progressive decreases in NaU values and increases in serum phosphate. In the above mentioned studies [2,5], low NaU values in AKI were followed by low fractional excretion of sodium (FENa) meaning that tubular capacity to retain sodium was well preserved. Renal recovery is usually followed by increased concentrations of NaU [4,5] and its fractional excretion [4] as well as decreases in serum phosphate [5].

We hypothesize that this sodium-retaining state occurs similarly in other non-septic SIRS states, including surgical trauma. This case report is an illustrative representation of a postoperative SIRS with its wide range of manifestations, in which we emphasize the serum phosphate and the sequential urinary biochemical changes that occurs in AKI development and recovery and that may be useful as additional methods of AKI monitoring. Blood and urine samples were collected simultaneously at ICU admission (around 5 p.m.) and then once daily around 4 a.m. until ICU discharge.

Case Presentation

A 86 year-old man with past medical history of arterial hypertension was admitted in the Intensive Care Unit (ICU) in the immediate postoperative period after a total left hip replacement under rachyanesthesia due to traumatic fracture of the femur that had occurred two weeks before ICU admission. Exams two days before surgery (D-2) revealed no significant alterations except mild anemia

(11.3 g/dL) and marginal renal function (creatinine 1.25 mg/dL). The procedure had no complications or unusual bleeding reported. At admission (D0), the patient had a mean arterial pressure (MAP) around 60 mmHg but there were no signs of active bleeding in the surgical site. The patient had borderline body temperature (36°C) and normal respiratory and heart rates (recent use of beta-blockers for hypertension). Lab exams at ICU admission revealed leukocytosis with normal C-reactive Protein (CRP) (Figure 1A), an elevation of 0.3 mg/dL in serum creatinine (sCr), configuring AKI stage 1 by acute kidney injury network (AKIN) criteria [6] (Figure 1B) and hyperlactatemia (Figure 1C). At day 1, the patient remained with borderline MAP, not responsive to fluid challenge, hyperlactatemia has worsened (5.6 mEq/L) and norepinephrine infusion was started. Hemoglobin level was stable around 9 g/dL. Troponin and brain natriuretic peptide levels were normal. Bedside echocardiography revealed only mild myocardial dysfunction due to diffuse ventricular hypokinesis (ejection fraction 50%) and, physical examination did not reveal any possible source of infection. A urinary and a central venous catheter were inserted. Due to low central venous saturation and low urine output compatible with AKIN stage 2, dobutamine was administered at D2. At that time, hyperlactatemia had resolved, leukocytosis was decreasing but CRP was still increasing (Figure 1A). Platelets count was decreasing daily. Norepinephrine was stopped at D3 but persistent oliguria has led to furosemide administration (single dose of 20 mg in the entire ICU stay). Both blood Urea Nitrogen (BUN) and sCr had their peak value at D4; in parallel, leukocytosis had resolved and CRP level was consistently decreasing. In the next few days, we observed a progressive improvement in renal function, with daily decreases in sCr and adequate

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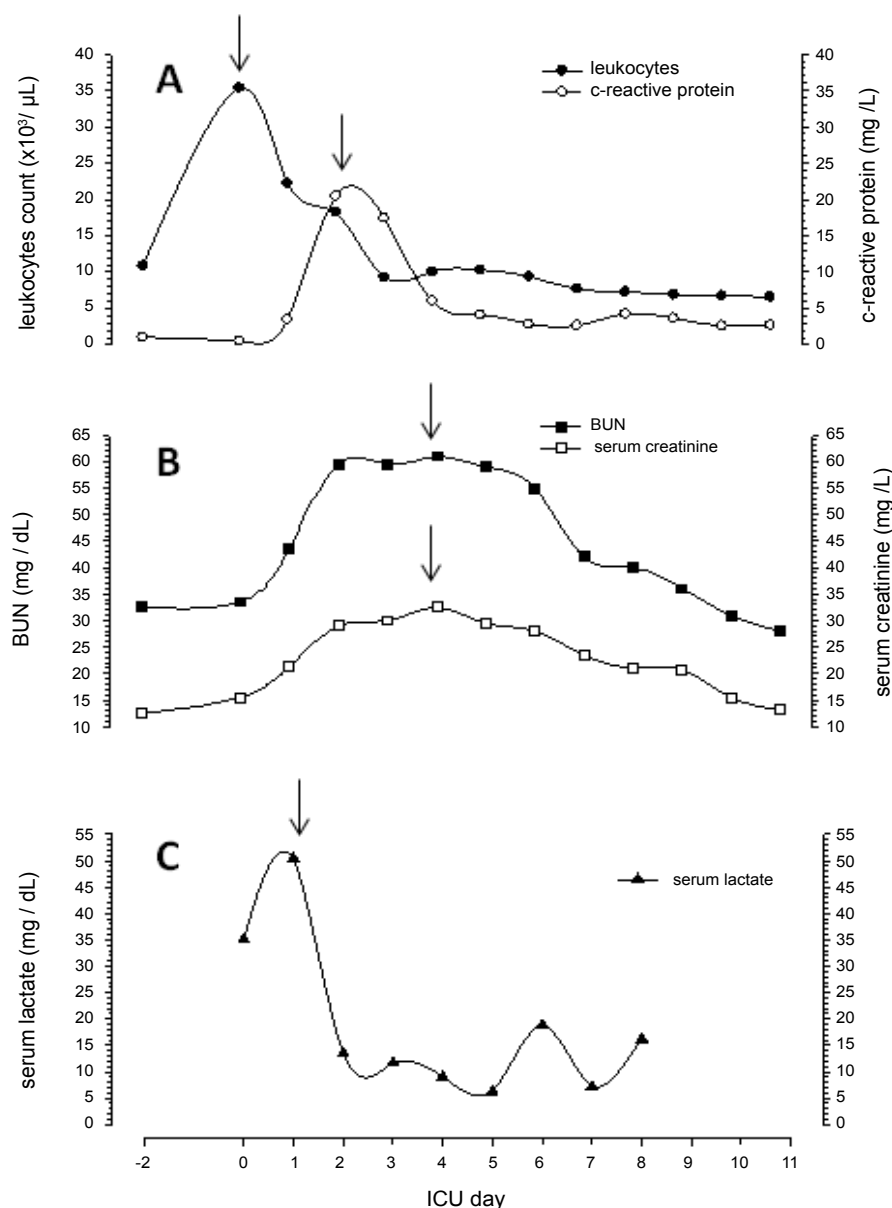


Figure 1: Temporal evolution of leukocytes and c-reactive protein (panel A), serum blood urea nitrogen and creatinine (panel B) and serum lactate (panel C) after being triggered by the systemic inflammatory response syndrome (SIRS) after surgery. The arrows indicate the day of the peak value of each one of these parameters. BUN: blood urea nitrogen ICU: intensive care unit.

urine output in the absence of diuretics. Platelet count decreased until D6 and then started to recover. At D6, dobutamine was stopped. At D8, both urinary and central venous catheters were removed. sCr returned to its baseline value at D11.

Discussion

In the case presented above, we have described the “up and down” and “down and up” behavior of many well-established parameters that we frequently monitor in SIRS. All the alterations in these parameters seemed to be triggered by the same stimulus - the surgical procedure. Infection, a common trigger of SIRS, was not found in this patient and he improved in the absence of antibiotics. It is noteworthy that each parameter had its own temporal behavior after being triggered and the

peak/ nadir of one of these parameters was eventually separated by days from the peak/nadir of the other parameters (Figure 1 and 2).

Revealing additional possible parameters to monitor in the AKI/ SIRS context

This case report also reveals some parameters that may behave in these similar “up and down” and “down and up” patterns but that we usually do not follow with the same attention. Hyperphosphatemia is considered one of the causes of metabolic acidosis in AKI [5,7]. Interestingly, the peak serum phosphate value occurred 3 days before the peak sCr value (Figure 2A). Decreases in serum phosphate might have signed for a renal recovery before decreases in sCr. In our previous study [5] increases and decreases in serum phosphate were simultaneous

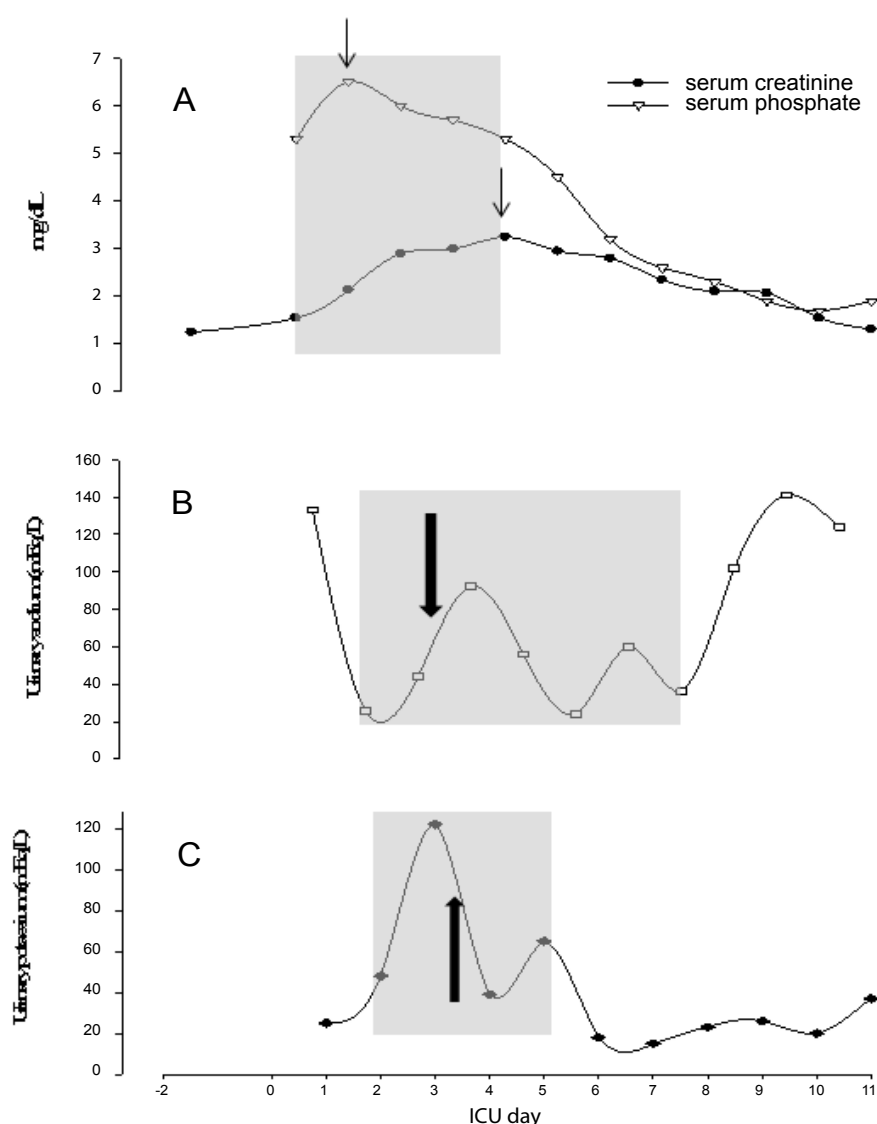


Figure 2: Temporal evolution of serum phosphate in comparison to serum creatinine (Panel A), urinary sodium and potassium (Panels B-C) in the development and recovery of acute kidney injury (AKI) due to systemic inflammatory response syndrome (SIRS) after surgery. Grey ranges correspond to the periods in which the parameters were changing due to AKI/SIRS. Small arrows in panel A indicate the peak values of serum creatinine and phosphate. Black arrows in panels B and C denote the period in which furosemide was administered.

with increases and decreases in sCr. Since this is a single case and we were not able to find additional previous literature specifically on this subject, these data only suggest that sCr and phosphate have similar behaviors in AKI and sequential serum phosphate measurement may be useful in AKI monitoring.

The behavior of some biochemical variables in urine also seems to be closely related to AKI/ SIRS development and recovery, as suggested by previous studies [2,4,5,8-11]. In the present case, NaU, as well as FENa and FEUr, had an abrupt decrease in the first 3 ICU days (Figure 2B and, Table 1), an “artificial” increase secondary to diuretic use at D4, and then a true NaU recovery occurred at D9. This avid sodium-retaining state in the first ICU days seems to be a characteristic of early AKI and SIRS. Urinary potassium (KU) had an opposite behavior in comparison to NaU, having an abrupt increase in AKI development, a decrease after diuretic use and a true recovery (fall) at D6 (Figure 2C).

In parallel, Fractional Excretion of K^+ (FEK) also had an “up and down” behavior (Table 1). This could be secondary to K^+ secretion in exchange to Na^+ reabsorption at the distal tubules. In fact, our group suggested in a recent article [10] that FEK may be a better monitoring tool in AKI than FENa and FEUr. Note that FENa and FEUr had oscillating values after the first three ICU days, making their values difficult to interpret. Other authors have also found only small fluctuations in FENa value in the course of AKI [12]. FEK values, on the other hand, had a better defined behavior, increasing significantly during AKI development and decreasing consistently in AKI recovery.

Significant increases in NaU and decreases in KU and FEK in the last ICU days are, in our view, part of the SIRS/AKI resolution process (diuretics absent). This could be a result of decreased activation of the sympathetic and renin-aldosterone systems, both of which are closely related to AKI development in critically ill patients [13].

| | D0 | D1 | D2 | D3 | D4 | D5 | D6 | D7 | D8 | D9 | D10 | D11 |
|----------------------------|------|------|------|------|------|------|------|------|------|------|------|------|
| pH | 7.33 | 7.33 | 7.38 | 7.39 | 7.35 | 7.38 | 7.36 | 7.38 | 7.35 | 7.36 | - | 7.37 |
| BE (mEq/L) | -1.9 | -4.5 | -2.5 | -2.6 | -3.2 | -3.1 | -2.7 | -0.4 | -1.5 | -2.1 | - | 0.7 |
| 24h urine output (ml/kg/h) | | 0.33 | 0.49 | 0.64 | 0.58 | 0.75 | 0.98 | 0.75 | 0.64 | 1.1 | 1.01 | - |
| Fluid balance (mL) | | 1436 | 288 | 1056 | 186 | -162 | -522 | -336 | -200 | -880 | -320 | - |
| FENa (%) | | 3.7 | 1.3 | 0.8 | 5.9 | 1.4 | 1.2 | 2.3 | 0.9 | 1.9 | 3.1 | 0.9 |
| FEUr (%) | | 45.4 | 37.1 | 25.1 | 47 | 51.2 | 49.2 | 58.2 | 44.6 | 53 | 48.2 | 34.9 |
| FEK (%) | | 19.1 | 71.2 | 70.1 | 82.1 | 55.9 | 31.1 | 20 | 19.3 | 15.3 | 14.6 | 9.4 |

BE: base excess; FENa, FEUr, FEK: fractional excretions of sodium, urea and potassium, respectively. D0: day of intensive care unit admission

Table 1: Temporal evolution of acid-base parameters, diuresis, fluid balance and fractional excretions of sodium, urea and potassium in the course of acute kidney injury development and recovery

Conclusion

AKI is a frequent complication of postoperative SIRS. Classical parameters monitored during SIRS have an “up and down” or a “down and up” behavior, which are not simultaneous among different parameters. Besides blood parameters, urinary parameters also follow this same behavior. We have previously reported the urinary biochemical changes that occur after cardiac surgery [11] and also in sepsis [8,9], according to AKI development and recovery.

We believe that sequential serum phosphate and urinary sodium and potassium have a role in postoperative AKI monitoring. The fact that they are easily assessed is an additional reason why they must be part of the diagnostic methods in AKI.

Conflict of interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

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