Letter

Serum uric acid, creatinine, and the assessment of antioxidant capacity in critical illness

Ivo Giovannini, Carlo Chiarla, Felice Giuliante, Federico Pallavicini, Maria Vellone, Francesco Ardito and Gennaro Nuzzo

Hepato-biliary Surgery Unit, Sub-intensive Care, and CNR-IASI Center for the Pathophysiology of Shock, Catholic University School of Medicine, Rome, Italy

Corresponding author: Ivo Giovannini, ivo.giovannini@rm.unicatt.it

Published: 4 September 2006

This article is online at http://ccforum.com/content/10/5/421

Critical Care 2006, 10:421 (doi:10.1186/cc5008)

© 2006 BioMed Central Ltd

See related research by Chuang et al., http://ccforum.com/content/10/1/R36

In their nice study on serum total antioxidant capacity (TAC) in sepsis [1] Chuang and coworkers have demonstrated an increase in TAC that was directly correlated to severity of illness and poor outcome, and to increasing levels of serum uric acid (UA). Although the increase in TAC might be interpreted as an extreme protective attempt against overwhelming inflammation, this must still be proved, as correctly commented on by the authors.

A critical point is that, although increasing UA enhances TAC, the pathophysiological relevance depends on the underlying mechanism, which may include detrimental factors, such as renal dysfunction. In this case the obvious concern is the organ dysfunction causing UA to increase, while the consequent increase in TAC should be considered coincidental.

To ease this interpretation one should at least examine the relationship between UA or TAC and plasma creatinine concentration (assuming that creatinine always accurately reflects renal function).

Simply excluding patients with plasma creatinine >3.0 mg/dl or on hemodialysis [1] may not be sufficient to rule out an impact of moderate changes in renal function on UA. We are mentioning this because, in an on-going study on changes in UA on more than 100 surgical patients with moderate to extreme illness, we found that 34% of the variability of UA was still controlled by creatinine concentration, even when excluding cases with creatinine >1.8: UA = 0.5 + 3.4(creatinine); r = 0.58, r² = 0.34, p < 0.001, n = 1,005 (means ± SD, ranges: UA = 3.6 ± 1.6 mg/dl, 0.2 to 9.2; creatinine = 0.9 ± 0.3 mg/dl, 0.3 to 1.8). Within this regression, septic patients showed a tendency for lower UA for any creatinine level, compared to nonseptics (p < 0.001).

Constructively, it would be interesting to know details of the relationship between UA or TAC and creatinine in the patients studied by Chuang and colleagues [1]. This might help to assess the impact of even moderate changes in renal function on TAC, or it may be an idea for future investigations. We would like to congratulate the authors once more for their nice study.

Authors’ response

Chia-Chang Chuang and Ming-Feng Chen

We agree that renal dysfunction will affect the association between serum TAC or UA and Acute Physiology and Chronic Health Evaluation (APACHE) II score. The correlation between serum TAC and APACHE II score showed a significant difference after excluding patients with a serum creatinine level >1.5 mg/dl (normal range 0.3 to 1.5 mg/dl; r = 0.518, p < 0.001, n = 43; Figure 1). However, the correlation between serum UA and APACHE II score showed no significant difference after excluding patients with a serum creatinine level >1.5 mg/dl (r = 0.224, p = 0.148, n = 43; Figure 2).

Some possible mechanisms for this should be considered. First, although serum UA had a major effect on TAC level,
Critical Care Vol 10 No 5 Giovannini et al.

some other measurable (for example, methyl-guanidine) and unmeasurable antioxidants were present in samples [2]. We believe that no single antioxidant can predict the outcome of a patient with severe sepsis. The integrated antioxidants (i.e. TAC), rather than serum UA alone, are more reliable at reflecting the whole spectrum of sepsis. Second, the kidney plays a major role in the excretion of urate [3] and some articles have described an association between renal dysfunction and serum total antioxidant status, and a stronger association between renal dysfunction and serum UA [4,5]. However, renal function is impaired during severe sepsis and it is very difficult to differentiate whether serum UA correlates with APACHE II score or not.

In our preliminary data, serum creatinine levels correlated with either UA levels ($r = 0.424, p = 0.005, n = 43$) or TAC levels ($r = 0.481, p = 0.001, n = 43$) on the first day in the emergency department in septic patients who have preserved their renal function (serum creatinine <1.5 mg/dl). Therefore, we could only conclude that serum UA was not significantly related to APACHE II score in septic patients who preserved their renal function (creatinine <1.5 mg/dl). Whether serum UA can reflect the outcome of septic patients with or without renal dysfunction is undetermined.

Finally, as we suggested in the Discussion, the increased serum UA or TAC in patients with severe sepsis or septic shock could not be a consequence of renal failure (creatinine >3.0 mg/dl) and whether hyperuricemia is a risk factor for severe sepsis is unknown. More studies are needed to establish the association between UA and clinical severity in severe sepsis.

Competing interests
The authors declare that they have no competing interests.

References
1. Chuang CC, Shiesh SC, Chi CH, Tu YF, Hor LI, Shieh CC, Chen MF: Serum total antioxidant capacity reflects severity of illness in patients with severe sepsis. Crit Care 2006, 10:R36.
2. Ghiselli A, Serafini M, Natella F, Scaccini C: Total antioxidant capacity as a tool to assess redox status: critical view and experimental data. Free Rad Biol Med 2000, 29:1106-1114.
3. Becker BF: Towards the physiological functions of uric acid. Free Rad Biol Med 1993, 14:815-831.
4. MacKinnon KL, Molnar Z, Lowe D, Watson ID, Shearer E: Measures of total free radical activity in critically ill patients. Clin Biochem 1999, 32:263-268.
5. Jackson P, Loughrey CM, Lightbody JH, Manane PT, Young IS: Effect of haemodialysis on the total antioxidant capacity and serum antioxidants in patients with chronic renal failure. Clin Chem 1995, 41:1135-1138.