Marano et al. Critical Care (2015) 19:177
DOI 10.1186/s13054-015-0746-7

CRITICAL CARE

LETTER Open Access

Relationship between reduced albumin and inflammation in the critically ill

Marco Marano

See related research by Zampieri et al. http://ccforum.com/content/18/4/r154

I read the interesting article by Zampieri and colleagues [1] reporting the new association between inflammatory cytokines and acid-base components in 87 ICU patients. I would like to note that whatever approach is used to investigate the acid-base status (the celebrated bicarbonate-centered approach, the base excess methodology or the physicochemical approach) most of the acid-base parameters have values within or slightly beyond the normal range [2,3]. Specifically, this is true for the pH, the pCO_2 and the HCO_3 values as well as for the standard base excess (SBE) value. As regards the physicochemical approach used by the authors, the independent variables determining the pH value show only a marginal distance, if any, from their reference value [2]. Notably, the SIDa (apparent strong ion difference) value is perfectly normal. The SIG (strong ion gap) value is above the upper normal threshold, but it should be remarked that such excess may be due, to a large extent, to the low amount of albumin (because the albumin value is one of the relevant parameters used to compute the effective strong ion difference and hence the SIG value). Therefore, the only acid-base parameter that the authors actually found to be abnormal is the albumin one. Since albumin is accepted as a basic element only in the physicochemical approach, and this approach is not unanimously adopted, the title of the article might be misleading. Concluding, it is my opinion that the innovative findings by Zampieri and colleagues should be more properly depicted as a relationship between reduced albumin and inflammation. My argument does not affect the validity of their findings and I agree with the authors that they could open a new field of research.

Authors' response

Fernando G Zampieri and John A Kellum

We would like to thank Dr Marano for his interest in our manuscript. While we agree that the main finding in our manuscript was the potential modulation of the inflammatory response by albumin, we do not believe that our other conclusions regarding the remaining components of the acid-base status should be diminished. We think so for two reasons.

First, the normal mean values of many acid-base components found in our study do not necessarily imply that all patients had close to normal values for SIG, SIDa or SBE. In fact, they were pretty abnormal. Regarding SIG, 29 patients had SIG values higher than 10 mEq/L, which cannot be accounted for only due to low albumin [4]. The range of SIDa was 24.1 to 52.1 mEq/L (Figure 1), with a quarter of the included patients presenting with values below 37 mEq/L.

Second, as shown in Additional file 1 of our paper, relationships were complex in nature and nonlinear. In fact, as shown in multi-adaptive analysis plots, albumin reduction *per se* was not always associated with inflammation (for example, no association was seen between low albumin and high MCP1 when SIG was low). In principal component analysis, albumin was part of both principal component 1 and 2, suggesting that it modulated the association but not necessarily was an independent factor. Thus, while we agree that albumin is important, and that our results support further research involving albumin, other acid-base variables were also important contributors to the overall findings of our study.

Correspondence: marano965@gmail.com
Hemodialysis Unit, Maria Rosaria Clinic, via Colle San Bartolomeo, 50, Pompeii 80045, Italy

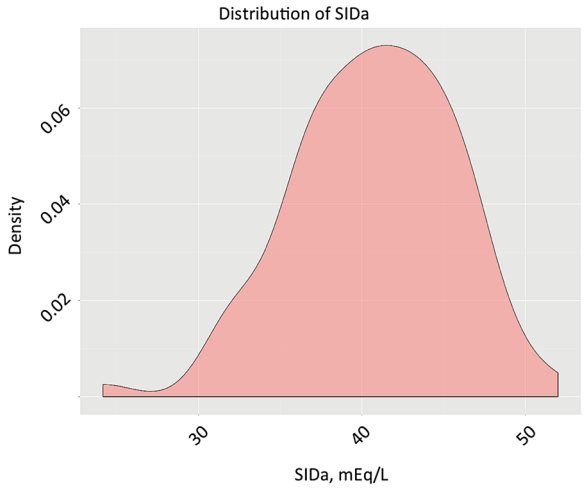

Figure 1 Density plot for SIDa (apparent strong ion difference) values.

Abbreviations
SBE: Standard base excess; SIDa: apparent strong ion difference; SIG: Strong ion gap.

Competing interests
The author declares that he has no competing interests.

Published online: 17 April 2015

References

1. Zampieri FG, Kellum JA, Park M, Ranzani OT, Barbeiro HV, de Souza HP, et al. Relationship between acid-base status and inflammation in the critically ill. Crit Care. 2014;18:R154.
2. Lindinger MI, Heigenhauser GJF. Effects of gas exchange on acid-base balance. Compr Physiol. 2012;2:2203–54.
3. Kellum JA. Clinical review: Reunification of acid-base physiology. Crit Care. 2005;9:500–7.
4. Gómez JL, Gunnerson KJ, Song M, Li J, Kellum JA. Effects of hypercapnia on BP in hypoalbuminemic and Nagase analbuminemic rats. Chest. 2007;131:1295–300.