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CORRESPONDENCE

Venous and arterial base excess difference: methodological error or physiological reality?

Luciano Gattinoni* and Mattia Busana

Dear Editor,

We thank Ziegenfuß and Zander for their interesting comments [1]. In our paper, we just acknowledged that all the blood gas analyzers implement algorithms which provide venous base excess values greater than the arterial ones, both in the whole blood and extracellular fluid (with the exception of GEM 4000 and 5000, Instrumentation Laboratory, which may implement, as an option, the Zander equation [2]). The more positive venous base excess is easily understandable looking at the NCCLS formula for extracellular base excess implemented in most blood gas analyzers:

$$\begin{aligned} \text{BE (mmol/L)} &= \text{HCO}_3^- \text{(mmol/L)} \\ &- 24.8 + 16.2(\text{mmol/L}) * (\text{pH} - 7.4) \end{aligned} \quad (1)$$

where HCO_3^- is the measured arterial bicarbonate, 24.8 mmol/L is the "ideal" arterial bicarbonate and pH 7.4 is the "ideal" arterial pH at PCO_2 40 mmHg. If in a healthy subject the measured arterial HCO_3^- is 24.8 mmol/L and the measured pH is 7.4 the base excess will be equal to 0 (see Eq. 1). However, if the blood of this healthy subject is drawn from a central venous catheter, due to the higher PCO_2, the HCO_3^- will be higher, e.g. 26.5 mmol/L, and pH will be lower, e.g. 7.36. In this case, the computed venous excess will be 1.05 mmol/L (see Eq. 1). However, if the base excess was computed inserting in Eq. 1 the ideal venous HCO_3^- and pH (e.g. 26.5 mmol/L and 7.36) its value will be zero as in the arterial side. Therefore, ideally, the arterial base excess should be computed referring to the "ideal" arterial values while the venous base excess referring to the "ideal" venous values.

*Correspondence: gattinoniluciano@gmail.com
Department of Anesthesiology, Emergency Medicine and Critical Care, University of Göttingen, Göttingen, Germany

The equations to compute the base excess (including the Zander's one [2]) derive from re-elaborations of Van Slyke's equation [3] and Siggaard-Andersen original data [4]. The coefficients used in the equations are computed according to several assumptions, such as (1) an "ideal" reference hemoglobin of 21 mmol/L in erythrocyte fluid, (2) 70 g proteins per liter of plasma, (3) a fixed ratio between HCO_3^- in erythrocyte fluid and in plasma, and (4) a fixed ratio between the blood volume and the extracellular volume. All these conditions are rarely met in critically ill patients. Despite these limitations, the equations proposed by Zander are the most adequate available today (Table 1).

Nonetheless, the physiological reasons for a more positive venous base excess in the whole blood do exist, and they have nothing to do with a misleading fixed acid generation from the lung, as provocatively stated by Dr. Ziegenfuß and Zander in their commentary. Base excess, according to Stewart's model [5], is equal to the deviation of the strong ion difference (SID) from the ideal: the SID, however, is actually different between venous and arterial sides due to the ion exchange between erythrocytes and plasma (Hamburger's effect) [6]. Indeed, the transition from the arterial to the venous side is characterized by a conformational change of hemoglobin which makes it more likely to bind H^+ and Cl^-. A net Cl^- shift from plasma to erythrocytes occurs, leading to an increase of extracellular SID and positive base excess in the venous side. The opposite occurs transitioning from the venous to the arterial side. SID differences have been documented across the membrane lung [7] and are particularly evident during minimally invasive CO_2 removal, where the PCO_2, pH and SID differences are extremely elevated [8]. Whether in these conditions the base excess can be correctly computed with standard equations is questionable and needs to be further elucidated. Nevertheless, the base excess remains a quick and effective tool

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Table 1 Summary of the currently available equations used to calculate the base excess, for the extracellular fluid and for the whole blood. PCO_2 is the partial pressure of carbon dioxide in mmHg, Hb the hemoglobin in g/dl and SO_2 is the oxygen saturation of the hemoglobin

		Plasma/blood redistribution coefficient	× Carbonic component	+ Non carbonic component	− Saturation correction
Zander	**BE(B)**	$(1 - 0{,}014 \cdot Hb)$	$0{,}0304 \cdot pCO_2 \cdot 10^{pH-6{,}1} - 24{,}26$	$(9{,}5 + 1{,}63 \cdot Hb) \cdot (pH - 7{,}4)$	$0{,}2 \cdot Hb \cdot (\frac{100 - SO_2}{100})$
	BE(ECF)	$(1 - 0{,}014 \cdot \frac{Hb}{3})$	$0{,}0304 \cdot pCO_2 \cdot 10^{pH-6{,}1} - 24{,}26$	$(9{,}5 + 1{,}63 \cdot \frac{Hb}{3}) \cdot (pH - 7{,}4)$	$0{,}2 \cdot \frac{Hb}{3} \cdot (\frac{100 - SO_2}{100})$
Siggaard Andersen	**BE(B)**	$(1 - 0{,}014 \cdot Hb)$	$0{,}0304 \cdot pCO_2 \cdot 10^{pH-6{,}1} - 24{,}8$	$(7{,}7 + 1{,}43 \cdot Hb) \cdot (pH - 7{,}4)$	
	BE(ECF)	$(1 - 0{,}014 \cdot \frac{Hb}{3})$	$0{,}0304 \cdot pCO_2 \cdot 10^{pH-6{,}1} - 24{,}8$	$(7{,}7 + 1{,}43 \cdot \frac{Hb}{3}) \cdot (pH - 7{,}4)$	
Van Slyke	**BE(ECF)**		$0{,}0304 \cdot pCO_2 \cdot 10^{pH-6{,}1} - 24{,}8$	$16{,}2 \cdot (pH - 7{,}4)$	

to understand at the bedside the acid–base disturbances of a critically ill patient [9].

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