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Negative alactic base excess is reversed by hemoperfusion in septic patients

Carlos Guido Musso[1,2], Juan P. Cordoba[3], Gustavo Aroca-Martinez[1,3,4], Sergio Terrasa[2], Adriana P. Barriga-Moreno[5], Marcela Lozano-Sanchez[5], Rafael A. Barón-Alvarez[5], Henry Gonzalez-Torres[1], Joaquin Cantos[6], Iván Huespe[6]

[1]Facultad de Ciencias de la Salud, Universidad Simón Bolivar, Barranquilla - Colombia
[2]Research Department, Hospital Italiano de Buenos Aires, Buenos Aires - Argentina
[3]Clínica de la Costa, Barranquilla - Colombia
[4]Universidad del Norte, Barranquilla - Colombia
[5]Critical Care Division, Clínica de la Mujer, Bogotá - Colombia
[6]Critical Care Division, Hospital Italiano de Buenos Aires, Buenos Aires - Argentina

Abstract

Introduction: Gattinoni et al. have recently introduced a new parameter: the "alactic base excess" (ABE). ABE is equivalent to the number of strong acids, other than lactate, which are present in the plasma in abnormal concentrations, negative ABE being associated with higher mortality in sepsis. Hemoperfusion (HPF) is an extracorporeal procedure that involves the passage of blood through an adsorption cartridge, where solutes are removed by direct binding to the sorbent material. Then, it was decided to explore the influence of HPF on negative ABE value in sepsis.

Materials and methods: Basal values of ABE, standard base excess (SBE), and lactate (mean, standard deviation [SD]) were obtained. The difference between these parameter values before and after four sessions of HPF (HA330) (delta value) was evaluated. Student's t-test and Wilcoxon test were applied.

Results: From 32 patients (age: 57±13) suffering from respiratory insufficiency secondary to COVID-19 who were treated with HPF in the critical care unit of Clinica de la Mujer, Bogotá (Colombia), 6 patients presented with metabolic acidosis with negative ABE value (–2.7±1) with negative SBE (–4.7±1) and high lactate serum value (2±0.7 mmol/L). Delta ABE, SBE, and lactate were: 7.7 ($p = 0.005$), 6.1 ($p = 0.003$), and 1.6 (p = NS), respectively. Thus, negative ABE was significantly reversed by HPF, since SBE value turned positive without significant change in lactate.

Conclusion: Negative alactic parameter was significantly reversed by HPF in septic patients. It is necessary to carry out evaluations in larger groups to estimate their impact on clinical outcomes.

Keywords: Alactic base excess, Hemoperfusion, Sepsis

Introduction

Gattinoni et al. have recently introduced a new internal milieu parameter: the "alactic base excess" (ABE), whose theoretical conception has been formulated according to Stewart's physicochemical approach, conceiving lactate as a strong negative ion that always produces acidemia *per se* by reducing the strong ion difference (SID), as long as there are no compensatory mechanisms (1).

The ABE parameter is obtained by applying the following equation:

ABE (mmol/L) = standard base excess (SBE, mmol/L) + lactate (mmol/L)

SBE (mmol/L) = (bicarbonate [mmol/L] – 24.8 [mmol/L]) + 16.2 mmol/L × (pH – 7.4)

ABE parameter is calculated by using SBE instead of measured base excess since the former has a better approach to extracellular fluid status than the latter (1). ABE is equivalent to the number of strong acids, other than lactate, which are present in the plasma in abnormal concentrations and it is strongly related to kidney function. Consistently, as renal

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Corresponding author:
Carlos Guido Musso
Research Department, Hospital Italiano de Buenos Aires
Perón 4190
Buenos Aires, Buenos Aires, C1199ABB - Argentina
carlos.musso@hospitalitaliano.org.ar

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function deteriorates, the concentration of these acids increases in plasma, represented by more negative values of ABE. This clinical scenario has been documented as associated with higher mortality in septic patients (1,2). Among currently available extracorporeal therapies for solute removal, hemoperfusion (HPF) is the procedure that involves the passage of blood (or plasma) through an adsorption cartridge, where solutes are removed by direct binding to the sorbent material (3,4).

An important advantage of HPF with respect to other extracorporeal blood purification techniques (e.g., high-volume hemofiltration, etc.) is that HPF minimizes unwanted molecule loss, such as nutrients or antibiotics (5). Thus, it was decided to explore the influence of HPF on negative ABE value in sepsis.

Materials and methods

In a group of patients who were submitted to four consecutive sessions of HPF (HA330; Jafron® – Colombian Medicare) procedure because they were suffering from a cytokine storm secondary to SARS-CoV2 pneumonia, ABE, SBE, and lactate values from arterial blood samples were obtained before and after the complete HPF treatment. From the above-mentioned parameters, mean, standard deviation, and differences between their pre-HPF and post-HPF values (delta value) were obtained. Student's t-test and Wilcoxon test were applied for data analyses. Informed consent was obtained from all patients included in the study and this study was approved by the Ethics Committee of the Clínica de la Mujer, Bogotá (Colombia).

Results

From 32 patients (age: 57±13 years, male 69%) suffering from respiratory insufficiency secondary to COVID-19 who were treated with HPF (HA330) in the critical care unit of Clinica de la Mujer, Bogotá (Colombia), 6 presented with metabolic acidosis (pH: 7.37±0.1, pCO_2: 36±14 mm Hg, bicarbonate: 20.5±3 mmol/L) with negative ABE value (–2.7±1) with negative SBE (–4.7±1) and high lactate serum value (2±0.7 mmol/L) before HPF treatment. Differences between ABE, SBE, and lactate value pre-HPF and post-HPF (delta value) were obtained. A significant difference in delta value of ABE: 7.7 ($p = 0.005$) and SBE: 6.1 ($p = 0.003$) parameters was documented, while there was no significant difference in delta lactate: 1.6 (p = NS) in this group.

Discussion

ABE is a novel parameter proposed by Gattinoni et al. in order to easily discriminate the presence of metabolic acidosis due to an excess of unmeasured strong acids different from lactate in septic patients (1), depending on the renal capability to compensate this disturbance. The importance of ABE negative value detection is based on the fact that it has been shown to be significantly associated with increased mortality in this population (1,3).

These unmeasured serum acids could be of renal origin, such as hippurate, sulfates, phosphates, or uremic toxins, which progressively accumulate in the presence of renal dysfunction (glomerular or tubular). In addition, they could be represented by Krebs cycle intermediate products, such as citrate, isocitrate, ketoglutarate, succinate, and malate, which could be increased in critically ill patients (1,6).

HPF is an extracorporeal technique developed to adsorb middleweight molecules: 5-60 kDa solutes, depending on the sort of cartridge used. HPF cartridges usually have a much higher weight cutoff than conventional high-flux hemodiafilters (4,7,8).

HPF cartridge contains biocompatible neutral macroporous adsorption resin made of coated polystyrene, which is capable of removing circulating solutes. Apart from its biocompatibility, other advantages of HPF are its lower risk of removal of nutrients and drugs (e.g., antibiotics) and its lower relative cost compared to other extracorporeal middle molecule-removing therapies, such as hemofiltration (8). HPF is highly effective in purifying blood from a number of endogenous (uremic) toxins or exogenous toxins (drug intoxication) and inflammatory cytokines (septic or non-septic inflammation) (4,9,10).

In this study, it was documented that a complete HPF treatment (four consecutive sessions), which was performed using HA330 cartridge, induced a significant reversion of negative ABE value, but not of serum lactate. This finding could signify that HPF (HA330) can significantly remove unmeasured acid serum excess but not lactate. However, perhaps the small number of studied patients could not allow detecting a significant lactate removal due to this procedure. It is worth mentioning that it has been hypothesized that HPF anti-inflammatory effect could be due to not only its solute adsorptive property but also its immunomodulatory effect, which could also be responsible for the observed unmeasured acid excess reduction (ABE value turned positive).

Future studies should be able to determine not only the substances that constitute this group of unmeasured acids, but also to evaluate if their removal by HPF contributes to reducing the mortality associated with them.

Conclusion

Negative alactic base excess was significantly reversed by HPF in septic patients. It is necessary to carry out evaluations in larger groups to estimate their impact on clinical outcomes.

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Disclosures

Conflict of interest: Juan P. Cordoba, MD has served as external scientific consultant for Colombian Medicare, which is the Jafron representative in Colombia, and he has received honoraria for his services; Adriana Barriga, MD has been speaker for Colombian Medicare. GCM, GA-M, ST, ML-S, RAB-A, HG-T, JC, IH declare no conflict of interest.

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Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all the participants included in the study.

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