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Mechanical Ventilation

Electrolyte shifts across the artificial lung in patients on extracorporeal membrane oxygenation: Interdependence between partial pressure of carbon dioxide and strong ion difference ☆,☆☆,★

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ABSTRACT

Purpose: Partial pressure of carbon dioxide (Pco_2), strong ion difference (SID), and total amount of weak acids independently regulate pH. When blood passes through an extracorporeal membrane lung, Pco_2 decreases. Furthermore, changes in electrolytes, potentially affecting SID, were reported. We analyzed these phenomena according to Stewart's approach.

Methods: Couples of measurements of blood entering (venous) and leaving (arterial) the extracorporeal membrane lung were analyzed in 20 patients. Changes in SID, Pco_2, and pH were computed and pH variations in the absence of measured SID variations calculated.

Results: Passing from venous to arterial blood, Pco_2 was reduced (46.5 ± 7.7 vs 34.8 ± 7.4 mm Hg, $P < .001$), and hemoglobin saturation increased (78 ± 8 vs 100% ± 2%, $P < .001$). Chloride increased, and sodium decreased causing a reduction in SID (38.7 ± 5.0 vs 36.4 ± 5.1 mEq/L, $P < .001$). Analysis of quartiles of ΔPco_2 revealed progressive increases in chloride ($P < .001$), reductions in sodium ($P < .001$), and decreases in SID ($P < .001$), at constant hemoglobin saturation variation ($P = .12$). Actual pH variation was lower than pH variations in the absence of measured SID variations (0.09 ± 0.03 vs 0.12 ± 0.04, $P < .001$).

Conclusions: When Pco_2 is reduced and oxygen added, several changes in electrolytes occur. These changes cause a Pco_2-dependent SID reduction that, by acidifying plasma, limits pH correction caused by carbon dioxide removal. In this particular setting, Pco_2 and SID are interdependent.

1. Introduction

Venovenous extracorporeal membrane oxygenation (ECMO), also known as "extracorporeal gas exchange," is a temporary support of the failing respiratory system [1,2] that is increasingly used as an adjunct to mechanical ventilation in patients who cannot be safely treated with mechanical ventilation alone [3,4]. Moreover, ECMO is increasingly used as a first-line treatment, that is, as an alternative to mechanical ventilation in patients bridged to lung transplantation [5], patients with exacerbation of chronic obstructive pulmonary disease (COPD) [6,7], and patients with acute respiratory distress syndrome (ARDS) [8,9]. During ECMO, a fraction of the patient's venous blood is drained from a catheter placed in a large vein, pumped through a membrane lung, and delivered back into the patient's venous system. The membrane lung is ventilated with varying amounts of oxygen mixtures (sweep gas flow [GF]), and gas exchange—oxygenation and carbon dioxide removal—takes place at the interface between blood and membrane fibers, similarly to the alveolar-capillary membrane of natural lungs.

When considering Stewart's approach to acid-base and electrolyte equilibrium [10,11], 1 of the 3 independent variables, the partial pressure of carbon dioxide (Pco_2), is acutely reduced when the blood passing through the membrane lung is ventilated, causing a reduction in plasma bicarbonate ion concentration (Hco_3^-) and an increase in plasma pH. Furthermore, although the total amount of weak acids (A_{TOT}) is expected to remain unchanged, electrolyte variations caused by changes in Pco_2 and hemoglobin (Hb) saturation have been described in vitro [12] and in experimental models [13,14]. These electrolyte variations can potentially lead to variations in plasma SID therefore affecting plasma pH and the final effect of ECMO in correcting arterial pH.

☆ Competing interests: The authors declare that they have no conflict of interest regarding the present study.

☆☆ Authors' contribution: TL and LG conceived the study; TL and MC contributed to data acquisition; TL, ES, EC, and LZ performed data analysis; TL, ES, and EC drafted the manuscript; AP, MC, PC, and LG critically revised the manuscript for important intellectual content; all authors read and approved the final version of the manuscript.

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The aim of the present study was to describe, in a cohort of critically ill patients with respiratory failure supported with ECMO, the variations in electrolytes and therefore SID occurring across the membrane lung as a consequence of extracorporeal gas exchange. In particular, we aimed to (i) describe accurately the electrolyte changes occurring across the membrane lung and (ii) investigate the possible impact of these electrolyte variations on plasma pH according to Stewart's quantitative approach to acid-base and electrolyte equilibrium.

Some of the results of the present study have been previously reported in the form of abstracts [15,16].

2. Materials and methods

This is a retrospective analysis of clinical data routinely collected in our intensive care unit. The study was approved by the institutional review board of our hospital; informed consent was waived because of the retrospective nature of the study.

All patients admitted to the general intensive care unit "Emma Vecla" of the Fondazione IRCCS Ca' Granda–Ospedale Maggiore Policlinico, Milan, Italy, between January 2010 and June 2011 requiring ECMO support were enrolled in the study.

Couples of measurements of blood gases and electrolytes (ABL 800 Flex; Radiometer GmbH, Willich, Germany) performed simultaneously, for clinical purposes, before (prelung, venous) and after (postlung, arterial) the membrane lung (Maquet Cardiopulmonary AG, Rastatt, Germany) were recorded. Moreover, settings of blood flow (BF) and sweep GF at the moment of sample drawing were recorded.

2.1. Definitions and calculations

Strong ion difference was calculated as reported in Eq. (1).

$$\left[SID\right] = \left[Na^{+}\right] + \left[K^{+}\right] + 2 \times \left[Ca^{2+}\right] - \left[Cl^{-}\right] - \left[Lac^{-}\right] \quad (1)$$

where Na^{+}, K^{+}, Ca^{2+}, Cl^{-} and Lac^{-} refer to plasma sodium, potassium, ionized calcium, chloride and lactate concentrations, respectively. All values are expressed as millimolar.

Theoretical postlung pH was calculated (MATLAB R2008a; The Math Works, Inc, Natick, MA) using premembrane lung acid-base values and the actual variation in P_{CO_2} as previously reported [17] (see also the electronic supplementary material for more details).

Actual and theoretical pH variations (ΔpH_A and ΔpH_T) induced by the passage of blood through the ventilated membrane lung were defined as follows:

$$\Delta pH_A = pH_{POST} - pH_{PRE} \quad (3)$$

$$\Delta pH_T = theoretical\ \ pH_{POST} - pH_{PRE} \quad (4)$$

Variations in other measured variables were defined similarly:

$$\Delta X = X_{POST} - X_{PRE} \quad (5)$$

where ΔX denotes the variation in any measured variable (X); footnotes POST and PRE denote blood exiting and entering the membrane lung, respectively.

2.2. Statistical analysis

Data are reported as mean ± SD unless otherwise stated. A paired *t* test or the Wilcoxon signed rank test was used, as appropriate, to compare prelung and postlung values. Moreover, data were divided into quartiles of P_{CO_2} variations (ΔP_{CO_2}), and the mean values of the resulting 4 groups were tested for statistical difference via one-way analysis of variance (ANOVA) or the Kruskal-Wallis test, as appropriate. Tukey or Dunn test was used for post hoc multiple comparisons.

The correlation between ΔP_{CO_2} and ΔpH_A and between ΔP_{CO_2} and ΔpH_T was assessed via linear regression analysis. Slopes of the resulting regressions were compared using the test for equality of slopes. Statistical significance was defined as $P < .05$. Analysis was performed with SAS v.9.2. (SAS, Cary, NC) and SigmaPlot v.12.0 (Systat Software Inc, San Jose, CA).

3. Results

Twenty patients were supported with ECMO during the study period. A total of 403 premembrane and postmembrane lung sample couples were collected (806 blood gas analyses), with a median number of 29 (interquartile range, 15-63) sample couples per patient.

Table 1 summarizes the most relevant demographic and clinical characteristics of the study population.

3.1. Prelung and postlung blood gases and electrolytes

Prelung and postlung values of blood gases and electrolytes are reported in Table 2. A significant reduction in P_{CO_2} associated with a consequent increase in pH and a reduction in HCO_3^- concentration was observed in postlung samples. Saturation of Hb increased significantly in blood passing through the membrane lung. Plasma concentration of chloride increased ($P < .001$), and concentration of sodium decreased ($P < .001$), causing a significant reduction in SID ($P < .001$) in postlung values. Moreover, a simultaneous variation of other electrolytes was observed: slight, although significant increase of lactate and minimal, although significant decrease for other cations (potassium and ionized calcium).

3.2. Analysis in quartiles of P_{CO_2} variation

To analyze the effects of different ΔP_{CO_2} on plasma acid-base variables and electrolyte concentrations, data were divided into quartiles of ΔP_{CO_2}. As variations in Hb saturation were similar in the different quartiles, this allowed us to normalize the samples for possible effects of Hb saturation changes. Results are summarized in Table 3. Fig. 1 represents the observed variations of SID associated to ΔP_{CO_2}.

3.3. Calculation of ΔpH_T

Theoretical ΔpH_T were significantly higher than the ΔpH_A (0.12 ± 0.04 vs0.09 ± 0.03, $P < .0001$). As shown in Fig. 2, both ΔpH_A and calculated pH correlated linearly to ΔP_{CO_2} ($r^2 = 0.69$, $P < .0001$ and $r^2 = 0.73$, $P < .0001$, respectively). Regression slopes significantly differed between calculated and ΔpH_A ($P < .001$).

Table 1
Demographic and clinical characteristics of the study population

Characteristics	(n = 20)
Age (y)	41 ± 18
Female sex—n (%)	8 (40)
Days on ECMO	15 ± 11
Cause of lung failure—n (%)	
ARDS	13 (65)
Bridge to lung transplantation	5 (25)
Primary graft dysfunction	1 (5)
COPD exacerbation	1 (5)
Spontaneous breathing—n (%)	8 (40)
Survival—n (%)	12 (60)

Abbreviations: *Primary graft dysfunction*, primary graft dysfunction after lung transplantation; *spontaneous breathing*, patients who have been treated with ECMO as an alternative to mechanical ventilation, in the absence of endotracheal intubation and invasive mechanical ventilation; plus-minus values are means ± SD.