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Assessment of Venous-to-arterial Carbon Dioxide Difference as a Marker of Global Perfusion in Sepsis Syndromes

Essay

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بسم الله الرحمن الرحيم

قالوا

سبحانك لا علم لنا

إلا ما علمتنا إنك أنت

العليم الحكيم

صدق الله العظيم

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Raed Mohamed Sherisher i

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List of Abbreviations

Abbrev.	**Full-term**
ACD	: Acidcitrate- dextrose
ADP	: Adenosine diphosphate
ARDs	: Acute respiratory distress syndrome
ATP	: Adenosine triphosphate
BPS	: Begin immediately
CI	: Cardiac index
CO	: Cardiac output
CRRT	: Continuous RRT
CVP	: Central venous pressure
DNA	: Deoxyribonucleic acid
DO2	: Oxygen Delivery (DO2
DPG	: Diphosphoglycerate
EEG	: Electroencephalography
EGDT	: Early goal-directed therapy
HbO2	: Hemoglobin-bound O2
HFOV	: High-frequency oscillatory ventilation
ICU	: Intensive care unit

IV : Intravenous

LMWH : Low-molecular- weight heparin

MR : Metabolic rate

NIV : Noninvasive ventilation

RBC : Red blood cells

RNA : Ribonucleotide acid

RRT : Renal replacement therapy

UFH : Unfractionated heparin

VTE : Venous thromboembolism

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Introduction

A shock is a form of acute circulatory failure associated with an inequality between systemic oxygen delivery (DO2) and oxygen consumption (VO2), which result in tissue hypoxia. Tissue hypoxia is a key trigger for organ dysfunction and the adequacy of oxygen delivery (DO2) to tissue oxygen metabolic demand is essential in septic patients. Optimization of DO2, using either or both fluid loading and inotropic support, to prevent tissue hypoxia in relation to increased oxygen consumption (VO2), could improve outcome. The use of central venous oxygen saturation (ScvO2), which reflects important changes in the DO2/VO2 relationship has been used to target the optimization of therapy ***(Cecconi et al., 2014).***

However normalizing systemic hemodynamic parameters does not guarantee adequate tissue perfusion and in fact some patients still progress to multi-organ dysfunction and death despite meeting ScvO2 targets ***(Yealy et al., 2014).***

Normalization of ScvO2 does not rule out persistent tissue hypoperfusion and does not preclude evolution to multi-organ dysfunction and death. The obvious limitation of ScvO2 is that normal high values cannot distinguish if DO2 is sufficient or in excess to demand. In septic conditions, normal/high ScvO2 values might be due to the heterogeneity of the microcirculation that generates capillary shunting and/or mitochondrial damage responsible of disturbances in tissue oxygen extraction ***(Mouncey et al., 2015).***

Lactate has also been proposed as a resuscitation endpoint. However, no benefits have been observed for lactate decrease-guided therapy over resuscitation guided by ScvO2 in septic shock patients ***(Gu et al., 2015).***

Moreover, given the nonspecific nature of lactate level elevation, hyperlactatemia alone is not a discriminatory factor in establishing the source of the circulatory failure. Hence, additional circulatory parameters such as the venous-to-arterial carbon dioxide tension difference are needed to identify patients with septic shock who presently may still insufficiently reanimated, especially when ScvO2 values are normal/high in the context of hyperlactatemia ***(Zhang and Xu, 2014).***

An inverse relationship between Pv-aCO2 and cardiac output was described, highlighting the importance of blood flow on venous CO2 accumulation. In cases of hemodynamic compromise and global hypoperfusion, the venous CO2 accumualtes and venous to arterial CO2 relationship is changed.Thus, the Pv-aCO2 aroused clinical interest as a marker of global perfusion in sepsis and during shock states ***(Vanbeest et al., 2013).***

A prospective observational study has shown that the central venous-to-arterial CO_2 difference may serve as a global index of tissue perfusion (***Vallee et al., 2013).***

Fifty consecutive septic patients with a $ScvO_2 > 70\%$ were included immediately after their admission into ICU following early resuscitation in the emergency room. The study demonstrated that the presence of a $P(cv\text{-}a)\ CO_2 > 6$ mmHg was associated with the largest lactate value and might have been a useful tool to identify patients who remained inadequately resuscitated despite a 70% $ScvO_2$ goal being reached. These results were in agreement with those of Bakker et al., who showed that, in patients with septic shock, the PCO_2 gap was smaller in survivors than in non survivors, despite quite similar cardiac index (CI), DO_2 and VO_2 values. These studies show that the difference between venous-arterial CO_2 can be used as a marker of hypoperfusion and as a guide to the optimization of therapy ***(Vanbeest et al., 2013).***

Aim of the Essay

View the role of Venous-to-Arterial CO_2 difference in the prognosis of septic patients during early resuscitation phases and correlation with other hemodynamic parameters as lactate and Base deficit.

Chapter (1):
Tissue Oxygenation

Physiology of oxygen delivery

The transfer of a gas across a membrane relies on physical principles and is summarized by Fick's first law of diffusion:

$$\mathbf{O2\ diffusion = K \times A/T \times \Delta P}$$

Where K is the diffusion constant for a particular gas, A is the surface of a membrane; T is the membrane's thickness and ΔP the difference in partial pressure across the membrane. As oxygen is poorly soluble in water, diffusion alone became insufficient to deliver oxygen to the cells, and novel methods of delivery have evolved, most notably the cardiovascular system. This provided the means to deliver oxygen around the body ***(van Boxel et al., 2012).***

Oxygen Delivery

Transport of oxygen to the cells can thus be divided into six simple steps reliant only on the laws of physics: (1) convection of oxygen from the environment into the body (ventilation); (2) diffusion of oxygen into the blood (oxygen uptake): (3) reversible chemical bonding with haemoglobin; (4) convective transport of oxygen to the tissues (cardiac output): (5) diffusion into the cells and organelles; (6) the redox state of the cell. This chain of events is oxygen delivery or more correctly oxygen flux (DO2) (***Kuper et al., 2004).***

Step 1: Convection – ventilation: The first step occurs in the lung in the form of pulmonary ventilation. At sea level the partial pressure of oxygen in environmental air is approximately 160 mmHg. On inspiration the air is humidified and mixed with exhaled carbon dioxide (CO_2) such that at the alveolus the PAO_2 is 100 mmHg. This will vary in different environments and different conditions. Much of oxygen therapy is based on increasing oxygen delivery into the lungs whether by masks or other devices (***Boyd O, 2003).***

Step 2: Diffusion – alveolus to blood: Oxygen within the alveolus diffuses across the alveolar–capillary membrane. The average thickness of the alveolar capillary membrane is 0.3µm and the surface area of the respiratory membrane between 50 and 100m2. This leads to a PaO_2 in the pulmonary capillaries of approximately 90 mmHg. Herein lies many of the problems seen in the critically ill where two mechanisms predominate: (1) the thickness and barrier effect of the space between alveolus and capillary usually a minor issue, and (2) the relationship between perfusion and ventilation at alveolar level (V/Q ratio) – in ARDS intrapulmonary shunt is the predominant cause of hypoxaemia (***Rivers et al., 2001).***

Step 3: Haemoglobin binding: Oxygen is poorly soluble in water, having a solubility of 0.003082g/100g H_2O. Having diffused across the alveolar capillary membrane, the oxygen binds rapidly to the respiratory pigment haemoglobin. The saturation of haemoglobin with oxygen (SaO_2) PO_2 relationship is not linear and forms a sigmoidal shape. The P_{50} is the PaO_2 at which 50% of the haemoglobin is saturated. Various factors are known to alter the affinity of haemoglobin for oxygen. These have teleological advantages as for example, a low pH or high CO_2 at tissue level could imply tissue hypoxia, and the reduction in oxygen-binding affinity increases oxygen availability. Similarly hyperthermia (fever), hypercarbia and an increase in the concentration of 2,3-diphosphoglycerate (2,3 DPG) all move the curve to the right and increase oxygen availability. 2,3-DPG is a by-product of glycolysis and therefore binds haemoglobin in predominantly hypoxic tissues, facilitating a release of oxygen. Conversely hypocarbia, alkalosis and low concentrations of 2,3-DPG result in a leftward shift of the curve and a higher affinity for binding for any given PO_2. Systemic interventions such as alteration in PCO_2 or pH will influence the curve and therefore oxygen dissociation and availability (***Grocott MP et al., 2009).***