Transfusion and Apheresis Science 45 (2011) 291–297

Contents lists available at SciVerse ScienceDirect

Transfusion and Apheresis Science

journal homepage: www.elsevier.com/locate/transci

Pathophysiological alterations in oxygen delivery to the tissues

Giuseppe Miserocchi *, Manuela Bartesaghi

Dipartimento di Medicina Sperimentale, Università Milano Bicocca, Via Cadore 48, 20052 Monza, Italy

ARTICLE INFO

Keywords:
Oxygen delivery
Anemia
Adaptive response to anemia

ABSTRACT

This paper reviews co-factors that impact on oxygen delivery and uptake, in the attempt to unravel the mechanisms underlying the correlation between the decrease in oxygen delivery and oxygen consumption. In sequence, the following factors are analyzed that, besides a decrease in haemoglobin concentration, impair tissue metabolism: (1) lung diffusion and perfusion limitation in oxygen transport, (2) decrease in cardiac output, (3) impairment of peripheral microvascular perfusion and (4) reduced ability of cells to extract oxygen. The contribution of the various factors is modeled aiming to present a decisional flow chart for the functional evaluation of the efficiency of the oxygen transport system.

1. Introduction

The management of anemic patients remains a difficult problem on clinical ground given the uncertainty to determine a correct benefit/cost ratio for blood transfusion [1,2]. Most of the debate develops around three basic questions:

(1) What is the minimum acceptable haemoglobin (Hb) concentration: 10 or 7 g/dl?
(2) Which objective symptoms should be considered as important determinants to suggest blood transfusion?
(3) Given a "satisfactory" Hb concentration, can one still cast doubts concerning the real oxygen delivery to the tissues?

This paper intends to review co-factors, either independent or only partially dependent on Hb concentration, that impact on oxygen delivery to the tissues. To cope with this aim, we will consider each step of the oxygen transport system in order to evaluate their potential limitation, as well as their interaction, that leads to an impairment of the oxygen made available to the tissues.

The four functional sequential steps that we will consider are:

(1) oxygen diffusion at the level of the air-blood barrier
(2) the role of cardiac output in the oxygen transport to the tissues
(3) the actual delivery of oxygen to the tissues due to potential limitation in vascular perfusion
(4) the ability of tissues to use oxygen

2. General overview of the oxygen transport system

Fig. 1 is a schematic model of the whole oxygen-transport system. The first step is O_2 gas diffusion through the air-blood barrier and solution in plasma; thereafter, based on its partial pressure, O_2 reacts with haemoglobin and is then carried by blood flow. One can now define the delivery of oxygen as $DO_2 = CO \times CaO_2$, where CO is cardiac output and CaO_2 is the arterial concentration of oxygen. As blood flows through the tissues, oxygen leaves blood to enter cells, and, considering the oxygen concentration in the venous blood (CvO_2), it is possible to write the fundamental equation (Fick's law) $VO_2 = CO(CaO_2–CvO_2)$. Under steady state conditions, VO_2 defined by Fick's law is exactly equal to the VO_2 estimated from gas analysis of inspired and expired air.

* Corresponding author. Tel.: +39 02 64488309; fax: +39 02 64488068.
E-mail address: giuseppe.miserocchi@unimib.it (G. Miserocchi).

1473-0502/$ - see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.transci.2011.10.011

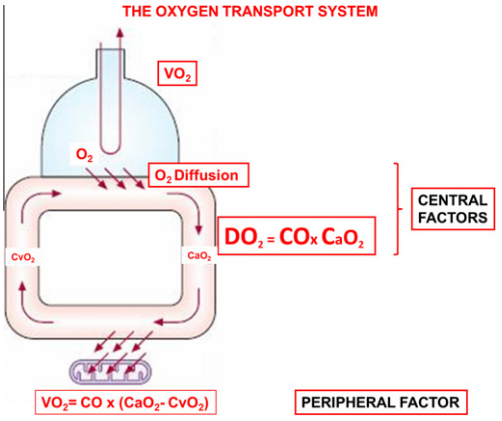

Fig. 1. General model of the oxygen transport system.

3. Potential limitation of oxygen diffusion at the level of the air-blood barrier

Fig. 2 allows to appreciate two mechanisms that may limit oxygen uptake in the lungs, namely diffusion "limitation" and perfusion "limitation" [3]. Gas diffusion is directly proportional to the pressure gradient of oxygen partial pressure between the alveolar gas (P_A) and the venous blood (P_v), it is also directly proportional to the surface available for diffusion (S) and inversely proportional to the thickness of the air-blood barrier (d), thus: $VO_2 = (P_A - P_v)\frac{S}{d}$. Diffusion limitation occurs for a decrease in P_A–P_v (as in alveolar hypoxia), in S (as in ventilation/perfusion mismatch, or alveolar edema), or an increase in d (thickening of the air blood-barrier due to interstitial lung edema or fibrosis). Perfusion "limitation" also occurs for O_2 transport in the blood as it is critically dependent upon blood flow, that is cardiac output. Both diffusion and perfusion limitation may obviously be present.

4. Potential limitation of lung perfusion in the oxygen transport

As can also be appreciated from Fig. 2, the delivery of oxygen to the left heart can be defined as:

$$DO_2 = CO \times CaO_2$$

where CO is cardiac output and CaO_2 is the arterial O_2 concentration. Note that CaO_2 is an average value resulting from mixing blood coming from regions where venous–alveolar equilibration was perfect (ventilation/perfusion ratio $\geqslant 1$) and regions where equilibration was not fully accomplished (ventilation/perfusion ratio <1). Note that the latter regions are those normally receiving a greater share of cardiac output and therefore their impact on CaO_2 is expected to be greater.

One can now define the oxygen extraction ratio (OER) defined as the VO_2/DO_2 ratio. Considering the definitions of VO_2 and DO_2 given above, one can write:

$$OER = \frac{CO \cdot (CaO_2 - CvO_2)}{CO \cdot CaO_2} \quad \text{that simplifies to :}$$

$$OER = 1 - \frac{CvO_2}{CaO_2}.$$

In physiological conditions the following average values hold: VO_2 ~250 ml/min, CO ~5000 ml/min, [Hb] = 15 g/dl, DO_2 ~1000 ml/min, OER ~0.25, and $\frac{CvO_2}{CaO_2} \sim 0.75$.

Fig. 3 shows a peculiar feature of the functional design for the interaction between oxygen diffusion and delivery [4]. Such interaction can be discussed by having on the ordinate the ratio $\frac{P_A - P_a}{P_A - P_v}$ that can vary between 0 (in case of perfect equilibration the alveolo-capillary difference P_A–P_a is equal to 0), to 1 when no oxygenation occurs for venous blood flowing through the lung (in this case the numerator becomes equal to the denominator). Thus, a shift of the ratio from 0 to 1 indicates a progressive increase in the alveolo-capillary difference. On the abscissa the ratio between total diffusive capacity for O_2 (Diff O_2) and O_2 delivery capacity (DO_2) is presented. In control conditions at rest the ordinate is 0 and the Diff O_2/DO_2 ratio equals 10, indicating that the architectural design of the lung is oversized for O_2 diffusion compared to O_2 transport. The response to an increase in oxygen needs (shown in the figure as a shift from a small to a large heart) is faced with an increase in DO_2 through an increase in cardiac output and since oxygen diffusive capacity cannot increase, the ratio Diff O_2/DO_2 is due to decrease: as shown in Fig. 3, the diffusion/transport model implies an increase in $\frac{P_A - P_a}{P_A - P_v}$. Note that an increase in oxygen needs can be matched also by an increased desaturation of the blood, yet since $\frac{P_A - P_a}{P_A - P_v}$ increases, the increase in P_A–P_a (the alveolo-capillary gradient) is greater than that of P_A–P_v. On biophysical ground, a greater alveolo-capillary gradient is mainly due to the decrease in transit time of the blood through the pulmonary capillaries that slows down the kinetics of oxygen equilibration.

5. Potential limitation in tissue perfusion

Two factors may be acting in a "critically ill patient" lying in bed, both causing a tissue pressure in the most

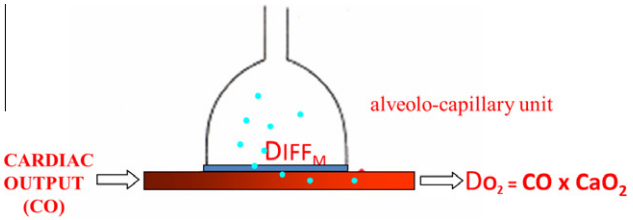

Fig. 2. Alveolar gas diffusion of oxygen and definition of oxygen delivery.