Oxygen transport during hemodilution with a perfluorocarbon-based oxygen carrier: effect of altitude and hyperoxia

Tatiana Gardeazábal,1 Mariana Cabrera,1 Pedro Cabrales,2 Marcos Intaglietta,2 and Juan Carlos Briceno1

1 Blood Substitutes Laboratory, Fundación Cardio Infantil, University of Los Andes, Bogotá, Colombia; and 2 Department of Bioengineering, University of California-San Diego, La Jolla, California

Submitted 8 February 2008; accepted in final form 29 May 2008

Gardeazábal T, Cabrera M, Cabrales P, Intaglietta M, Briceno JC. Oxygen transport during hemodilution with a perfluorocarbon-based oxygen carrier: effect of altitude and hyperoxia. J Appl Physiol 105: 588–594, 2008. First published June 5, 2008; doi:10.1152/japplphysiol.00152.2008.—Oxygen delivery and consumption after hemodilution with a perfluorocarbon-based oxygen carrier (PFCOC) was evaluated at sea level and at 2,600 m above sea level. Fifteen anesthetized rats were subjected to a two-exchange normovolemic hemodilution of 40% of the circulating blood volume each. First exchange was performed with a colloid solution. Second exchange was with 80% PFCOC and 20% colloid. Animals were then ventilated with 100% oxygen. Experiments were performed at barometric pressure of 1.0 atm (sea-level group, n = 9) or 0.74 atm (2,600-m group, n = 6). Blood gases, hematocrit, fluorocrit, and hemoglobin content were measured at baseline and 15 min after each exchange. After hemodilution, total arterial content was not modified by the PFCOC in either group. In contrast, arteriovenous oxygen difference increased significantly in both groups, as did the oxygen extraction ratio. In the second exchange, although total arterial content was similar between the two groups, the perfluorocarbon and plasma phases contributed significantly more at sea level. Arteriovenous oxygen difference was significantly less at sea level with a higher contribution from the perfluorocarbon and plasma phases. In conclusion, hemodilution with a PFCOC induced changes in oxygen delivery and consumption that differ with altitude. The 2,600-m group exhibited a higher oxygen extraction ratio and arteriovenous oxygen difference, with reduced oxygen delivery and unloading from both the fluorocarbon and plasma phase. Therefore, the efficacy of PFCOCs at 2,600 m above sea level is reduced, and altitude must be taken into account when PFCOCs are used.

perfluorocarbon oxygen carriers; normovolemic hemodilution; altitude; hyperoxia

PERFLUOROCARBON-BASED OXYGEN CARRIERS (PFCOCs) provide an interesting perspective for acute blood loss and presur- }

0.8. The oxygen carrying capacity of PFCOCs has been extensively documented (7, 12). They transport dissolved oxygen that can easily be taken up by the tissues because oxygen is transported by van der Waals interactions, a much weaker bond than the coordination bond found in hemoglobin (11). The amount of oxygen carried in perfluorocarbon (PFC) molecules depends on the partial pressure of oxygen, which in turn, depends on the barometric pressure. Hence, it is reasonable to believe that PFCOCs perform differently in terms of oxygen delivery and consumption with different barometric pressures.

Our objective was to investigate how oxygen delivery and consumption with a PFCOC varied at sea level (barometric pressure: 760 mmHg) and at 2,600 m above sea level (560 mmHg) in a murine model of hemodilution. Additionally, we examined the effect of normovolemic hemodilution on blood gas parameters at sea level and 2,600 m above sea level.

MATERIALS AND METHODS

Emulsion Preparation

Emulsions were prepared using 38% (wt/vol) perfluorooctylbromide (Perflubron, F2 Chemicals), 3% soybean lecithin-epicuron 170 (Deggussa), alphatocopherol as antioxidant, and glycerol, glucose, and sodium chloride as osmolarity stabilizers. A microemulsifier (M-110Y, Microfluidics) was used to prepare the emulsion until a droplet size between 100 and 150 nm was attained as measured with a laser scattering size analyzer (90 plus, Brookhaven Instruments). Osmolarity was between 299 and 310 mosM to maintain baseline plasma osmolarity and viscosity 5.6 cP at 160 s⁻¹.

Perfluoroochemical blood substitutes exert oncotic pressure only if a plasma volume expander such as Hydroxyethylstarch is present. However, such substances may induce particle aggregation in the presence of salts. For this reason, a prepared mixture of 80% PFCOC and 20% hydroxyethylstarch (HES 10%) was administered.

Sea-Level Model

The institutional Review Board (University of California-San Diego) approved the protocol, and the animals were kept according to the Guide for the Care and Use of Laboratory Animals (National Research Council, 1996).

Adapted male Sprague-Dawley rats (provided by Charles River; San Diego, CA), weighting 260 ± 40 g (mean ± SD) were subjected to the procedure (n = 9). The experiments were performed in La Jolla at the Microhemodynamics Laboratory of the University of California-San Diego at 20 m above sea level (barometric pressure 1.0 atm). Animals were starved 2 hours prior to the experiment.

Animals were sedated with intraperitoneal pentothal sodium (60 mg/kg). Once the animal was dissociated, supine position was adopted with neck hyperextension under light microscope (Leica S6E). Oxygen was supplied at 1 l/min.

Venous and arterial catheters were inserted through the left common femoral artery and right external jugular vein using 0.58-mm (0.023-in.) polyethylene tubing to do the exchanges. These catheters were previously filled with heparin solution (30 UI/ml). The arterial line was used to take samples and extract blood volume. The venous line was used to infuse the exchange solution and obtain venous samples. Both extraction and infusion were performed at a rate of 200 μl/min.

A thermal transducer was inserted through right common carotid artery to register body temperature. Cardiac output (CO) was measured through this transducer in three of the animals by a modified thermodilution technique.

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

Address for reprint requests and other correspondence: J. Carlos Briceno, Carrera 1 Este No. 19-40, Office ML817, Univ. of Los Andes, PO Box 4976, Bogotá, Colombia (e-mail: jbriceno@unianandes.edu.co).

588 8750-7587/08 $8.00 Copyright © 2008 the American Physiological Society http://www.jap.org
Two exchanges of 40% blood volume (6 ml/100 g wt) were performed, following a previous model (11). During the first exchange, rodents were hemodiluted using a plasma expander [hydroxyethylstarch 10% (HES 10%), Fresenius]. In the second exchange, animals were submitted to a 40% exchange with a solution of 80% PFC emulsion and 20% of 10% HES. When the second exchange was over, rodents were submitted to 100% inhaled oxygen for 15 min.

High-Altitude Model

The institutional Review Board (Fundación Cardio Infantil) approved the protocol, and the animals were kept according to the Guide for the Care and use of Laboratory Animals (National Research Council, 1996).

Altitude-native Wistar male rodents, 210 ± 10 g of weight, were subjected to the procedure (n = 6). Experiments were performed at the Experimental Surgery Facility of the Blood Substitutes Laboratory at the Fundación Cardio Infantil in Bogotá at 2,600 m above sea level (barometric pressure 0.74 atm). Animals were starved 2 h before the experiment. The model is identical to the sea-level model except that the arterial catheter was inserted through the left common carotid artery and CO was not measured.

Samples

Blood gases, hematocrit (Hct), and hemoglobin content (Hb) were measured at baseline (BL) and 15 min after each exchange (L1, L2). Arterial oxygen content (CaO2) and arteriovenous oxygen content difference (Ca-vO2) were calculated. The fractional contribution of each phase [red blood cell (RBC), PFC, and plasma] to CaO2 and to Ca-vO2 were determined.

Fluorocrit measurement. PFC volumetric content or fluorocrit (Fct) was assessed by centrifugation of a capillary with blood (Readacrit Centrifuge, Clay Adams) and is expressed as a percentage, representing the length of PFC emulsion (indicated by the white color) in the centrifuged capillary tube relative to the entire length of the centrifuged blood (6).

Data Analysis

Total CaO2, and total Ca-vO2 were used as indicators of oxygen delivery and consumption, respectively. The formulas used throughout the study are shown in appendix.

Statistical Analysis

Results are presented as means ± SD. Differences between groups were analyzed using two-way ANOVA for repeated measurements and post hoc Bonferroni tests. Data within each group were analyzed using one-way ANOVA for repeated measurements and post hoc Bonferroni tests (Prism, GraphPad Software). Differences were considered significant at P < 0.05.

RESULTS

Experiments at Sea Level

Blood gases. Arterial and venous blood gases are presented in Table 1. At sea level, the arterial pH (pHa) maintained constant at BL and L1, with a slight but significant increase at L2 (P < 0.05). The venous pH (pHv) was not modified at any of the three time points.

Arterial PO2 (PaO2) increased significantly at L2 because of the increased inspired oxygen fraction (FIO2); the arterial oxygen saturation (SaO2) and venous oxygen saturation (SvO2) remained constant.

Hb, Hct, and Fct. Hb content was 15.4 ± 0.6 g/dL at BL, 9.7 ± 1.2 g/dL at L1, and 8.2 ± 1.2 g/dL at L2. Hct was 48.1 ± 0.6% at BL, 30.6 ± 3.6% at L1, and 24.2 ± 2.0% at L2. Fct was 5 ± 2% at L2.

CaO2. The results for CaO2 are presented in Fig. 1. CaO2 decreased at L1 significantly (P < 0.001) and then increased at L2 (P < 0.05), although it remained significantly lower than at BL (BL vs. L2: P < 0.001).

The fractional contribution by phase (PFC, plasma, and RBCs) to CaO2 is shown in Fig. 2A. The absolute contribution (in ml O2/100 ml of blood) by PFC was small: 1.55 ± 0.67, which accounted for 11.2 ± 4.2% of the total CaO2. This was similar to the fractional contribution of plasma: 9.3 ± 1.7%.

Ca-vO2. The results for Ca-vO2 are shown in Fig. 3. Ca-vO2 decreased significantly from BL to L1 and then recovered at L2, which was similar to baseline levels (BL vs. L2: P > 0.05).

The fractional contribution by phase (PFC, plasma, and RBCs) to Ca-vO2 is shown in Fig. 4A. The fractional contributions by RBCs decreased drastically from BL (98.4 ± 0.6%) and L1 (95.6 ± 2.2%) to L2 (38.3 ± 19.3%). The fractional contributions of PFC and plasma became very significant at L2 (33.3 ± 12.9% and 28.3 ± 10.4%, respectively).

The experiments performed at sea level included the recording of CO for three of the animals. We found a linear correlation (r2 = 0.82) between oxygen consumption (Vo2) and Ca-vO2, which is why we believe Ca-vO2 to be a valid estimate of Vo2. These results are shown in Fig. 5.

Oxygen extraction ratio. At L1 the oxygen extraction ratio (OER) decreased slightly and then increased at L2, being significantly higher than both L1 and BL (P < 0.01) (Fig. 6).

Experiments at 2,600 m Above Sea Level

Blood gases. Arterial and venous blood gases at 2,600 m above sea level are also presented in Table 1. In this set of results, the pHa at BL and L1 is similar, but L2 is very low in comparison. However, the pHa at L2 has a large variability (7.28 ± 0.20), and there is no significant difference between

<table>
<thead>
<tr>
<th></th>
<th>BL</th>
<th>L1</th>
<th>L2</th>
</tr>
</thead>
<tbody>
<tr>
<td>pHa</td>
<td>7.42±0.03</td>
<td>7.43±0.05</td>
<td>7.48±0.03</td>
</tr>
<tr>
<td>pHV</td>
<td>7.36±0.06</td>
<td>7.36±0.12</td>
<td>7.28±0.20</td>
</tr>
<tr>
<td>PAO2</td>
<td>7.42±0.03</td>
<td>7.43±0.03</td>
<td>7.40±0.02</td>
</tr>
<tr>
<td>PvO2</td>
<td>7.33±0.06</td>
<td>7.30±0.09</td>
<td>7.21±0.18</td>
</tr>
</tbody>
</table>

pHa, arterial pH; pHv, venous pH; PaO2, arterial PO2; PvO2, venous PO2; SaO2, arterial oxygen saturation; SvO2, venous oxygen saturation.
the pH at any of the time points ($P > 0.05$). A similar scenario occurred with the pHv, where a large decrease in L2 is observed but is not significant due to the variability of the values ($P > 0.05$).

$PaO_2$ increased significantly at L2 because of the increased FIO2. $SaO_2$ remained constant throughout the experiments. A decrease in the $SvO_2$ can be seen at L2, although this decrease was not statistically significant ($P > 0.05$).

$Hb$, $Hct$, and $Fct$. $Hb$ content was $16.5 \pm 0.8$ g/dl at BL, $10.2 \pm 1.2$ g/dl at L1, and $8.0 \pm 0.9$ g/dl at L2. $Hct$ was $48.4 \pm 1.8\%$ at BL, $30.4 \pm 3.1\%$ at L1, and $24.0 \pm 2.6\%$ at L2. Due to technical problems, $Fct$ was not measured in this group. Given that the $Hb$ and $Hct$ in this group were similar to the sea-level group, we used the $Fct$ value of the sea-level group for all calculations in the 2,600-m group.

$CaO_2$. The $CaO_2$ at 2,600 m is also shown in Fig. 1. $CaO_2$ decreased significantly at L1 ($P < 0.001$), which was not modified at L2 (L1 vs. L2, $P > 0.05$; BL vs. L2, $P < 0.001$).

The fractional contribution by phase (PFC, plasma, and RBCs) to $CaO_2$ is shown in Fig. 2B. The fractional contribution by PFC was $6.7 \pm 1.7\%$ of the total $CaO_2$ and the contribution of plasma was $5.4 \pm 1.5\%$.

$Ca-vO_2$. The results for $Ca-vO_2$ are shown in Fig. 3. $Ca-vO_2$ decreased from BL to L1 and then recovered at L2. The increase from L1 to L2 was significant ($P < 0.01$), and L2 ended up significantly higher than BL ($P < 0.05$). The fractional contribution by phase (PFC, plasma, and RBCs) to $Ca-vO_2$ is shown in Fig. 4B. The contribution of RBC decreased from $97.3 \pm 1.8\%$ at L1 to $78.6 \pm 9.3\%$ at L2. The contribution of plasma increased from $2.7 \pm 1.8\%$ at L1 to $9.6 \pm 4.1\%$ at L2. The fractional contribution of PFC at L2 was $11.8 \pm 5.2\%$.

$OER$. The OER increased from $17.7 \pm 6.7\%$ at BL to $23.8 \pm 17.8\%$ at L1 and $52.9 \pm 15.7\%$ at L2. This value is significantly higher than BL and L1 ($P < 0.01$) (Fig. 6).

Sea Level vs. 2,600 m Above Sea Level

Blood gases. Comparing the sea-level group vs. the 2,600-m group, there were no significant differences between the blood gases at baseline and after the first exchange. At L2, both arterial and venous pH were significantly lower in the 2,600-m group.

At L2, $PaO_2$ at sea level was significantly higher than at 2,600 m ($562 \pm 30$ Torr vs. $296 \pm 87$ Torr, respectively; $P < 0.001$). Venous $PO_2$ and $SvO_2$ were also significantly higher in the sea-level group at L2.
Hb, Hct, and Fct. The Hb and Hct values were similar between the three groups at all time points.

$Ca_{O_2}$ was similar at BL for the two groups and did not differ significantly at any time point (Fig. 1). The absolute contribution (in ml O$_2$/100 ml of blood) by PFC was relatively small and similar for both groups. However, in terms of fractional contribution to total $Ca_{O_2}$, the PFC phase was significantly higher in the sea-level (Fig. 2A) group than in the 2,600-m group (Fig. 2B) ($11.2 \pm 4.2\%$ vs. $6.7 \pm 1.7\%$, respectively; $P < 0.05$). Likewise, in the plasma fraction, the absolute contribution was similar in both groups, but as a fraction of the total $Ca_{O_2}$ in L2, the sea-level group had a higher percentage.

Although the absolute value in milliliters of oxygen provided by the RBC phase was similar in both groups at the three time points, the fractional contribution from the RBC phase at L2 was significantly lower at sea level (sea level, $79.5 \pm 4.4\%$ vs. 2,600 m, $87.9 \pm 3.2\%$; $P < 0.01$).

$Ca_{-vO_2}$. $Ca_{-vO_2}$ decreased from BL to L1 and then recovered at L2 for both groups (Fig. 3).

$Ca_{-vO_2}$ at L2 was significantly higher at 2,600 m than at sea level ($6.33 \pm 1.82$ vs. $4.36 \pm 1.82$ ml O$_2$/100 ml blood, respectively; $P < 0.05$).

Fractional contribution to $Ca_{-vO_2}$ from the PFC and plasma phases at L2 were significantly higher at sea level (Fig. 4A) than at 2,600 m (Fig. 4B) ($P < 0.01$), and fractional contribution from the RBC phase at L2 was significantly lower at sea level ($P < 0.001$).

$OER$. Oxygen extraction was similar for both groups at BL. The OER was slightly higher at 2,600 m at BL and L1, but at L2 it became significantly higher compared with the sea-level group ($P < 0.01$) (Fig. 6).

**DISCUSSION**

Our results show that hemodilution has an important effect on the oxygen consumption and delivery in rodents, which varies on whether the animal is at sea level or at 2,600 m above sea level. Additionally, the PFCOC performed differently in the two places, transporting and delivering more oxygen at sea level and becoming a more significant source of oxygen than at 2,600 m.

**Blood Gases**

Previous experiments have shown that altitude acclimatized rodents are more resistant to hemodilution at sea level (3), but it is not clear how they behave when hemodilution is per-
formed at 2,600 m. It has been reported that altitude-dwelling animals have a better tolerance to hypoxia due to policythemia and/or changes in hemoglobin oxygen affinity (4). Contrary to our expectations, the 2,600-m rodents had less tolerance to hemodilution, becoming more acidotic than the sea-level animals. This could be due to a more traumatic catheterization, although acidosis was noted predominantly at L2, a significant while after the catheterization procedure. Is it possible that the 2,600-m group was in fact less tolerant to the hemodilution as such? It is interesting to note that, at L2, the 2,600-m rodents are acidotic despite acceptable levels of Hb (8 g/dl) and PaO2 (295 Torr). This finding is similar to previous reports, where animals who received PFCOCs showed acidosis, despite improved tissue oxygenation parameters (1). This phenomenon has been explained by the interference of PFCs on lactate homeostasis rather than to deficient tissue oxygenation (2, 14).

PaO2 was predictably elevated at sea level more than at 2,600 m due to higher atmospheric pressure. The 2,600-m rats had a lower venous PO2 because it was initially lower and because of a larger V˙O2.

Hb and Hct content were similar in both groups, perhaps because of an alternative method of acclimatizing other than policythemia-like hyperventilation and alteration in the oxygen affinity of hemoglobin. This could also affect oxygen delivery and consumption values. It is possible that the 2,600-m group had a larger blood loss during the catheterization (which is significant due to a small circulating volume), although that is unlikely.

CaO2

The use of the PFCOC did not significantly modify CaO2. Both groups began with a similar CaO2 at BL, a similar decrease at L1, which at L2 was not modified at 2,600 m, and increased slightly at sea level (not significant). PFCOC was less effective at transporting oxygen at 2,600 m due to a smaller PaO2, even with a maximal FIO2. Regarding the PFC and plasma phases, absolute values were not significantly higher at sea level, but as a fraction of CaO2, were significantly higher, further supporting the notion that PFCOCs are more effective at sea level. The absolute contribution by RBCs in L2 was similar in both groups, but the fractional contribution was significantly higher at 2,600 m, explained in part because PFC and plasma contributed lesser percentages.

Ca-vO2

As with previous experiments (1), although the PFC fraction did not increase CaO2, it did affect the Ca-vO2 significantly, facilitating oxygen unloading and becoming a significant source for V˙O2.

Ca-vO2 decreases at L1 in part because of insufficient delivery and a defense mechanism of decreased oxygen requirements and increases at L2 to compensate the oxygen debt generated. Ca-vO2 is similar at BL and L1 between the two groups, then increases in both groups, but significantly more at 2,600 m. The 2,600-m group had higher V˙O2, perhaps due to metabolic stress and the generation of a higher oxygen debt. It is likely that the sea-level animals tolerated the hemodilution better with smaller oxygen demands and a smaller oxygen debt, reflected in a reduced increase at L2.

The contribution of PFC was significantly higher at sea level both in the absolute values (1.36 ± 0.64 vs. 0.72 ± 0.25) and even more in the percentage of total Ca-vO2 (33.3 ± 12.9% vs. 11.8 ± 5.2%). The PFC fraction became an important source of oxygen, although much more important at sea level.

The plasma fraction was also significantly higher at sea level than at 2,600 m with similar percentages to the PFCOC contribution, showing that at sea level even fluid resuscitation is more effective than it is at 2,600 m. The efficiency of PFCOC is evident since only a 5% fluorocrit contributes as much as a plasma volume of 70%. In addition, the lower oxygen pressure made plasma less significant at 2,600 m, highlighting the need for an efficient oxygen carrier. In this study, at 2,600 m, the mechanism of adaptation was to increase the oxygen extraction from RBCs (associated with the higher %SaO2 from increased FIO2) since the PFC and plasma phases were minor sources of oxygen. The alkalosis in the sea-level
HEMODILUTION WITH PFCOCs AND ALTITUDE

593

group could have contributed to less unloading of oxygen by the RBCs, but probably not in a significant manner. Additionally, it is possible that, at sea level, the RBC fraction became less significant because there was a larger oxygen supply more easily taken up from the PFCOC. In fact, at sea level, the PFC fraction contributed an amount of oxygen similar to RBCs, despite a smaller volume of PFCOC. This was not true at 2,600 m, where RBCs continued to contribute ~80% of the total Ca-vO₂.

OER

The OER was significantly higher at 2,600 m than at sea level at L2, reflecting that the 2,600-m group had a higher VO₂ and lower oxygen supply. The OER has been proposed as an indicator of transfusion requirement when it is above 50% (9, 15). The normal OER range is between 20 and 30%, and it has been shown that, when the OER is above 50%, there is significant lactate production indicative of anaerobic metabolism (10). It takes into account not only the anemic insult but also the adequacy of the organism to respond to this blood loss. From our indicator of the whole body OER, the sea-level animals not only had a smaller OER than the 2,600-m animals, but their OER was below 50% even after L2 (mean OER: 32 ± 13%), indicating that they did not reach the threshold required for transfusion. On the other hand, the OER of the 2,600-m group was 53 ± 16% at L2, which shows that, not only did these animals have less tolerance to the blood loss, but a transfusion was indicated, despite the use of the PFC. It is interesting to note that these elevated OER values at L2 in the 2,600-m group were concomitant with acidosis.

From our results, we could see that, despite the fact that at 2,600 m the PaO₂ was much higher than it normally is (295.8 ± 86.6 Torr), it was not enough for the PFCOC to be as effective as it was at sea level (with a similar FIO₂). Therefor, at altitude, even with the highest oxygen supplementation therapy, PFCOCs may not be as efficient. This means that, for future preparations to be used at altitude, intrinsic characteristics of the emulsion such as PFC concentration, oxygen solubility, osmolality, and viscosity would have to be modified, keeping in mind the limitations of PFCOCs with altitude.

Limitations of the Study

The use of rodents for hemodilution is convenient and inexpensive, but because they are small animals, the catheterization is a significantly traumatic procedure, possibly affecting the results. Additionally, the procedure was performed by different investigators (except for one, T. Gardeazábal) in the two centers, and this could have further modified the response, although this is unlikely since baseline parameters were similar. In the future, larger species could be utilized and more parameters could be measured (such as heart rate, blood pressure, and CO) to provide a higher degree of accuracy.

Conclusions

Hemodilution with PFCOCs at 2,600 m above sea level produced profound changes in blood gases, fractional arterial oxygen content, and arteriovenous oxygen content difference. These changes can be explained by the different mechanisms of oxygen transport: at higher altitude, lower PaO₂ is achieved, reducing oxygen delivery and unloading from both the PFC and plasma phase. The consequent decrease in oxygen carrying capacity is compensated by increased transport by the RBC phase. Therefore, PFCOCs can be less effective at higher altitudes.

This study also provides more information regarding resuscitation at 2,600 m and sea level, because with a high enough supplementation of oxygen, plasma could become a significant source of oxygen at sea level but not at 2,600 m.

To our knowledge, this study shows for the first time the effect of altitude on hemodilution with PFCOCs. These findings stimulate new research into the development of PFCOCs with properties that increase their efficacy at altitude. The changes in oxygen delivery and consumption induced by altitude must be taken into account in the implementation of oxygen supplementation therapy as well as in the design of blood substitutes.

APPENDIX

Calculations Used in the Study

Total oxygen content. Equations used for arterial total oxygen content in red blood cells (CaO₂RBC):

\[ Hb \cdot 1.34 \cdot SaO_2 \% \]  (1)

in PFC (CaO₂PFC):

\[ (Fct \cdot \alpha_{PFC}) \text{ arterial PO}_2 \]  (2)

in plasma [Pl] (CaO₂Pl):

\[ [(1 - Hct - Fct)\alpha] \text{ arterial PO}_2 \]  (3)

and total arterial oxygen content (CaO₂):

\[ \text{CaO}_2\text{RBC} + \text{CaO}_2\text{PFC} + \text{CaO}_2\text{Pl} \]  (4)

Equations used in venous total oxygen content in red blood cells (CaO₂RBC):

\[ Hb \cdot 1.34 \cdot SvO_2 \% \]  (5)

in PFC (CaO₂PFC):

\[ (Fct \cdot \alpha_{PFC}) \text{ venous PO}_2 \]  (6)

in plasma (CaO₂Pl):

\[ [(1 - Hct - Fct)\alpha] \text{ venous PO}_2 \]  (7)

and total venous arterial oxygen content (CaO₂):

\[ \text{CvO}_2\text{RBC} + \text{CvO}_2\text{PFC} + \text{CvO}_2\text{Pl} \]  (8)

Arteriovenous oxygen difference. Equations used for total arteriovenous oxygen difference in RBC (CaO₂RBC):

\[ \text{CaO}_2\text{RBC} - \text{CvO}_2\text{RBC} \]  (9)

in PFC (CaO₂PFC):

\[ \text{CaO}_2\text{PFC} - \text{CvO}_2\text{PFC} \]  (10)

in plasma (CaO₂Pl):

\[ \text{CaO}_2\text{Pl} - \text{CvO}_2\text{Pl} \]  (11)

and total arteriovenous oxygen difference (CaO₂):

\[ \text{CvO}_2\text{RBC} + \text{CvO}_2\text{PFC} + \text{CvO}_2\text{Pl} \]  (12)
Other equations. Other equations used are for oxygen extraction ratio:

\[
(CavO_2/CaO_2) \times 100
\]

(13)

and oxygen consumption:

\[
CO \times CavO_2 \times weight(kg)^{-1} \times 100
\]

(14)

In all of the above equations, Hb is the hemoglobin in RBCs expressed as grams per deciliter of blood, 1.34 is the oxygen-carrying capacity (in ml O_2/g Hb) of Hb at 100% saturation, SaO_2 is the arteriovenous oxygen saturation of RBCs, SvO_2 is the venous oxygen saturation, 1 − Hct is the fractional plasma volume, 1 − Hct − Fct is the fractional plasma volume when PFCs are present, α is the solubility of oxygen in plasma and equal to 3.14×10^−3 ml O_2·dl plasma^−1·mmHg^−1, α_Pfc is the solubility of oxygen in the PFC emulsion and equal to 5.4×10^−2 ml O_2·dl plasma^−1·mmHg^−1 (5), and CO is cardiac output (in ml/min).

ACKNOWLEDGMENTS

We thank C. I. Castro, S. E. Cuervo, and L. F. Ponce for the emulsion preparation.

GRANTS

This study was funded by Colciencias contract no. 286-2004.

REFERENCES