Decrease in the Oxygen Extraction Ratio in Surgical Patients after Blood Transfusion

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Abstract

Introduction: To establish if there is a relationship between the decrease in the oxygen extraction ratio (O2ER) and the administration of erythrocyte concentrate (EC) using central venous saturation for the calculation of O2ER.

Method: Samples were obtained for blood gas analysis before starting the transfusion and 15 minutes after EC administration. Changes related to blood transfusion in patients with O2ER < 45% and ≥ 45% were analyzed. The statistical test of paired T was used to compare both groups.

Results: Thirty patients were included, of which 5 were eliminated due to massive bleeding and 25 patients were followed, 14 men (56%) and 11 women (44%). Prior to transfusion, 16 patients (64%) showed a O2ER < 45% with a mean of 26.8 ± 8.06% without significant change in post-transfusion O2ER and 9 patients (36%) reported a O2ER ≥ 45% with a mean of 50.07 ± 5.12%. Having a significant decrease of -10.26 (-23.93 to -5.77) in O2ER; p < 0.001.

Conclusion: After the transfusion of CE, there was a significant decrease in that of O2ER in the patients that presented a value > 45% before transfusion.

Keywords: Blood Transfusion; Central Venous Catheter; Hemorrhage; Hemoglobin; Oxygen Extraction Ratio

Introduction

Management of intraoperative bleeding is a complex and changing area that requires multiple evaluations and appropriate strategies to optimize the patient’s clinical conditions. In the practice of transfusion medicine, the use of a defined value of hemoglobin is frequently used as an indicator of transfusion of erythrocyte concentrate (EC); however, there is no consensus among the various medical societies. As examples of this, are the guidelines of the European Society of Anesthesiology, which suggest a hemoglobin (Hb) concentration of 7.0 - 9.0 g/dL during active trans-operative bleeding [1]. The guidelines of the American Society of Anesthesiology (ASA) suggest an Hb concentration of 6 to 10 g/dL, depending on the clinical state of the patient [2]. In the absence of acute myocardial or cerebrovascular ischemia, the Australian National Blood Authority recommends that postoperative transfusion may be inappropriate for patients with an Hb level > 8 g/dL. Patients should not receive a transfusion when the hemoglobin level is ≥ 10 g/dL [3]. However, these sources suggest not taking hemoglobin levels as the only factor in the decision to start an allogeneic blood transfusion.
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The main rationale for EC transfusion is to increase the oxygen transport capacity, reduce morbidity and mortality, in addition to improving the functional capacity resulting from anemia and the inadequate supply of oxygen to the tissues [4]. Allogeneic blood transfusion involves risks such as: transfusion-associated lung damage (TRALI), hemolytic transfusion reactions, transfusion-associated sepsis, and transmission of other infectious diseases such as human immunodeficiency virus, hepatitis B, hepatitis C, cytomegalovirus, parvovirus B19, Treponema pallidum, prion disease, among others [5]. Transfusion therapy and the number of units transfused have been linked to an increased risk of mortality and prolonged stay in the intensive care unit (ICU) and in the hospital [6,7]. In addition to the inherent risks of blood transfusion, there are also high costs and the supply depends on altruistic donation [8-10].

The oxygen extraction index (O₂ER) is the amount of consumed oxygen (VO₂), as a fraction of oxygen availability (DO₂); The latter is a product of cardiac output (CO) and arterial oxygen content (CaO₂). VO₂ is essentially the difference between CaO₂ and venous oxygen content (CvO₂); CvO₂ is mainly determined by Hb concentration and mixed venous oxygen saturation (vSO₂), while CaO₂ is determined by Hb concentration and arterial oxygen saturation (SaO₂) [11]. The O₂ER normal value is 25 - 30% and is used as a marker for oxygen extraction in tissue and is expected to increase in the presence of elevated VO₂ or decreased DO₂ [12]. To calculate O₂ER, measurement of mixed venous saturation (vSO₂) is required using a pulmonary artery catheter; instead, the measurement of central venous saturation (ScvO₂) can be obtained more easily, with less cost and risk for the patient, by means of a central venous catheter (CVC) [13]. ScvO₂ is reported to have a lower value than vSO₂ by approximately 2% to 3%, largely due to the lower rate of oxygen extraction by the kidneys [13]. Although the absolute values differ, the trends in ScvO₂ closely reflect the trends in vSO₂ [14,15].

The hypothesis of this study proposes that the administration of EC will decrease the O₂ER to a greater extent when it is found with a value > 45%. The objective of this prospective observational cohort study is to describe the modification of O₂ER after globular package administration; which would help us determine a value from which the patient’s clinical status benefits from the administration of the blood product.

Materials and Methods

The Research Ethics Committee of the University Hospital “Dr. José Eleuterio González” from the Autonomous University of Nuevo León evaluated and approved this study carried out in the period from March to October 2019, with the registration number AN18-00006. We included patients who gave their verbal consent to participate in the study, aged 18 to 65 years and who were scheduled for elective intermediate or high risk surgical procedures according to the updated ACC/AHA Guidelines [16] with classification ASA I to III [17], who were able to perform central venous and arterial blood gas analysis. Patients with heart failure, cardiomyopathies, ventricular septal defect and chronic obstructive pulmonary disease, pulmonary embolism, acute respiratory distress syndrome, as well as sickle cell anemia and thalassemias, hemophilia, thrombocytopenia, liver failure, patients in septic status and pregnant women were excluded, in whom the measurement O₂ER could be altered. Furthermore, patients who had massive bleeding [4] or any surgical procedure that affected venous return were eliminated from the study.

Heart rate, blood pressure, arterial oxygen saturation, the number of packets transfused and the results of central and arterial venous blood gases were recorded at the start of the procedure, prior to the administration of the blood product and within 15 minutes after at the end of the administration. All blood gases were analyzed in the gas laboratory of the Clinical Pathology department, with a blood gas system using a RAPIDPoint® 500 kit (Siemens Healthcare Diagnostics Inc. 511 Benedict Avenue Tarrytown, NY 10591-5005 USA). Because there is no transfusion protocol established in our institution, the decision to transfuse was made by the Resident of Anesthesiology in accordance with his clinical judgment and with the authorization of a professor from the Anesthesiology Service.

The parameters were determined based on the following calculations [18]:

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\[ \text{CaO}_2 = (\text{Hb} \times 1.34 \times \text{SaO}_2) + (\text{arterial PO}_2 \times 0.0031) \]

\[ \text{CvO}_2 = (\text{Hb} \times 1.34 \times \text{ScvO}_2) + (\text{central venous PO}_2 \times 0.0031) \]

\[ \text{Da-vO}_2 = \text{CaO}_2 - \text{CvO}_2 \]

\[ \text{O}_2\text{ER} = \left( \frac{\text{Da-vO}_2}{\text{CaO}_2} \right) \times 100 \]

Where \( \text{CaO}_2 \) refers to arterial oxygen content, \( \text{Hb} \) to hemoglobin, 1.34 is the amount of oxygen transported by hemoglobin in mL/g, \( \text{SaO}_2 \) to arterial oxygen saturation, \( \text{PO}_2 \) to partial pressure of oxygen, 0.0031 is the solubility of oxygen in plasma at 37°C reported in ml/mmHg, \( \text{CvO}_2 \) at venous oxygen content, \( \text{ScvO}_2 \) at central venous saturation, \( \text{Da-vO}_2 \) at arteriovenous oxygen difference.

\( \text{O}_2\text{ER} \) values were calculated at the time of statistical analysis. The physicians in charge of the case were blinded to the results obtained from the \( \text{O}_2\text{ER} \) at the time of the surgical procedure.

\( \text{O}_2\text{ER} \) of 50% to 60% has been suggested as a critical value that reflects a deficit in oxygen supply [19], from 40 to 50% in the intraoperative period and in the intensive care unit [4], for which reason we propose the value of 45% of \( \text{O}_2\text{ER} \) because it is an early \( \text{O}_2 \) deficit value, and it must also be taken into account that blood loss, changes in oxygen availability and consumption are usually more sudden in the intraoperative setting. The cases were divided depending on whether they reported an \( \text{O}_2\text{ER} \leq 45\% \) or an \( \text{O}_2\text{ER} \geq 45\% \).

The laboratory results were compared pre and post-transfusion between both groups with the paired student’s T statistical test and statistical significance was considered with \( p < 0.05 \). SPSS version 23.0 was used for Windows.

Results

Thirty patients scheduled for an elective surgical procedure were included, of whom 5 were eliminated due to massive bleeding and 25 patients, 14 men (56%) and 11 women (44%) were followed up (See table 1).

<table>
<thead>
<tr>
<th>Demographic values</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>25</td>
</tr>
<tr>
<td>Age (years)</td>
<td>48.76 ± 16.93</td>
</tr>
<tr>
<td>Size (cm)</td>
<td>164 ± 8.35</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>73.42 ± 13.19</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Female n (%)</td>
<td>11 (44%)</td>
</tr>
<tr>
<td>Male n (%)</td>
<td>14 (56%)</td>
</tr>
</tbody>
</table>

**Table 1:** Demographic characteristics of the patients.

Before the transfusion, 16 patients (64%) presented an \( \text{O}_2\text{ER} \leq 45\% \) with a mean of 26.8 ± 8.06% and 9 patients (36%) reported an \( \text{O}_2\text{ER} > 45\% \) with a mean of 50.07 ± 5.12% (See table 2 and 3). The mean \( \text{Hb} \) in pretransfusion venous blood in the \( \text{O}_2\text{ER} \) group < 45% was 9.2 ± 2.2 g/dL (5.9 g/dL - 12.4 g/dL), while in the \( \text{O}_2\text{ER} \) group > 45%, it was from 8.8 ± 1.7 g/dL (5.6 g/dL - 13.0 g/dL); the mean of the intraoperative bleeding was 600 ml (362 - 787.5 ml) and 700 ml (350 - 1100 ml), respectively. Patients received an average of 1.77 ± 0.59 globular packages (1 - 3 packages); no patient was transfused with whole blood (See table 3).
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<table>
<thead>
<tr>
<th>Variable</th>
<th>O₂ER patients &lt;45% pre-transfusion (n = 16)</th>
<th>O₂ER patients &gt; 45% pre-transfusion (n = 9)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transfused packages</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>6</td>
<td>2</td>
<td>0.134</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Bleeding</td>
<td>600 (362-787.5)</td>
<td>700 (350-1100)</td>
<td>0.487</td>
</tr>
<tr>
<td>O₂ER difference</td>
<td>3.36 (-3.03 - 7.55)</td>
<td>-10.26 (-23.93 - -5.77)</td>
<td>&lt; 0.001*</td>
</tr>
</tbody>
</table>

Table 2: Blood transfusion variables.
*P < 0.05, O₂ER: Oxygen Extraction Index.

The reported post-transfusion results showed a mean of 29.31 ± 9.03% (P = 0.14) and 36.19 ± 8.29% (P = 0.003) for the O₂ER group < 45% and > 45%, respectively, evidencing a statistically significant difference for the second group. Post-venous blood transfusion Hb reported a mean of 10.2 ± 1.5 g/dL, with a minimum concentration of 8.4 g/dL and a maximum of 13.3 g/dL in the O₂ER group < 45% and a mean of 10.2 ± 1.5 g/dL, with a minimum concentration of 8.1 g/dL and a maximum of 11.2 g/dL in the O₂ER group > 45%. The difference in reported hemoglobin levels in pre and post-transfusion venous blood was statistically significant in both groups. Hemoglobin in arterial blood is shown in table 3.

O₂ER patients <45% before blood transfusion (n = 16) O₂ER patients > 45% before blood transfusion (n = 9)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pre-transfusion</th>
<th>Post-transfusion</th>
<th>p</th>
<th>Variable</th>
<th>Pre-transfusion</th>
<th>Post-transfusion</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central venous blood gas</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lactate (mmol/L)</td>
<td>1.75 ± 0.88</td>
<td>2.23 ± 1.14</td>
<td>0.028*</td>
<td>Lactate (mmol/L)</td>
<td>2.23 ± 1.36</td>
<td>2.01 ± 1.03</td>
<td>0.586</td>
</tr>
<tr>
<td>Hb (g/dL)</td>
<td>9.2 ± 2.2</td>
<td>10.2 ± 1.5</td>
<td>0.02*</td>
<td>Hb (g/dL)</td>
<td>8.8 ± 1.7</td>
<td>10.2 ± 1.5</td>
<td>0.004*</td>
</tr>
<tr>
<td>ScvO₂ (%)</td>
<td>75 ± 8.7</td>
<td>72.6 ± 10.9</td>
<td>0.188</td>
<td>ScvO₂ (%)</td>
<td>53.1 ± 5.6</td>
<td>61.8 ± 10.8</td>
<td>0.021*</td>
</tr>
<tr>
<td>Variables calculated</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CvO₂ (ml/dL)</td>
<td>9.28 ± 2.10</td>
<td>9.80 ± 1.97</td>
<td>0.314</td>
<td>CvO₂ (ml/dL)</td>
<td>6.31 ± 0.68</td>
<td>8.52 ± 1.59</td>
<td>0.002*</td>
</tr>
<tr>
<td>CaO₂ (ml/dL)</td>
<td>12.76 ± 2.75</td>
<td>13.99 ± 2.24</td>
<td>0.042*</td>
<td>CaO₂ (ml/dL)</td>
<td>12.73 ± 1.57</td>
<td>13.54 ± 1.39</td>
<td>0.056</td>
</tr>
<tr>
<td>DavO₂ (ml/dL)</td>
<td>3.45 ± 1.44</td>
<td>4.23 ± 1.60</td>
<td>0.014*</td>
<td>DavO₂ (ml/dL)</td>
<td>6.42 ± 1.33</td>
<td>4.90 ± 1.13</td>
<td>0.024*</td>
</tr>
<tr>
<td>O₂ER (%)</td>
<td>26.81 ± 8.06</td>
<td>29.31 ± 9.03</td>
<td>0.14</td>
<td>O₂ER (%)</td>
<td>50.07 ± 5.12</td>
<td>36.19 ± 8.29</td>
<td>0.003*</td>
</tr>
</tbody>
</table>

Table 3: Laboratory variables.
*p < 0.05. ScvO₂: Central Venous Saturation; CvO₂: Mixed Venous Saturation; CaO₂: Arterial Oxygen Concentration; DavO₂: Arterial Venous Oxygen Difference; O₂ER: Oxygen Extraction Index.

Another finding is the increase in ScvO₂ after hemotransfusion when O₂ER is greater than 45% (See table 3). Within lactate levels in the group of patients with O₂ER < 45%, significant changes were observed pre- and post-transfusion, but not in the group with O₂ER > 45%. While DavO₂ presented statistically significant changes before and after the transfusion in both groups (See table 3).
Discussion

In our study we found that the level of $O_2$ER is modified in relation to the $O_2$ER figure prior to hemotransfusion, being more notable when it is above 45% of $O_2$ER. Nasser, et al. found statistically significant differences between $O_2$ER and ScvO2 pre and post-transfusion when $O_2$ER was greater than 40% or 50% but not in the group with $O_2$ER < 40% [20]. Our findings demonstrate that incorporating the $O_2$ER figure in decision-making to initiate hemotransfusion will decrease the need for blood components in surgical patients. Similarly, Sehgal, et al. demonstrated that using $O_2$ER as an indicator of transfusion can potentially reduce the number of blood transfusions; They stated that if they had used an $O_2$ER value of 50% from their study group, only 7 of 41 patients would have been transfused [21]. The main findings of our study are compared with other similar ones in figure 1.

Figure 1: Characteristics of similar studies.

During a surgical procedure, considerable blood loss can occur, which can have repercussions on the patient’s hemodynamic state, reducing $DO_2$, causing hypoxia and, therefore, the need to administer EC [22]. It can be assumed, in a clinical situation in which we have an $O_2$ER value of less than 45% in the absence of organic failure, that affects any system involved in $DO_2$, or in the face of current massive bleeding, there will be no benefit in the administration of hemotransfusion with the aim of increasing oxygen transport to meet metabolic demands, regardless of the hemoglobin level.

We may be faced with a clinical situation in which we find an $O_2$ER within normal parameters (less than 30%) and present tissue hypoxia due to severe alteration of the capacities in oxygen extraction as it can occur in septic patients [23]. EC administration can increase $DO_2$ but would not necessarily increase $VO_2$ [24]. A current problem is the inability to prospectively identify patients who would respond to blood transfusion with increased $VO_2$ [25]. $O_2$ER is a marker of global oxygenation, it does not reflect the oxygen utilization of a specific organ; therefore, it does not rule out the need for hemotransfusion at a low $O_2$ER value.

The present study also evidences a significant increase in ScvO2 when the $O_2$ER value is > 45%. In a prospective observational study by Vallet, et al. In which the correlation between ScvO2 and the recommendations of the French Society of Intensive Care Medicine (Société De Réanimation De Langue Française, SRLF) for blood transfusion was evaluated, the utility of ScvO2 as a physiological parameter for indication of hemotransfusion was demonstrated [26].

Using the ScvO2 obtained by CVC has the advantage that its insertion, has a lower cost and lower inherent risks in the placement compared to a pulmonary artery catheter that is required for the measurement of vSO2. A study by Scheinman, et al. showed that

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there is a good correlation between changes in ScvO₂ and vSO₂; however, this difference increases up to 10% in patients with heart failure or cardiogenic shock [27].

Cardiac output and core body temperature are variables that could not be documented at the time of the study since there were no tools to measure it; they are also factors that would affect O₂ER when modifying DO₂ and VO₂. We will continue investigating, including parameters that help the decision to transfuse a patient.

Conclusion

We conclude based on the results that there is a significant statistical change in O₂ER after EC administration in the intraoperative period when a figure greater than > 45% is presented.

The O₂ER is an additional parameter to the hemoglobin figure, it could be a guide in the decision making to transfuse a patient. The joint use of physiological parameters should replace the arbitrary use of a defined value of hemoglobin as an indicator of hemotransfusion; This could help us by avoiding unwanted adverse effects, promoting the optimized use of blood components and saving in hospital costs [28]. These physiological parameters can be based on signs of global alteration (vSO₂, lactate, O₂ER, excess base) and regional (ST segment alteration on electrocardiogram, near-infrared spectrometry, p300 latency on electroencephalogram) in addition to hemodynamic parameters such as mean arterial pressure, heart rate, and pulse oximetry.

We will continue investigating for other parameters that would be useful in the decision to transfuse a patient.

Conflict of Interests

The authors declare that does not exist an interest conflict.

Ethical Responsibilities

- **Protection of people and animals:** The authors declare that the procedures followed were in accordance with the ethical standards of the responsible human experimentation committee and in accordance with the World Medical Association and the Declaration of Helsinki.

- **Confidentiality of the data:** The authors declare that they have followed the protocols of their workplace regarding the publication of patient data.

- **Right to privacy and informed consent:** The authors declare that no patient data appear in this article.

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