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

Research Article

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Abstract

Introduction:

To establish if there is a relationship between the decrease in the oxygen extraction ratio (O_2ER) and the administration of erythrocyte concentrate (EC) using central venous saturation for the calculation of O_2ER.

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 $O_2ER < 45\%$ and $\geq 45\%$ 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 $O_2ER < 45\%$ with a mean of 26.8 $\pm$ 8.06% without significant change in post-transfusion O_2ER and 9 patients (36%) reported a $O_2ER \geq 45\%$ with a mean of 50.07 $\pm$ 5.12%. having a significant decrease of -10.26 (-23.93 to -5.77) in O_2ER; $p < 0.001$.

Conclusions:

After the transfusion of CE, there was a significant decrease in that of O_2ER in the patients that presented a value $\geq$ 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 thepractice of transfusion medicine, the use of a definedvalue of hemoglobin is frequently used as an indicator of transfusion of erythrocyte concentrate (EC); however, thereis 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 in appropriate for patients with an Hb level> 8 g/dL. Patients should notreceive a transfusionwhenthehemoglobinlevelis≥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.

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 in adequate 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 immuno deficiency virus, hepatitis B, hepatitis C, cytomegalo virus, parvovirus B19, Treponema pallidum, prion diseases, 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 (O_2ER) is the amount of consumed oxygen (VO_2), as a fraction of oxygen availability (DO_2); The latter is a product of cardiac output (CO) and arterial oxygen content (CaO_2). VO_2 is essentially the difference between CaO_2 and venous oxygen content (CvO_2); CvO_2 is mainly determined by Hb concentration and mixed venous oxygen saturation (vSO_2), while CaO_2 is determined by Hb concentration and arterial oxygen saturation (SaO_2) [11]. TheO_2ERnormal valueis 25-30% and isused as a marker for oxygen extraction in tissue, and is expected to increase in the presence of elevated VO_2 or decreased DO_2 [12]. To calculate O_2ER, measurement of mixed venous saturation (vSO_2) 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 venouscatheter (CVC) [13]. $ScvO_2$ is reported to have a lower value than $vSO_2$by approximately 2% to 3%, largely due to the lower rate of oxygen extraction by the kidneys [13]. Although the absolute values differ, thetrends in $ScvO_2$ closely reflect the trends in vSO_2 [14,15].

The hypothesis of this study proposes that the administration of EC will decrease the O_2ER to a greater extent when it is found with a value> 45%. The objective of this prospective observational cohor tstudy is to describe the modification of O_2 ER after globular package administration; which would help us determine a value for 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" 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 O_2ER could be altered. Further more, 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]:

- CaO_2: (Hb X 1.34 X SaO_2) + (arterial PO_2 X 0.0031)
- CvO_2: (Hb X 1.34 X $ScvO_2$) + (central venous PO_2 X 0.0031)
- Da-vO_2: CaO_2 - CvO_2
- O_2ER: (Da-vO_2 / CaO_2) X 100

Where CaO_2 refers to arterial oxygen content, Hb to hemoglobin, 1.34 is the amount of oxygen transported by hemoglobin in mL / g, SaO_2 to arterial oxygen saturation, PO_2 to partial pressure of oxygen, 0.0031 is the solubility of oxygen in plasma at 37 oC reported in ml / mmHg, CvO_2 at venous oxygen content, $ScvO_2$ at central venous saturation, Da-vO_2 at arteriovenous oxygen difference.

O_2ER values were calculated at the time of statistical analysis. The physicians in charge of the case were blinded to the results obtained from the O_2ER at the time of the surgical procedure.

O_2ER of 50% to 60% has been suggested as a critical value that reflects a deficit in oxygensupply [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 O_2ER because it is an early 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 O_2ER<45% or an O_2ER≥ 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%) werefollowedup (Table 1).

Table1: Demographic characteristics of the patients.

Demographicvalues	
Patients	25
Age (years)	48.76 ± 16.93
Size (cm)	164 ± 8.35
Weight(kg)	73.42 ± 13.19
Gender	
Female n (%)	11 (44%)
Male n (%)	14 (56%)

Before the transfusion, 16 patients (64%) presented an O_2 ER<45% with a mean of 26.8 + 8.06% and 9 patients (36%) reported an O_2ER> 45% with a mean of 50.07 + 5.12% (Table2,3). The mean Hb in pretransfusion venous blood in the O_2ER group <45% was 9.2 + 2.2 g/dL (5.9 g/dL - 12.4 g/dL), while in the O_2ER 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 (Table3).

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 O_2ERgroup <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 O_2ER 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 O_2ER group> 45%. The difference in reported hemoglobin levels in pre and post-transfusion venous blood was statistically significant in both groups. Hemoglobin in arterial bloodisshown in (Table3).

Another finding is the increase in $ScvO_2$ after hemotransfusion when O_2ER is greaterthan 45% (Table3). Within lactate levels in the group of patients with O_2ER<45%, significant changes were observed pre- and

Table2: Blood transfusion variables

Variable	$O_2ER_{patients<45\%\ pre\text{-}transfusion\ (n = 16)}$	$O_2ER_{patients>45\%\ pre\text{-}transfusion\ (n = 9)}$	P
Transfusedpackages			
1	6	2	0.134
2	10	5	
3	0	2	
Bleeding	600 (362-787.5)	700 (350-1100)	0.487
O_2ERdifference	3.36 (-3.03 - 7.55)	-10.26 (-23.93 - -5.77)	<0.001*

*P <0.05, O2ER: oxygen extraction index

Table3: Laboratory variables

O_2ERpatients<45% beforebloodtransfusion (n = 16)				O_2ERpatients> 45% beforebloodtransfusion (n = 9)			
Central venousblood gas							
Variable	Pre-transfusion	Post-transfusion	p	Variable	Pre-transfusion	Post-transfusion	p
Lactate (mmol/L)	1.75 ± 0.88	2.23 ± 1.14	0.028*	Lactate (mmol/L)	2.23 ± 1.36	2.01 ± 1.03	0.586
Hb (g/dL)	9.2 ± 2.2	10.2 ± 1.5	0.02*	Hb (g/dL)	8.8 ± 1.7	10.2 ± 1.5	0.004*
$ScvO_2$ (%)	75 ± 8.7	72.6 ± 10.9	0.188	$ScvO_2$ (%)	53.1 ± 5.6	61.8 ± 10.8	0.021*
Variables calculated							
Variable	Pre-transfusion	Post-transfusion	p	Variable	Pre-transfusion	Post-transfusion	p
CvO_2 (ml/dL)	9.28 ± 2.10	9.80 ± 1.97	0.314	CvO_2 (ml/dL)	6.31 ± 0.68	8.52 ± 1.59	0.002*
CaO_2 (ml/dL)	12.76 ± 2.75	13.99 ± 2.24	0.042*	CaO_2 (ml/dL)	12.73 ± 1.57	13.54 ± 1.39	0.056
$DavO_2$(ml/dL)	3.45 ± 1.44	4.23 ± 1.60	0.014*	$DavO_2$(ml/dL)	6.42 ± 1.33	4.90 ± 1.13	0.024*
$O_2ER_{(}$%)	26.81 ± 8.06	29.31 ± 9.03	0.14	O_2ER(%)	50.07 ± 5.12	36.19 ± 8.29	0.003*

*p <0.05. $ScvO_2$: central venous saturation; CvO_2:mixed venous saturation; CaO_2: arterial oxygen concentration; $DavO_2$: arterial venous oxygen difference; O_2ER: oxygen extraction index

post-transfusion, but not in the group with $O_2ER \geq 45\%$. While $DavO_2$ presented statistically significant changes before and after the transfusion in both groups(Table3).

Discussion

In our study we found that the level ofO_2ER ismodified in relation to the O_2ER figure prior to hemotransfusion, being more notable when it is above 45% of O_2ER. Nasser et al., found statistically significant differences between O_2ER and ScvO2 pre and post-transfusion when O_2ER was greater than 40% or 50% but not in the group with $O_2ER<40\%$ [20]. Our findings demonstrate that incorporating the O_2ER 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_2ER as an indicator of transfusion can potentially reduce the number of blood transfusions; They stated that if they had used an O_2ER value of 50% from their study group, only 7 of 41 patients would have been transfused [21]. The main findings of ourstudy are compared with other similar ones in (Figure 1).

During a surgical procedure, considerable blood loss can occur, which can have repercussions on the patient's hemodynamic state, reducing DO_2, causinghypoxia and, therefore, theneedtoadminister EC [22]. It can be assumed, in a clinical situation in which we have an O_2ER 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_2ER within normal parameters (less than 30%) and present tissue hypoxia due to severe alteration of the capacities in oxygenextraction as it can occurin

Figure 1. Characteristics of similar studies

Study	Orlov et al						Nasser et al.						Elizondo et al.					
Characteristic	Adult patients for non-emergent cardiac surgery who required cardiopulmonary bypass						Children for curative or palliative cardiac surgery and with blood transfusion in the postoperative period of the cardiac intensive care surgical unit						Surgical patients from 18 to 65 years in the transoperative period for mayo surgery of medium to high risk					
Population	$O_2ER \leq 30\%$ prior to transfusion (n= 35)			$O2ER > 30\%$ (n = 27) prior to transfusion			$O_2ER \leq 40\%$ (n = 75) prior to transfusion			$O_2ER < 40\%$ (n = 28) prior to transfusion			$O_2ER < 45\%$ (n = 16) prior to transfusion			$O_2ER \geq 45\%$ (n = 9) prior to transfusion		
Variables	Pre transfusion	Post transfusion	P value	Pre transfusion	Post transfusion	P value	Pre transfusion	Post transfusion	P value	Pre transfusion	Post transfusion	P value	Pre transfusion	Post transfusion	P value	Pre transfusion	Post transfusion	P value
Hb	78.3 ± 16.7 g/L	88.5 ± 22.3 g/L	NS	78.1 ± 7.6 g/L	87.0 ± 8.3 g/L	NS	9.3 ± 1.1 (g/dL)	12 (1.5) (g/dL)	.0001*	9.03 ± 1.1 (g/dL)	11.8 ± 1.4 (g/dL)	.0001*	9.2 ± 2.2 (g/dL)	10.2 ± 1.5 (g/dL)	0.02*	8.8 ± 1.7 (g/dL)	10.2 ± 1.5 (g/dL)	.004*
Lactate (mmol/L)	No data						1.9 ± 0.2	1.6 ± 0.2	.3	1.7 ± 0.2	1.4 ± 0.1	.18	1.75 ± 0.88	2.23 ± 1.14	.028*	2.23 ± 1.36	2.01 ± 1.03	.586
ScvO2 (%)	No data						67.5 ± 1.4	67.5 ± 1.2	1	51.3 ± 1.8	58.9 ± 2	.0065*	75 ± 8.7	72.6 ± 10.9	.188	53.1 ± 5.6	61.8 ± 10.8	.021*
O_2ER (%)	23.1 ± 4.9	23.9 ± 7.8	<.001*	39.8 ± 9.0	33.4 ± 10.2	<.001*	25.0 ± 9.6	25.8 ± 9.8	.6	46 ± 4.7	36.4 ± 9.5	.0001*	26.81 ± 8.06	29.31 ± 9.03	0.14	50.07 ± 5.12	36.19 ± 8.29	.003*

Hb = hemoglobin, NS = not significant, ScvO2 = central venous saturation, O_2ER = oxygen extraction index

septicpatients [23]. ECadministration 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 transfusión with in creased VO_2 [25]. O_2ER 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_2ER value.

The present study also evidences a significant increase in $ScvO_2$ when the O_2ER value is> 45%. In a prospective observational study by Vallet et al. In which the correlation between $ScvO_2$ 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 $ScvO_2$ obtained by CVC has the advantage that its insertion is easier, has a lower cost and lower inherent risks in the placement compared to a pulmonary artery catheter that is required for the measurement of vSO_2. A studyby Scheinman et al., showed that there is a good correlation between changes in $ScvO_2$ and vSO_2; however, this difference increases up to 10% in patients With heartfailure 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 O_2ER when modifying DO_2 and VO_2. We will continue investigating, including parameters that help the decisión to transfuse a patient.

Conclusions

We conclude based on the results that there is a significant statistical change in O_2ER after EC administration in the intraoperative period when a figure greater than> 45% is presented.

The O_2ER 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 bloodcomponents and saving in hospital costs [28]. These physiological parameters can be based on signs of global alteration (vSO_2, lactate, O_2ER, 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, heartrate, and pulse oximetry. We Will continue investigating for other parameters that would be useful in the decision to transfuse a patient.

Ethical Responsibilities

Protection of people and animals: Theauthors 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: Theauthors declare that they have followed the protocols of their workplace regarding the publication of patient data.

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Righttoprivacy and informedconsent: Theauthors declare that no patient data appear in this article.

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