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## ORIGINAL RESEARCH

### Blood transfusion and oxygen extraction ratio in patients admitted to the general intensive care unit: A quasi experimental study



#### *Transfusion sanguine et ratio d'extraction de l'oxygène chez des patients admis en unité de soins intensifs généraux: Une étude quasi expérimentale*

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**Introduction:** Blood transfusion is commonly undertaken in critically ill patients; and studies have suggested the use of oxygen extraction ratio (O<sub>2</sub>ER) as an additional transfusion trigger in critically ill patients. The aim of this study was to establish the relationship between blood transfusion and oxygen extraction ratio in adult patients admitted to the general intensive care unit, using central venous oxygen saturation instead of mixed venous oxygen saturation.

**Methods:** Arterial and central venous blood samples were drawn and a blood gas analysis immediately before commencement of blood transfusion was undertaken. At least 15 min after completion of the transfusion, similar samples were drawn and the blood gas analysis was repeated. The O<sub>2</sub>ER before and after transfusion was then calculated. Using paired student's *t*-test, we checked whether the mean difference between the two O<sub>2</sub>ERs was statistically significant.

**Results:** We enrolled 58 patients in the study, the mean ( $\pm$ SD) haemoglobin concentration before transfusion was 7.38 g/dl ( $\pm$  1.71). The mean change in haemoglobin concentration following blood transfusion was 2.29 g/dl ( $\pm$  1.18), after transfusing an average of 1.95 ( $\pm$  0.83) units of packed cells. Mean O<sub>2</sub>ER was 0.27 ( $\pm$  0.11) before, and 0.25 ( $\pm$  0.12) after RBC transfusion. The mean change in O<sub>2</sub>ER was  $-0.018$  SD  $\pm$  0.10 (95% CI,  $-0.043$ – $0.007$ ;  $P = 0.15$ ). Linear regression analysis showed no statistically significant relationship between change in haemoglobin concentration and change in O<sub>2</sub>ER;  $p$ -value = 0.12.

**Discussion:** The change in oxygen extraction ratio was not statistically significant following blood transfusion in adult patients admitted to the general ICU at a tertiary teaching hospital. Further studies are required especially in patients with increased pre transfusion O<sub>2</sub>ER to evaluate the usefulness of this measurement as a possible transfusion trigger.

**Introduction:** La transfusion sanguine est effectuée de façon courante chez les patients en état critique ; et des études ont suggéré l'utilisation du ratio d'extraction de l'oxygène (REO<sub>2</sub>) comme déclencheur supplémentaire d'une transfusion chez les patients en état critique. Le but de cette étude était de déterminer le lien entre transfusion sanguine et ratio d'extraction de l'oxygène chez les patients adultes admis en unité de soins intensifs généraux en utilisant la saturation veineuse centrale en oxygène au lieu de la saturation veineuse mixte en oxygène.

**Méthodes:** Des échantillons sanguins artériels et veineux centraux ont été prélevés et une analyse des gaz du sang a été effectuée juste avant le commencement de la transfusion sanguine. Au moins 15 min après l'achèvement de la transfusion, des échantillons similaires ont été prélevés et l'analyse des gaz du sang à nouveau effectuée. Le REO<sub>2</sub> avant et après la transfusion a ensuite été calculé. En utilisant des tests de Student appariés, nous avons vérifié si la différence moyenne entre les deux REO<sub>2</sub> était statistiquement significative.

**Résultats:** Nous avons inclus 58 patients dans l'étude, le taux moyen ( $\pm$ écart-type) d'hémoglobine avant la transfusion était de 7.38 g/dl ( $\pm$  1.71). Le changement moyen de taux d'hémoglobine à la suite de la transfusion sanguine était de 2.29 g/dl ( $\pm$  1.18), après avoir transfusé une moyenne de 1.95 ( $\pm$  0.83) unités de globules concentrés. Le REO<sub>2</sub> moyen était de 0.27 ( $\pm$  0.11) avant, et de 0.25 ( $\pm$  0.12) après la transfusion de globules rouges. Le changement moyen de REO<sub>2</sub> était de  $-0.018$ , l'écart-type de  $\pm$  0.10 (intervalle de confiance de 95%,  $-0.043$ – $0.007$ ;  $P = 0.15$ ). Une analyse de régression linéaire n'a montré aucun lien statistiquement significatif entre le changement du taux d'hémoglobine et le changement de REO<sub>2</sub>;  $p = 0.12$ .

**Discussion:** Le changement du ratio d'extraction de l'oxygène suite à une transfusion sanguine n'était pas statistiquement significatif chez les patients adultes admis aux soins intensifs généraux dans un centre hospitalier universitaire. Des études supplémentaires sont nécessaires surtout chez les patients dont le REO<sub>2</sub> avant la transfusion a augmenté afin d'évaluer l'utilité de cette mesure comme déclencheur possible d'une transfusion.

#### African relevance

- Minimising unnecessary blood transfusion by using accurate transfusion triggers may ensure appropriate use of a scarce resource.
- Samples from central venous catheters can be used to measure central venous oxygen saturation.
- Oxygen extraction ratio is a useful, additional transfusion trigger to haemoglobin when deciding on blood transfusion.

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## Introduction

Little is known about oxygen extraction ratio and its relationship with anaemia and red blood cell (RBC) transfusion, as well as its ability to potentially supplement haemoglobin (Hb) concentration as a transfusion trigger. Oxygen extraction ratio ( $O_2ER$ ) is the amount of oxygen consumed ( $VO_2$ ), as a fraction of oxygen delivered ( $DO_2$ ); the latter being a product of cardiac output (CO) and arterial oxygen content ( $CaO_2$ ).<sup>1</sup>  $VO_2$  is essentially the difference between  $CaO_2$  and venous oxygen content ( $CvO_2$ );  $CvO_2$  being determined mainly by the Hb concentration and mixed venous oxygen saturation ( $SvO_2$ ), while  $CaO_2$  is determined by Hb concentration and arterial oxygen saturation ( $SaO_2$ ).<sup>1</sup> Orlov et al. examined temporal changes in Hb concentration and  $O_2ER$  following RBC transfusion post cardiac surgery with cardiopulmonary bypass, and suggested that;  $O_2ER$ , a readily available index of systemic oxygenation may be used to supplement Hb concentration as a RBC transfusion trigger.<sup>2</sup>

Oxygen extraction ratio is used as a marker for tissue oxygen extraction, and is expected to increase in the presence of either increased  $VO_2$  or decreased  $DO_2$ . A reduction in  $DO_2$  may be due to decreased  $CaO_2$  from anaemia and/or low  $SaO_2$ , while an increase in  $VO_2$  may be due to stress, fever, shivering and pain.<sup>2,3</sup> Studies have shown that oxygen extraction ratio can be used to supplement haemoglobin concentration as a trigger for blood transfusion in ICU patients<sup>4,5</sup>; however, for purposes of measuring  $SvO_2$ , these studies involved placement of a Swan-Ganz catheter which requires technical expertise. In addition, the benefit of inserting a Swan-Ganz catheter in critically ill patients is still questionable.<sup>6</sup>

To the best of our knowledge, no published study has investigated the value of using blood samples from the central venous catheter to measure central venous oxygen saturation ( $ScvO_2$ ) for purposes of calculating the oxygen extraction ratio; despite oxygen saturations in this samples showing good correlation with those from the pulmonary artery ( $SvO_2$ ), drawn via the pulmonary artery catheter.<sup>6-8</sup>

The purpose of our study therefore, was to investigate how blood transfusion affects  $O_2ER$  in adult patients admitted to the general ICU at a tertiary teaching hospital; using  $ScvO_2$  instead of  $SvO_2$  in the calculation of  $O_2ER$ .

## Methods

The study was undertaken in the ICU at the Aga Khan University hospital, Nairobi; between July 2011 and January 2012. We obtained written approval from the institution's research and ethics committee followed by written informed consent from patients themselves whenever possible; or from the next of kin as indicated in the hospital records; and in adherence to the declaration of Helsinki. The study was funded by the postgraduate medical education programme through the department's budget. Patients were included if they underwent blood transfusion (packed red blood cells or whole blood), were aged above 18 years and a written informed consent was given, had a mean arterial blood pressure (MAP) not less 65 mmHg and an hourly urine output of at least 0.5 mls/kg. The exclusion criteria included age below 18 years, MAP below 65 mmHg, oliguria, on-going haemorrhage, congestive

heart failure, carbon monoxide or cyanide poisoning and shock of any origin. Since there are no blood transfusion protocols in place, the attending physician for each patient made all RBC transfusion decisions; based on his or her own judgement. Patient's age, gender and physiological parameters (temperature, mean arterial blood pressure, heart rate and central venous pressure) were collected in all study patients as per protocol.

The number of units of blood (packed cells or whole blood) transfused per study patient during the study period was recorded. The reasons for the blood transfusion, the Hb concentration and  $O_2ER$  immediately before and a minimum of 15 min after the end of the blood transfusion were subsequently recorded.<sup>9,10</sup> If a patient was scheduled to receive more than 1 unit of packed cells, the Hb and  $O_2ER$  were recorded immediately before commencing the first unit and at least fifteen minutes after completion of the last unit.

To calculate  $O_2ER$ , blood gas analysis on samples obtained from indwelling arterial and central venous catheters was undertaken. The primary outcome was the change in  $O_2ER$  following blood transfusion; while our secondary outcomes were: how the APACHE II score on admission correlated with the change in  $O_2ER$  after blood transfusion and the effect of haemoglobin concentration on  $O_2ER$ .

All blood samples were analysed using the blood gas analyser located in a centralised room within the ICU (RADIOMETER COPENHAGEN ABL-800 BASIC). The study was registered with the pan African clinical trials register; PACTR: 201109000317141.

We determined that a sample size of 58 patients undergoing blood transfusion would be sufficient to estimate the mean percentage (%) change in oxygen extraction ratio within  $\pm 2$  of the true value with 95% confidence.<sup>2</sup> Data analysis was undertaken using the SPSS statistics 17.0 software (IBM Corporation). The oxygen extraction ratio before and after transfusion was compared using paired student's *t*-test, while linear regression analysis was used to analyse the relationship between changes in haemoglobin concentration and oxygen extraction ratio. Data are presented as mean  $\pm$  standard deviation unless otherwise specified, and a *p*-value < 0.05 was considered to be statistically significant.

## Results

A total of fifty-eight patients were included in the study; 36 (62.1%) were non-surgical patients while 22 (37.9%) were surgical (post-operative). The patient's baseline characteristics are summarised in Table 1. Measured clinical variables pre and post blood transfusion are summarised in Table 2.

The mean haemoglobin concentration before blood transfusion was 7.37 g/dl (SD 1.71) with the lowest being 3 g/dl and the highest being 14 g/dl. Post blood transfusion, the mean haemoglobin concentration was 9.67 g/dl (SD 1.68), with the lowest being 5 g/dl and the highest being 15 g/dl. The average number of packed red blood cell units transfused per patient was 1.95 (with a range between 1 and 5 units); no patient was transfused with whole blood. The mean change in haemoglobin concentration was 2.29 g/dl (SD 1.18). The lowest increase in haemoglobin concentration was by 1 g/dl while the highest increase in haemoglobin concentration was by 6 g/dl. The mean (SD = 0.10) difference in the pre and post

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