

Red Cell Transfusion Practices and the Impact of Phlebotomy in an Adult Intensive Care Unit in Trinidad

A Prospective Observational Study

N Bedayse, S Hariharan, D Chen

ABSTRACT

Objectives: To determine the pattern of current red cell transfusion practices in an adult intensive care unit (ICU) in Trinidad and the impact of phlebotomy on transfusions.

Methods: A prospective observational study was conducted over a six-month period to include all patients who received transfusions in the ICU of Port-of-Spain General Hospital, Trinidad. Demographic data including age, gender and weight were recorded. Clinical data recorded were the admission APACHE II scores, daily phlebotomy volumes, haemoglobin levels, transfusions and outcome during the first thirty days following ICU admission. Patients were grouped according to diagnoses and transfusion patterns.

Results: Of 134 patients admitted, 40 (29.8%) were transfused packed red cells 18 (29%) of the requests were for single unit transfusion. The mean phlebotomy volume was 13.5 ± 4.3 (SD) mL day. The adjusted phlebotomy volume to body weight did not correlate with the amount of transfusions.

The mean haemoglobin level for triggering blood transfusion was 6.73 g dL. The mean transfusion rate was 2.9 ± 1.8 (SD) units per patient. Ten per cent of the patients received more than 5 units. Twenty nine per cent of the units were transfused on the first day of ICU admission and 69% were transfused during the first week of ICU stay.

Conclusions: Transfusion practices in the study ICU pointed towards a restrictive strategy, although there were some inappropriate transfusions. The phlebotomy volumes did not contribute towards transfusion requirements.

Keywords: ICU transfusions, phlebotomy, developing country

La Práctica de la Transfusión de Glóbulos Rojos y el Impacto de la Flebotomía en una Unidad del Cuidados Intensivos para Adultos en Trinidad

Un Estudio Observacional Prospectivo

N Bedayse, S Hariharan, D Chen

RESUMEN

Objetivos: Determinar el patrón de las prácticas actuales de transfusión de glóbulos rojos en una Unidad de Cuidados Intensivos (UCI) para adultos en Trinidad y el impacto de la flebotomía en las transfusiones.

Métodos: Se llevó a cabo un estudio observacional prospectivo por un periodo de seis meses, que incluyó a todos los pacientes que recibieron transfusiones en la UCI del Hospital General de Puerto España, Trinidad. Se registraron los datos demográficos, incluyendo edad, género y peso. Los datos clínicos recogidos fueron las puntuaciones APACHE II a la hora del ingreso, los volúmenes de flebotomía diarios, los niveles de hemoglobina, las transfusiones y el resultado durante los primeros treinta días tras el ingreso a la UCI. Los pacientes fueron agrupados según los diagnósticos y patrones de transfusión.

From: Anaesthesia and Intensive Care Unit, Faculty of Medical Sciences, The University of the West Indies, St Augustine, Trinidad and Tobago, West Indies.

Correspondence: Dr S Hariharan, Anaesthesia and Intensive Care, Faculty of Medical Sciences, The University of the West Indies, St Augustine, Eric Williams Medical Sciences Complex, Mount Hope, Trinidad, West Indies. Fax: (868) 662-4030, e-mail: uwi.hariharan@gmail.com

Resultados: De 134 pacientes ingresados, a un total de 40 (29.8%) se les transfundió glóbulos rojos empaquetados; 18 (29%) de las solicitudes fueron para una transfusión de una sola unidad. El volumen promedio de flebotomías fue 13.5 ± 4.3 (SD) mL/día. El volumen de flebotomía ajustado al peso del cuerpo no guardaba correlación con la cantidad de transfusiones.

El nivel promedio de hemoglobina para realizar la transfusión de sangre fue 6.73 g/dL, la tasa promedio de transfusión fue 2.9 ± 1.8 (SD) unidades por paciente. El diez por ciento de los pacientes recibió más de 5 unidades. El veintinueve por ciento de las unidades fueron transfundidas en el primer día de admisión a la UCI, y el 69% se transfundió durante la primera semana de estancia en la UCI.

Conclusiones: Las prácticas de la transfusión en la UCI de estudio, apuntaron hacia una estrategia restrictiva, aunque hubo algunas transfusiones impropias. Los volúmenes de flebotomía no contribuyeron a los requisitos de la transfusión.

Palabras claves. Transfusiones en la UCI, flebotomía, país en vías de desarrollo

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INTRODUCTION

Red cell transfusion in critically ill patients has long been an area of controversy. The trigger for transfusion based on a haemoglobin (Hb) concentration has been repeatedly questioned by clinical studies (1, 2). The logic of transfusing a patient based on a value rather than signs and symptoms of anaemia has been the main subject of dispute. The Canadian Transfusion Requirements in Critical Care (TRICC) trial found that a conservative transfusion strategy (at Hb 7 g/dL) was as effective and possibly superior to a liberal transfusion strategy (at Hb10 g/dL). The CRIT study (Anaemia and blood transfusion in the critically ill – current clinical practice in the United States of America) observed that the number of red blood cell units transfused is an independent predictor of worse clinical outcome (2). Patients who received transfusions had longer ICU stays, increased mortality and were more likely to experience complications related and unrelated to transfusions. Using propensity scores for a subgroup of patients with nadir haemoglobin of < 9.0 g/dL, the study found that red cell transfusion was associated with an increased risk of death.

However, the most recent ‘Sepsis Occurrence in Acutely ill Patients’ (SOAP) study evaluating hundreds of ICUs across Europe reported that blood transfusion has not been associated with an increase in mortality (3).

Critically ill patients may experience blood loss due to a variety of reasons. A surgical patient may have continued bleeding from the operative site. Routine procedures during intensive care therapy such as placement of invasive lines eg central venous and arterial catheters, changing the urinary catheter in a patient with urethral or bladder trauma or even change of dressing, may be associated with significant blood loss. Critically ill patients are also at the risk of developing stress ulcers that may cause significant bleeding. Phlebotomy for routine and specialized laboratory investigations also contributes to the blood loss. Comorbid illnesses in ICU patients may also contribute to anaemia and may have a greater impact on the hospital mortality and morbidity (4).

Although the term ‘transfusion trigger’ is commonly used, the implication of this terminology has been questioned (5). Since the publication of the trials documenting no added benefits of liberal transfusion in the ICU patients, there appears to be a change in the clinical practice. A recent survey of transfusion practices found that more clinicians prefer to transfuse at a lower ‘transfusion trigger’ (6). This seems to be true for even patients with ischaemic heart disease in ICU, as reported by a recent Scottish study, which concluded that only small adjustments in transfusion triggers were made for these patients (7).

Most of the studies regarding transfusions in ICU have been published from the developed world and few have been reported from the ICUs of the developing world. With this background, the present study was conducted to determine the current red cell transfusion practices in an adult multi-disciplinary ICU of a University teaching Hospital in Trinidad, West Indies, and evaluate the relationship between phlebotomy and red cell loss and transfusions.

SUBJECTS AND METHODS

Approval of the Ethics Committee of the University of the West Indies, St Augustine, Trinidad, was obtained prior to the study. The Institutional Review Board of the Port-of-Spain General Hospital also approved the study. The study was a prospective observational, cross-sectional analysis to include all patients who had blood transfusions during the time period from September 2005 to February 2006 (six-month period) in the ICU of the Port-of-Spain General Hospital, Trinidad.

Hospital setting

Trinidad and Tobago is a twin-island nation of the English-speaking Caribbean, with a population of 1.3 million. The Port-of-Spain General Hospital is one of the three major public hospitals in Trinidad, affiliated to the University of the West Indies. The ICU at the Port-of-Spain General Hospital is a 10-bed open unit admitting adult medical and surgical

patients. The ICU has state-of-the-art equipment facilitating a wide range of therapeutic interventions and investigations including facilities for blood gas analyses, portable radiograph, ultrasound and fiberoptic scopes *etc.* Most of the patients admitted to the ICU have invasive lines which include arterial and a central venous line. Two House Officers and a Specialist Registrar take care of patients under the supervision of a Consultant Anaesthetist.

Data collection

All patients who received blood transfusions during the first 30-day stay in ICU were included for data collection which was done on a daily basis. Case notes were examined and demographic data such as age, weight, gender and ethnicity of the patients were recorded. Further clinical data including Acute Physiology and Chronic Health Evaluation (APACHE) II score on admission to assess the severity of illness, diagnoses on admission, co-morbid illnesses and the daily haemoglobin level were collected.

The amount of blood withdrawn for investigations from each patient was recorded on a daily basis. In the ICU every morning, samples are taken for complete blood count (3 mL), urea and electrolytes (2 mL), random blood sugar (2 mL) and arterial blood gas analysis (1 mL). Most samples are usually taken from the arterial line except for prothrombin time/partial thromboplastin time (PT/PTT) and blood culture which are taken from separate venous sites by phlebotomy. Other than the above routine ones, any additional blood investigations done on the patients were also noted with regards to the volume of blood withdrawn.

Details regarding transfusions received by patients during the first 30-day stay in ICU were recorded. The indications for transfusion, the number of units transfused and the total volume were recorded. The outcome of patients at the end of the first 30 days following admission was recorded.

For the purpose of analysis, the patients were divided into the following groups *post hoc*:

- * Septic and non-septic patients
- * Surgical or non-surgical patients
- * Survivors and non-survivors

Patients were also grouped according to the Canadian Transfusion Requirements in Critical Care (TRICC) trial (1):

- * Liberal transfusion group, when they received transfusions for diagnoses such as anaemia with low platelets, anaemia with known coronary artery disease, bleeding without anaemia and for unsure reasons.
- * Restricted transfusion group, when they were transfused for anaemia of critical illness, anaemia with sepsis, preoperative anaemia, anaemia requiring renal replacement therapy and anaemia with bleeding.

Descriptive analyses of all data were done. Independent *t* test was used to compare interval scale data between groups of patients. Mann-Whitney U test was used for comparison of APACHE II scores and predicted mortality between survivors and the non-survivors as well as septic and non-septic patient groups. Statistical significance was fixed at the level of $p < 0.05$. The Statistical Package for Social Sciences (SPSS)TM – version-12.0 (Chicago IL, USA) software was used to analyse the data.

RESULTS

During the six-month period of study, a total of 134 patients were admitted to the ICU. Of these patients, 40 patients (29.8%) received blood transfusions during the first 30 days of their stay in ICU. Since data regarding haemoglobin values and phlebotomy volumes were collected on all these patients from the day of admission to the day of discharge/death during the first 30-days, a total of 742 patient-days were encountered.

The demographic data of the transfused patients are shown in Table 1. Overall 23 (57.5%) were females and the

Table 1: Demographic data of transfused patients

Gender	Male	17 (42.5)
n (%)	Female	23 (57.5)
Age (years)	Male	46 (20)
Mean (SD)	Female	47 (14)
Ethnicity	African	17 (42.5)
n (%)	Indian	15 (37.5)
	Mixed	7 (17.5)
	Caucasian	1 (2.5)

ages between the gender were comparable. The diagnostic categories of patients are shown in Fig. 1, respiratory illnesses being the most common reason for ICU admission.

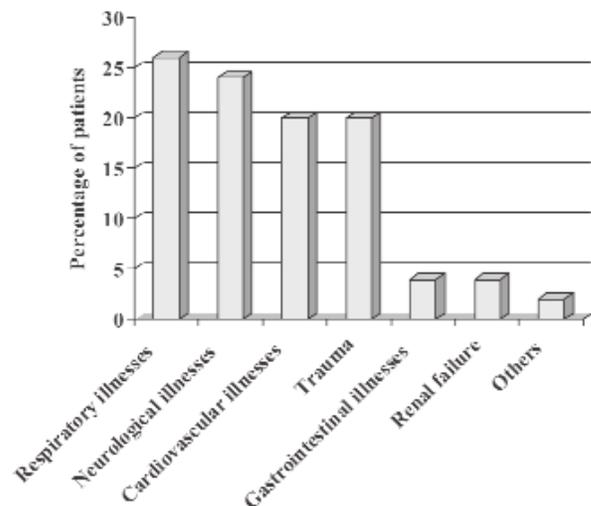


Fig. 1: ICU admission categories

A total of 117 units were transfused to the patients during the study period. Twenty-nine per cent of the requests for blood transfusion were for 'single-unit' packed red cells. The mean transfusion rate was 2.9 ± 1.8 (Standard Deviation, SD) units per patient. Ten per cent of the patients received more than 5 units during their ICU stay. Twenty-nine per cent of the units were transfused on the first day of ICU admission and 69% were transfused during the first week of ICU stay. The overall mean transfusion trigger of haemoglobin was 6.73 g dL. The indications for transfusion, mean trigger for transfusion and the number of units transfused are shown in Table 2.

Table 2: Indications for transfusion, haemoglobin and number of units transfused

Indications	Number	Haemoglobin	Number of units transfused n (%)
		(g dL) Mean (SD)	
Anaemia of critical illness	11	6.6 (1.1)	58 (49.6)
Suspected bleeding	4	11.6 (2.5)	19 (16.3)
No reason recorded	7	9.1 (4.0)	11 (9.4)
Anaemia with sepsis	5	6.0 (1.4)	8 (6.8)
Preoperative anaemia	5	7.1 (0.8)	7 (6.0)
Anaemia due to blood loss	2	9.6 (3.9)	4 (3.4)
Anaemia with renal failure requiring RRT	3	6.8 (1.6)	4 (3.4)
Anaemia with ischemic heart disease	2	7.3 (0.3)	4 (3.4)
Anaemia with low platelets	1	7.3	2 (1.7)

RRT = renal replacement therapy

Twenty-five surgical patients received transfusions, compared to 15 non-surgical patients. The baseline haemoglobin concentration and daily phlebotomy volumes were similar in both groups. Among the patients transfused, there were 25 with sepsis. Eighty-six per cent of the non-surgical patients had sepsis as compared to 48% of surgical patients. The patients with sepsis had significantly lower baseline haemoglobin when compared to non-septic patients. However, the daily haemoglobin, phlebotomy volumes and the amount of packed cells transfused were comparable.

A relatively restrictive pattern of transfusion was followed in 77% of cases. There was a statistically significant difference between the mean haemoglobin levels at which blood was transfused according to the restrictive and

liberal strategies. The comparisons between groups are shown in Table 3.

Table 3: Transfusion details in groups of patients

Group of patients	Baseline haemoglobin (g dL) mean (SD)	Daily haemoglobin (g dL) mean (SD)	Units transfused mean (SD)	Phlebotomy volume (mL) mean (SD)
Surgical (n = 25)	10.1 (3.0)	9.0 (1.7)	3.3 (2.0)	13.7 (4.0)
Non-surgical (n = 15)	11.1 (3.4)	9.0 (1.3)	2.1 (0.8)	13.2 (4.5)
Septic (n = 25)	9.6 (3.3)	8.7 (1.1)	2.5 (1.7)	13.4 (3.5)
Non-septic (n = 15)	11.9 (2.5)*	9.4 (2.1)	3.5 (1.8)	13.6 (5.2)
Restrictive (n = 31)	6.7 (1.4)	7.8 (1.4)	3.2 (1.6)	15.4 (6.6)
Liberal (n = 9)	9.4 (3.4)†	9.2 (1.3)	2.9 (1.9)	13.3 (3.9)

* $p = 0.02$, when compared to septic patients by t-test

† $p < 0.05$, when compared to restrictive group by t-test

The mean APACHE II score of the septic patients (22.7) was not significantly different from that of the non-septic group (16.9) as determined by Mann-Whitney U test. The mean APACHE II score and predicted mortality was not significantly different between survivors and non-survivors as determined by Mann-Whitney U test (p value = 0.86). Also, there were no statistically significant differences between the haemoglobin levels and the amount of transfusions between survivors and non-survivors.

The overall mean phlebotomy volume was 13.5 ± 4.3 (SD) mL. The mean volume of red cells transfused was 308 ± 14 mL per patient. Data were analysed to determine if larger phlebotomy volumes in patients with lesser body-weight would influence transfusion requirements. The mean phlebotomy volume was divided by patient weight to get an adjusted phlebotomy factor (mL kg) and no significant correlation was found between transfusions and the adjusted phlebotomy factor.

For the entire hospital, during the year 2005, the blood bank received requests for 14 710 units, of which only 7101 (48.3%) units were cross-matched and transfused. The ICU requested 472 (3% of the total) units in the same year, of

Table 4: APACHE II and 30-day mortality in transfused patients

Variables	Number	Number of units transfused mean (SD)	Haemoglobin (g dL) mean (SD)
APACHE II < 20	32	2.8 (1.9)	9.2 (1.6)
APACHE II ≥ 20	8	3.3 (1.7)	8.2 (1.1)
30-day mortality Died	22	2.7 (1.9)	9.1 (1.7)
30-day mortality Survived	18	3.2 (1.7)	8.8 (1.4)

APACHE II: Acute Physiology and Chronic Health Evaluation (II) Score

which 291 (61.7%) were transfused. Hence the ICU was responsible for 4% of the total transfusions in the hospital.

DISCUSSION

The major finding of the present study is the overall lower rate of transfusion in the study ICU, although there were instances of inappropriate transfusions. The transfusion rate of the present study is less than that of the CRIT trial and closer to that of the restrictive group of the TRICC trial (1, 2).

The mean pre-transfusion haemoglobin was less than 7.0 g·dL⁻¹. Restrictive transfusion practice accounted for the majority of the transfusions in the ICU during the study period. Only 13% of the transfusions were given according to the liberal strategy, for indications such as anaemia with low platelets and unsure indications. Similarly, the proportion of single-unit transfusions within the first 30 days of ICU was less than the follow-up study to the TRICC trial (29% versus 56%) (6). All these facts may suggest that the study ICU may be adopting restrictive transfusion practices. A recent study has proposed, by a simulation model, that restrictive transfusion practice in ICU improves the quality of care and cost savings (8).

The lower transfusion trigger in the present study may reflect the adherence to the current evidence based recommendations which suggest that the lower haemoglobin concentration is a physiological adaptation that may benefit the critically ill patient. In fact, the practice of liberal transfusion is associated with adverse outcomes such as higher incidence of blood-stream infections in ICU patients (9). However, the apparent lower transfusion trigger in our setting may also be attributed to a combination of difficulty in getting donors and scarcity of banked blood in the study hospital.

Studies suggest that 40–50% of transfusions occur in the first week of critical illness (10). In the present study, the first week accounted for 69% of transfusions and 45% of patients were transfused within the first two days of ICU admission.

There was the practice of red cell transfusion for anaemia with thrombocytopenia, although there was no documentation of ongoing bleeding. For a critically ill patient even with ongoing bleeding, clinical assessment of impaired oxygen delivery is necessary before red-cell transfusion is recommended. Also, there were no platelet transfusions in the study ICU during the study-period. Platelet transfusions should be considered only if counts are $\leq 5 \times 10^9 \text{ L}^{-1}$ regardless of apparent bleeding and when counts are $5\text{--}30 \times 10^9 \text{ L}^{-1}$ if there is a significant risk of bleeding (11).

Also in the present study, 11% of patients (with a mean pre-transfusion haemoglobin of 9.06 g·dL⁻¹) received red cell transfusions without a clear indication. Frequently, there is a time-lag between the decision to transfuse, request being sent to blood-bank, arranging donors, cross-matching and receiving packed red cells for transfusion. Even though the patient's haemoglobin level might have changed during this

time-period, the requested units were often transfused just because they were made available, without considering the therapeutic benefit and the risks of transfusions. A computerized physician entry may assist to avoid inadvertent transfusions (12). Nevertheless, the number of inappropriate transfusions in the present study compares favourably with previous studies which report ranges from 4% to as high as 57% (1, 2).

The mean daily phlebotomy volume in the present study (13.5 mL) was less than those quoted in previous studies [65 mL per day] (13). A previous study documented a mean daily phlebotomy volume of 41 mL which had a significant positive correlation to organ dysfunction (14). In the present study, none of the patients was phlebotomized more than one unit of blood (450 mL) within the first 30 days in ICU. Hence phlebotomy losses were unlikely to be associated with the development of anaemia.

The lower phlebotomy volumes in the present study may be due to relative conservative practices for blood sampling in the ICU. Blood was taken by the exact volume for routine investigations and any extra blood withdrawn was usually returned to the patient *via* the arterial line. Published reports of discarded blood from arterial lines following phlebotomy vary from 2 to 10 mL (15). Also there have been strategies recommended to minimize blood loss by phlebotomy (16). Reducing phlebotomy volumes have been associated with shorter length of hospital stay and may suggest less morbidity (17). Another possible explanation for the low phlebotomy volumes in the study ICU may be the lesser number of blood investigations requested in a given ICU patient in this study compared to those in the developed countries.

The overall transfusion requirement of the ICU was only 4% of the hospital blood supply. A previous study showed that ICUs require almost 7–8% of the national blood supply (18).

The diagnosis of the patient *per se* would not have probably influenced the transfusion practices in the study ICU. This is evident from the fact that the patterns of transfusions were similar between different groups of patients such as surgical and non-surgical patients, septic and non-septic patients (Table 3).

The present study has some limitations. Data collection was limited to patients who had blood transfusions. Thus, no comparisons could be made with patients who did not receive blood transfusions to determine the risk factors associated with blood transfusion. Other factors such as the age of red cells transfused, the use of other methods to treat anaemia in the critically ill patient *eg* use of iron and folic acid supplementation for microcytic anaemia and the use of erythropoietin were not recorded. While recording phlebotomy volumes, there could have been some errors such as missing some repetition of blood tests, although care was taken not to miss any data.

In summary, the blood transfusion rate in the adult multidisciplinary ICU of a tertiary care teaching hospital in Trinidad is low and comparable to that of the published reports from the developed countries. Although there was no specific trigger for transfusion, the mean haemoglobin level at which patients were transfused was low. Phlebotomy volumes were also smaller suggesting that it may not be a contributing factor to anaemia in the ICU patients in our setting.

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