BLOOD TRANSFUSION TRIGGER IN BURNS: A FOUR-YEAR RETROSPECTIVE ANALYSIS OF BLOOD TRANSFUSIONS IN ELEVEN BURN CENTERS IN UKRAINE

SEUIL TRANSFUSIONNEL CHEZ LES BRULES: UNE ANALYSE RETROSPECTIVE SUR QUATRE ANS EN UKRAINE

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SUMMARY. One focus of improvement of burn care in Ukraine was the management of blood loss and blood transfusions in burn patients. The aim of this project was to analyze blood transfusion triggers in burn patients and outcomes at eleven major burn centers in Ukraine. This multicenter retrospective study reviewed four years of data on blood-transfused burn patients admitted to eleven major burn centers in Ukraine. Data analyzed included: demographics, characteristics of the burns, complications of burn injury, triggers for blood transfusions and outcomes. A total of 928 burn patients who received 2,693 blood transfusions from 11 major burn centers over a four-year period, were studied. Regardless of the total body surface area (TBSA) that was burned, blood transfusions were administered with a hemoglobin (Hb) trigger value of around 9 g/dL. Roughly one third (30.5%) of all transfusions were given in patients with a TBSA ≤ 10%. We demonstrated that Ukrainian doctors were using the same Hb trigger for blood transfusions for all Ukrainian burn patients, which suggested a need to change blood transfusion policy.

Keywords: blood transfusion, burn injury, Ukraine

RÉSUMÉ. *Un des objectifs de l'amélioration des soins aux brûlés en Ukraine est la prise en charge de la perte de sang et des transfusions sanguines chez les patients brûlés. Le but de cette étude était d'analyser les seuils de transfusions sanguines et le devenir des patients brûlés dans onze grands centres de brûlés en Ukraine. Cette étude multicentrique rétrospective a examiné les dossiers de 928 patients brûlés traités dans 11 CTB ukrainiens sur une période de 4 ans et transfusés. Les données analysées étaient: la démographie, les caractéristiques des brûlures, les complications, les seuils de transfusion sanguine et le devenir des patients. Les 928 patients ont reçu 2693 transfusions. Le seuil d'Hb se situait aux environs de 9g/dL, et les indications de transfusion n'étaient pas corrélées à la surface corporelle totale (SCT) brûlée (environ un tiers -30.5%-) des transfusions ont été prescrites à des patients avec une SCT de 10%. Nous avons ainsi montré le seuil transfusionnel est le même pour tous les patients brûlés ukrainiens, et concluons qu'il serait nécessaire de changer la politique de transfusion sanguine dans les CTB ukrainiens.*

Mots-clés: *transfusion sanguine, seuil, brûlés, Ukraine*

Introduction

According to the World Health Organization, burn injuries claim the lives of around 300,000 people worldwide each year.[1] Mortality due to burns and barriers to effectively treating them are mainly issues in low and middle-income countries (LMICs).[2,3] Ukraine, a LMIC with a population of 46 million people, has 40,000 patients who suffer from burn injuries each year.[4] During our annual mission trips to Ukraine in 2011, 2012 and 2013, we found

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Manuscript: submitted 31/12/2014, revised 06/05/2015, accepted 04/03/2015.

multiple areas of burn care that could be improved with minimal investment of resources, including burn prevention programs, and in-hospital care.[5-7] We also found evidence indicating that an unusually high number of burn patients received blood transfusions, including those with less severe burns.[6] Using two years' worth of data collected by hospitals in a single province, we found that 25% of all patients who received a blood transfusion had a burn area of <10% TBSA.[7] Burn patients often become anemic and, because there are no established guidelines for blood transfusions, practice can vary widely among physicians caring for burn patients.[8] The cause of anemia is multifactorial and includes heat and inflammatory damage of erythrocytes, hemodilution from resuscitation, impaired erythrocyte production, and multiple staged surgeries for excision and grafting of burned tissue.[9-14] Nonetheless, the indications for transfusions were not clear to us at the time.

Historically, blood transfusions were triggered by a hemoglobin value of 10g/dL and a hematocrit value of 30%, the so-called "10-and-30" rule. This rule was not based on solid evidence. The Transfusion Requirements in Critical Care (TRICC) Trial was a large-scale prospective trial, which compared the outcomes of a restrictive transfusion policy to the traditional standard, with hemoglobin treatment trigger values of 7-8 g/dL vs. 10-12 g/dL, respectively. The restrictive strategy was as effective as the traditional and had lower in-hospital mortality and cardiac complication rates.[15] This landmark trial led many critical care physicians to rethink the need for transfusions in their patients and develop transfusion guidelines.[16-19]

In the burn care literature there have been similar data to support a restrictive strategy for blood transfusion. Sittig et al. found that patients who were transfused for a hemoglobin trigger level of 6.0 g/dL had similar outcomes to patients transfused for hemoglobin values of 9.5-10 g/dL.[20] Palmieri et al found no difference in outcomes in pediatric burn patients who were transfused with a restrictive strategy, but there was considerable financial cost to the institution when a more liberal transfusion policy was used.[21] Kwan et al demonstrated a lower mortality rate when patients were transfused using a restrictive strategy that includes a trigger hemoglobin level of 7 g/dL.[22] These studies imply that unless clinicians use a restrictive strategy for blood transfusions, some patients are receiving blood without an apparent benefit. Importantly, these patients are still exposed to considerable risk from the transfusions including blood type mismatching, suppression of immunity, infection, circulatory overload, pulmonary edema, acute lung injury, and microcirculatory alterations among others.[8,23-28]

Morbidity from blood transfusions is also considerably higher in low and middle-income countries (LMICs) than in high-income countries like the United States. The screening processes in LMICs are less stringent and transfusion transmissible disease rates are much higher. A national policy for the collection, testing, processing, storage, and distribution of blood is present in only 60% of middle-income countries as opposed to 81% of high-income countries. According to the WHO Global Database on Blood Safety, the median rate of transfusion-transmissible infections in high-income countries is 0.003% vs. 0.1% in middle-income countries.[29] The UN AIDS report in 2011 indicated that there is no strategy in place to prevent HIV transmission during blood transfusions.[30] This implies that in Ukraine, which is a middle-income country, blood transfusions should be administered only when a clear benefit is present, given the associated risks. The purpose of our review was to determine current transfusion practice for patients with burn injuries in the Ukraine.

Materials and methods

The Partners Human Research Committee and the Office of the Ministry of Health in Ukraine approved this study ((Protocol Number: 2013P002282) in November 2013.

Our study is a retrospective multicenter cohort analysis of data collected over a four-year period (January 2010-December 2013) on burn patients admitted to 11 out of 35 major burn centers in Ukraine. The patients were collected via examination of patient records during the aforementioned time period. The burn centers participating in this study provided input into our study design and data collection process. Ukrainian physicians at these burn centers provided us with this data and recorded it in a digital Case Report Form, which was pretested with the physicians at each center. They collected the patient data from the hospital paper medical records. After the data collection was complete, the chief of the burn service at each center audited the data to verify accuracy.

We obtained demographic information: age (younger than 5 years-old, 5 to 15, 15-55, and over 55 years of age), gender, and weight of pediatric patients; the characteristics of the burn injury: type of burn, TBSA, burn depth, and presence of inhalation injury; co-morbidities: presence of CAD, HIV, hepatitis B, hepatitis C, diabetes mellitus, renal failure; complications of burn injury: infection, sepsis, need for mechanical ventilation pre- transfusion Hemoglobin, which was obtained 1-3 hours before transfusion; and outcome: hospital length of stay and mortality.

Data Analysis

The data points were analyzed using Microsoft Excel (Microsoft Corp., Redmond, WA) and SAS® Version 9.3 (SAS institute, Cary, NC). Chi-Square analysis was used to assess the difference in outcomes between the two groups.

Results

Data included 2,693 blood transfusions in 928 burn patients at 11 different major Ukrainian burn centers over a four-year period (January 2010 - December 2013). These patients were divided into two groups: those that survived and were eventually discharged versus those that died. Of the total number of transfused burn patients, 742 (80%) survived and were discharged (*Table I*). The largest age category in both groups was 15 to 55 years old (44.0% vs. 46.2%). There was no statistically significant difference in age between the two groups except for the 0 to 5 years category (28.7% vs. 2.7%, p<0.001). There was also no statistically significant difference in gender between the two groups. Not surprisingly, a lower percent TBSA was seen among patients who survived compared with those that died (24% vs. 33.1%, p<0.001). Similarly, a greater depth of burn and percent BSA was seen in patients who died. Regarding the type of burn, there was a predominance of flame burns in both groups, with a greater percentage seen in patients that died (57.2 % survivors vs. 90.2 % fatal, 90.2%, p<0.001).

Regarding complications of burns between the two groups, sepsis (19% vs. 62.9%, p<0.001) and pneumonia

Table I - Demographic and severity of burn injury in transfused patients

	Discharge N (%)	Death N (%)
Total Number of transfused patients	742	186
Age (years)		
<5	212 (28.7)	5 (2.7)
5-<15	37 (5)	2 (1.1)
15-<55	332 (44.9)	86 (46.2)
>55	159 (21.5)	93 (50)
Gender		
F	256 (34.5)	78 (41.9)
M	486 (65.5)	108 (58.1)
Total Body Surface Area, %	24 (20.3)	33.1 (26.9)[a]
Total Body Surface Area, deep burn, %	13.6 (12.4)	30 (21.4)[a]
Type of Burn Injury		
flame	378 (57.2)	148 (90.2)[a]
scald	206 (31.2)	10 (6.1)
contact	33 (5.0)	2 (1.2)
chemical	4 (0.6)	0 (0)
electrical	23 (3.5)	2 (1.2)
other	17 2.6)	2 (1.2)
Inhalation Injury	127 (17.2)	90 (48.7)[a]

[a] p<0.001 by Chi Square Test
Variables expressed as actual number with percentages in parentheses.

Table II - Complication of burns and coexisting disease

	Discharge N (%)	Death N (%)
Wound Infection	426 (57.4)	115 (61.8)[a]
Sepsis	141 (19)	117 (62.9)[a]
Pneumonia	117 (15.8)	112 (60.2)[a]
Other burns complication[b]	166 (24.7)	130 (72.6)[a]
Patients with co-existing disease (N)	228 (30.7)	109 (58.6)
coronary artery disease	65 (20.6)	53 (46.1)
diabetes mellitus	9 (2.9)	1 (0.9)
hepatitis (B,C)	2 (0.6)	1 (0.9)
renal failure	4 (1.3)	2 (1.7)

[a] p<0.001 by Chi Square Testing
[b] other complications include Urinary Tract Infections and Cellulitis

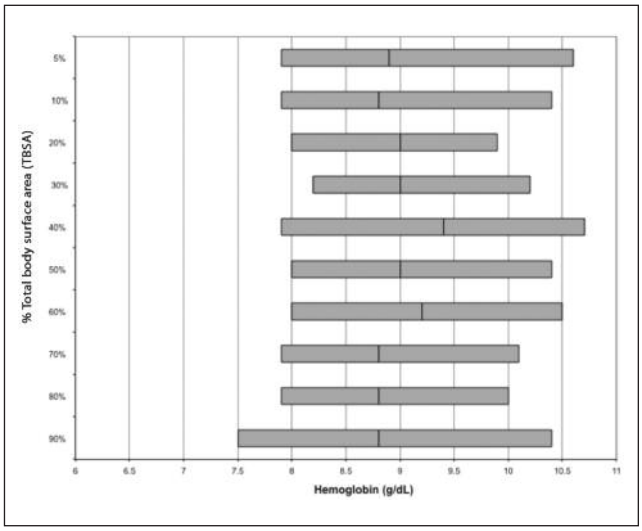

Fig. 1 - Hemoglobin level at time of transfusion in different total body surface area percentage groups.
The mean of the hemoglobin level was in the middle mark of the box, and the upper and lower bounds represented the range.

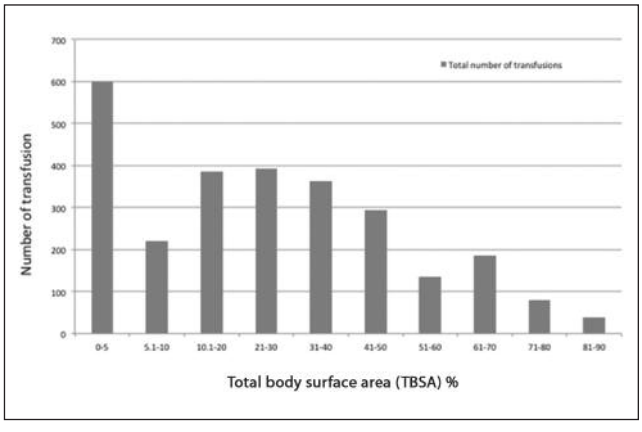

Fig. 2 - Total number of transfusions by TBSA.
The total number of transfusions in each TBSA% group does not depict the number of patients given that one patient may have had multiple transfusions.

(15.8% vs. 60.2%, p<0.001) was far less common among the surviving discharge group (*Table II*). Coexisting diseases, especially coronary artery disease, was more commonly found among fatal cases (30.7% vs. 58.6%, p<0.001). *Fig. 1* depicts the average and range of hemoglobin triggers for transfusing based on the %TBSA. Of note, 599 transfusions were administered to patients with TBSA 5% with average hemoglobin close to 9 g/dL (*Fig. 2*). Similar findings were seen in 220 transfusions, which were administered to patients who had TBSA less than 10%. A total of 30.4% of all transfusions were done on patients with a TBSA of 10% or less (44.7% with a TBSA of 20% or less). In fact, all the different TBSA groups were transfused close to a hemoglobin value of 9 g/dL, with TBSA groups in the 40%, 50%, and 60% having an average hemoglobin trigger of >9 g/dL.

Discussion

The results of this study show that the same hemoglobin trigger (~9 g/dL) was used to transfuse patients regardless of the TBSA %. Almost a third of all transfusions conducted were given to patients with a TBSA% of 10 or less. Hemoglobin triggers for blood transfusions remains an issue all across the world, especially in regions with limited resources for this precious commodity. More importantly, the burn centers in Ukraine, and likely other parts of the world, are continuing to give blood excessively despite the wealth of literature regarding the lack of benefit and potential for increased morbidity that accompany liberal transfusions. The reasons for such discrepancies are likely multifactorial and include: 1) insufficient influence from trained specialists in Transfusion Medicine and 2) lack of education regarding safe and appropriate use of blood products combined with dogmatic beliefs regarding the need for transfusion in burns.

Our study is a snapshot into the transfusion practices of a developing country, practices that are unlikely to be isolated, and indicate a possible area for improvement within other regions around the world as well.

Despite our findings noted above, limitations of this study include a lack of data on burn patients who were not transfused at these centers. Also, other complications and co-morbidities may serve as confounding factors that affect the decision to transfuse other than hemoglobin and TBSA% (e.g. the need for greater oxygen carrying capacity in those with inhalation injury). Furthermore, our study does not analyze the number of transfusions per patient or the time course of blood transfusions at these various burn centers. Nevertheless, the high hemoglobin trigger and large amount of transfusions given to patients with lower TBSA% is apparent.

During our visits to Ukraine and ongoing telemedicine conferencing, we noticed a general lack of education with respect to updated transfusion practices. While we found physicians to be highly intelligent and dedicated, they had not been exposed to the relatively recent data regarding transfusion medicine. Blood transfusions were well intended and meant to help patients, but there was little awareness of the potential complications as noted in our introduction. The policies and guidelines in place to help shape the physicians' practices dated from the 1970s.

After analyzing the process of blood administration and understanding the reasons for the excessive transfusions in Ukraine, it became clear that this problem is likely amenable to intervention in the form of teaching sessions with the Ukrainian physicians. We found the healthcare professionals in the burn centers to be very receptive to education and learning new techniques to help improve the quality of the care. Our plan is to develop a targeted education program to help the Ukrainian physicians update their practice model for blood transfusions while concurrently implementing new guidelines for blood transfusion in Ukraine. Following the completion of these steps, we will evaluate the results of the intervention by reexamining the blood transfusion practices in burn patients.

Conclusion

Our plan is to develop a targeted education program to help the Ukrainians update their practice model for blood transfusions. This project will be an excellent opportunity to update the practices of dedicated physicians in another country as part of our larger mission to improve burn care in Ukraine. The time is ripe for changes in Ukraine and this is an excellent opportunity to help both doctors and patients in this country, which is rapidly reforming. If we succeed in disseminating an educational program and implementing transfusion guidelines, we will use this as a model to help make changes in other countries. We plan to collaborate with the International Outreach Committee of American Burn Association, International Society of Blood Transfusion and others, and to disseminate educational programs on burns in other parts of the world.

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Author Contributions. Gennadiy Fuzaylov, M.D. was involved in the literature search, study design, data analysis, data interpretation, writing, editing, figures, and tables. Richard Anderson, M.D. was involved in literature search, study design, data analysis, data interpretation, and writing. Jason Lee, M.D was involved in literature search, data analysis, writing, editing, figures, and tables. Sergey Slesarenko, M.D., Vasyliy Nagaychuk, M.D., Tamara Grigorieva, M.D., and Georgiy Kozinec, M.D were involved in study design, data collection and auditing. All authors have seen and approved the final version.

Funding. There were no funders involved in the study design; in the collection, analysis or interpretation of data; in the writing of the report; or in the decision to submit for publication. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Acknowledgements. The study team would like to acknowledge the help of:
- Kwun Yee Trudy Poon of the Clinical Research Core in the Department of Anesthesia, Critical Care and Pain Medicine at Massachusetts General Hospital, Boston, MA for contributions to the design of the figures and tables, and statistics.
- Charles Coté, M.D. from the Department of Anesthesia, Critical Care and Pain Medicine at Massachusetts General Hospital, Boston, MA for the final revision of the manuscript;
- Walter Dzik, M.D. from the Blood Bank at Massachusetts General Hospital, Boston, MA for revision of manuscript and guidelines on this project;
- Robert Sheridan M.D. for the help with designing the study;
- Alexandr Akimenko, M.D. , Vladimir Moroz, M.D., Elena Ponomarenko, M.D., Vladimir Capenko, M.D., Svyatoslav Dykalo, M.D., Vasyl Savchyn, M.D., Oleksandr Grinchak, M.D. for helping to collect data.