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

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

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...
multiple areas of burn care that could be improved with minimal investment of resources, including burn prevention programs, and in-hospital care.\textsuperscript{37} We also found evidence indicating that an unusually high number of burn patients received blood transfusions, including those with less severe burns.\textsuperscript{4} 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.\textsuperscript{1} 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.\textsuperscript{5} 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.\textsuperscript{6,14} 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.\textsuperscript{15} This landmark trial led many critical care physicians to rethink the need for transfusions in their patients and develop transfusion guidelines.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{4,12-24}

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.\textsuperscript{29} The UN AIDS report in 2011 indicated that there is no strategy in place to prevent HIV transmission during blood transfusions.\textsuperscript{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, necessity 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\textsuperscript{®} 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

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

Variables expressed as actual number with percentages in parentheses.

Table II - Complication of burns and coexisting disease

<table>
<thead>
<tr>
<th></th>
<th>Discharge N (%)</th>
<th>Death N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wound Infection</td>
<td>426 (57.4)</td>
<td>115 (61.8)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>141 (19)</td>
<td>117 (62.9)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>117 (15.8)</td>
<td>112 (60.2)</td>
</tr>
<tr>
<td>Other burns comp.</td>
<td>166 (24.7)</td>
<td>130 (72.6)</td>
</tr>
<tr>
<td>Patients with co-existing disease (N)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>coronary artery disease</td>
<td>228 (30.7)</td>
<td>109 (58.6)</td>
</tr>
<tr>
<td>diabetes mellitus</td>
<td>65 (20.6)</td>
<td>53 (46.1)</td>
</tr>
<tr>
<td>hepatitis (B,C)</td>
<td>9 (2.9)</td>
<td>1 (0.9)</td>
</tr>
<tr>
<td>renal failure</td>
<td>2 (0.6)</td>
<td>1 (0.9)</td>
</tr>
</tbody>
</table>

Variables expressed as actual number with percentages in parentheses.

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 dis-
ases, especially coronary artery disease, was more com-
monly found among fatal cases (30.7% vs. 58.6%, p<0.001).
Fig. 1 depicts the average and range of hemoglobin trig-
gers 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). Simi-
lar findings were seen in 220 transfusions, which were ad-
ministered 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%
less). In fact, all the different TBSA groups were trans-
fused 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 con-
ducted were given to patients with a TBSA% of 10 or less.
Hemoglobin triggers for blood transfusions remains an is-
ssue all across the world, especially in regions with limit-
ed resources for this precious commodity. More impor-
tantly, the burn centers in Ukraine, and likely other parts
of the world, are continuing to give blood excessively de-
spite the wealth of literature regarding the lack of benefit
and potential for increased morbidity that accompany lib-
eral 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 with
in 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 capac-
ity 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 TBS-
SA% 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 in-
tended 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 trans-
usions in Ukraine, it became clear that this problem is like-
ly amenable to intervention in the form of teaching ses-
sions with the Ukrainian physicians. We found the health-
care 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 up-
date their practice model for blood transfusions while con-
currently implementing new guidelines for blood trans-
fusion in Ukraine. Following the completion of these steps,
we will evaluate the results of the intervention by reex-
amining 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 im-
plementing 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 educa-
tional 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 Sli-sarenko, M.D., Vasylly Nagaychuk, M.D., Tamara Grig-orieva, M.D., and Georgiy Kozenee, M.D were involved in study design, data collection and auditing. All authors have seen and approved the final version.

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