Root cause analysis of non-infectious transfusion complications and the lessons learnt

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Abstract

Background: Transfusion of blood and blood products can be associated with hazards which may be at times fatal. Timely reporting of transfusion reactions is imperative for root cause analysis and their prevention in future.

Methods: We retrospectively reviewed the transfusion reactions at our institution during last seven years. The data was retrieved from our computerized blood bank information system and by reviewing the medical charts of patients. The frequency of adverse effects, implicated products, wrong blood transfusion and its outcome were observed.

Results and conclusions: During study period (2006–2012), a total of 393,662 blood or blood products were transfused. There were 458 adverse events with an estimated rate of 1.16 per 1000 blood products administered. During 2011–2012, 121 transfusion reactions were reported of 119,921 transfused units. The most common adverse effects were allergic reactions (70 episodes of 121 or 57.8%) followed by febrile non hemolytic transfusion reactions or FNHTR (43 events of 121 or 35.5%). Transfusion associated dyspnea, circulatory overload and transfusion associated lung injury were less frequent. During the study period, 142,066 red cell units were transfused with nine recognized ABO-mismatch transfusions and two fatalities. The computed incidence of ABO-mismatch transfusion was 1 in 15,785 with a mortality rate of 1 in 71,033 units transfused. Etiology included: errors in final bed side check (n = 5), blood bank clerical errors (n = 3) and mislabeled tube (n = 1). A review of these cases prompted hospital transfusion committee for re-enforcing policies and protocols to minimize accidental ABO incompatible transfusions. We concluded that urticaria and FNHTR are the most frequent transfusion reactions in our setting. ABO mismatched blood transfusions are rare but preventable errors and result mainly from clerical imprecisions.

1. Introduction

The concept of blood transfusion evolved about 200 years back when animal blood was transfused to humans for various illnesses. In the 19th century, the first inter-human transfusion was done and was reserved as the ultimate life-saving therapy for patients with severe blood loss [1]. Since then, clinical blood transfusion has become an essential and life-saving therapeutic option. However, blood transfusion had never been absolutely safe and has been associated with significant risks [2]. The major risks of blood transfusion are transmission of infections and adverse transfusion reactions which may be fatal [3]. The risk of transmission of infectious agents by transfusion was minimized by improvements in donor screening and infectious disease testing in 1980s and 1990s. Now, the residual risks of noninfectious complications of transfusion have become more apparent [4]. Severe noninfectious complications account for most of the significant morbidity and mortality from blood transfusion. Based on
the time of occurrence of transfusion reaction, they are categorized as acute and delayed [4,5].

Acute transfusion reactions (ATRs) occur within 24 h of the administration of blood or blood components [6]. The most commonly reported ATR are allergic and febrile non-hemolytic transfusion reactions (FNHTR). The actual incidence of ATR is uncertain but rates of 0.5–3% of transfusions have been reported [7].

Of all ATR, acute hemolytic transfusion reaction is of major concern as it can lead to significant morbidity and mortality. Acute hemolytic transfusion reaction occurs due to mismatch transfusion as a result of incorrect blood component transfused (IBCT) to the patient due to misidentification [8].

Delayed transfusion reactions occur after 24 h of transfusion. Transfusion reactions included in this category include transfusion associated graft versus host disease (TA-GVHD), post-transfusion purpura and delayed hemolytic transfusion reactions [9].

Blood transfusion is a life-saving therapeutic option but it is also associated with significant risks or hazards [10]. Recently, many developed countries have promoted safe transfusion practices through hemovigilance programs by reporting of transfusion reactions. There is variance in reporting ranging from voluntary reporting of only serious and incompatible blood component transfusion reactions in United Kingdom to mandatory reporting of all reactions in France [11]. In Pakistan, a national task force for safe blood transfusion is struggling for establishing a national hemovigilance program [12]. At our institutional level, it is mandatory to report every transfusion reaction.

Hemovigilance programs worldwide aim to detect and analyze untoward effects of blood transfusion in order to correct the causes and prevent their recurrence. Reporting of transfusion reactions helps in understanding the root causes and improves transfusion safety [13]. It has been observed that since wrong blood transfusion has a legal implication, the mismatched transfusions are often suppressed and under reported in hospitals. We consider it of utmost importance that not only these should be reported but thoroughly investigated to minimize their future occurrence. Sharing experiences is beneficial and promotes good transfusion practices. The objective of our study was to evaluate frequency of all transfusion reactions including ABO-mismatch incompatible red cell transfusions and their root cause analysis in our institute. Secondary objective was to discuss the preventive measures to avoid such happenings in future.

2. Materials and methods

2.1. Setting

Situated in the Southern Pakistan, Aga Khan University Hospital is a 700-bedded tertiary care academic institute. The institutes serve a number of specialized treatment including bone marrow and peripheral blood stem cell transplantations. It has a 100 bedded emergency department which provides comprehensive trauma management as well. Transfusion needs of all admitted patients are catered by hospital’s own blood bank which was established in 1985. This was accredited by International Organization for Standardization (ISO) in 1998 and by the Joint Commission International (JCI) in 2006. Blood Bank is manned by a team of experienced and fully trained medical technologists who work under the supervision of full time hematologist to provide quality service round the clock. The blood bank is equipped with sophisticated instruments and skilled technologists. Annually 30,000 non-remunerated individuals donate blood following careful donor evaluation. The blood units are dispensed only after serological and nucleic acid amplification testing. The blood products are non-leucoreduced due to cost issues. However, in patients with repeated transfusions bedside filters are used for leucoreduction. For platelets, both whole blood derived and apheresis platelets are used.

AKUH Blood bank policies are derived from the guidelines of British Committee for Standards in Hematology (BCSH) and AABB, formerly the American Association of Blood Banks. The working guidelines adapted from these are available on blood bank website and printed copies are available in all units of the hospital. This allows all the staff involved in blood transfusion to be familiar with the local policy.

2.2. Medical training programme in pathology and transfusion medicine

The blood bank is owned by the Department of Pathology and Microbiology. There are five subsections of the department, namely, Hematology, Histopathology, Microbiology, Molecular Pathology and Chemical Pathology. The Hematology section is responsible for the blood bank. The Department offers post-graduation training in all the disciplines. About 40 residents are enrolled in the post-graduation training of which 12 are Hematology residents at any one time. It is the responsibility of the hematology resident rotating in blood bank to look after all the blood bank related issues including transfusion matters and report to the Consultant hematologist. In addition, the laboratory also offers Trainee Technologist Program. Trainees who have completed their masters in clinical sciences, are inducted each year in this one-year trainee technologist programme. The one-year trainee technologist programme is unique in Pakistan and has been very successful. Every year more than 30 trainees are inducted who rotate in each section including blood bank through a pre-defined programme. The trainees who are found competent are employed as full-time technologist in blood bank.

2.3. Transfusion reaction reporting

Any untoward event that occurs during or after blood transfusion not related to patients underlying illness is considered as a transfusion reaction. Additionally, if a wrong component is administered to the patient irrespective of any adverse effect is considered IBCT. A transfusion reaction form adapted from AABB is available in all the hospital units. Whenever a transfusion reaction occurs or is suspected, the form is filled by the patients’ primary
The process. Regular audits are conducted to assess the completeness of file in the blood bank and stored for a period of ten years.

The completed form is assessed the laboratory results and consults the hematologist upon receiving the transfusion reaction form by the technologist who then informs post donation samples, direct coombs test, culture of the bag and urine DR. The information is filled in the transfusion reaction form by the technologist who then informs the rotating blood bank resident. The blood bank resident visits the patient, reviews file chart for details of reaction including signs and symptoms, vital signs at the time of reaction and any intervention carried out at that time, assesses the laboratory results and consults the hematologist. The latter is responsible for finalizing every reaction report according to AABB criteria. The completed form is filed in the blood bank and stored for a period of ten years. Regular audits are conducted to assess the completeness of the process.

2.4. Transfusion reactions audit by hospital transfusion committee

The blood bank owns a computerized in-house blood bank information system and maintains all records and historical data. A quarterly report is prepared and discussed within hospital transfusion committee (HTC) called blood utilization committee (BUC). The monitoring of transfusion reactions is also one of the dashboard quality indicators of the hospital quality indicator control committee and submitted to Medical director. A wrong transfusion is considered as a sentinel event demanding comprehensive root cause analysis. The report thus made is shared with all stake holders including medical director. Gaps identified are bridged through reinforcement of existing guidelines and in-service training under the supervision of BUC.

2.5. This study

This was a retrospective review of blood transfusions during past seven years (January 2006 to December 2012). The statistics regarding the total number of transfusions was derived from electronic blood bank information system while type of transfusion reaction and ABO-mismatch transfusions were retrieved from manual review of reported transfusions forms. Rate of transfusion reaction per 1000 blood products was computed by dividing the transfusion reactions by total number of all blood units transfused.

From 2006 to 2010, the incidence of transfusion reactions was reported in totality and record of the type of transfusion reactions was not available apart from ABO mismatch transfusions for which a separate file is available in the blood bank with complete information and results of root cause analysis. Similarly, the record of the different component types transfused was also not available for this period. From January 2011 onwards all transfusion reactions were reported according to the type and incidence of each type along with the type of component implicated in each case was analyzed. The transfusion reactions were categorized as follows: acute hemolytic transfusion reaction, allergic reactions, anaphylactic reactions, febrile non-hemolytic transfusion reaction, transfusion associated acute lung injury (TRALI), transfusion associated circulatory overload (TACO), transfusion associated dyspnea (TAD), hypotension associated with use of ACE inhibitors and septic reaction. Reactions that were reported but on detailed investigation found to be not related to transfusion were classified as ‘false reports’.

All reports of comprehensive root cause analysis of ABO-mismatch transfusions were evaluated for etiology, preventive and corrective measures.

2.6. Ethical issues

Ethical review committee of The Aga Khan University does not require approval for the analysis of retrospective data provided anonymity is maintained. During data entry, all personal identifiers were removed.

3. Results

3.1. Type and frequency of transfusion reactions

Overall 393,662 blood units were transfused from January 2006 till December 2012 to 154,105 recipients. An aggregate of 458 transfusion reactions were reported during this period. Thus, the rate of transfusion reaction was 1.16 per 1000 blood products administered. Table 1 summarizes the annual incidence of transfusion reactions which has been constant over a period of time.

From 2011 to 2012, total number of transfusions given were 119,921. During this period, 142 transfusion reactions were reported, of which 21 (14.8%) were classified as false reports. The details of false reports is as follows: in some patients, fever was reported but on investigation it was found that patient was already febrile before transfusion and there was not an increase in >1°C in temperature during transfusion, so these reports were excluded. In others, vague symptoms were reported such as headache in a patient who already had headache complaint. Thus, the final analysis was done on the 121 actual transfusion reactions.

Table 2 summarizes these 121 transfusion reactions according to the type of blood product administered. Of these, allergic reactions or urticaria was the most frequent adverse event accounting for 70 (57.8%) of all transfusion reactions. In our setting, febrile non-hemolytic transfusion reaction was observed as the second common event (n = 43 or 35.5%). The incidence of allergic reaction was 0.06% in all blood products transfused. The incidence of FNHTR reaction was 0.08% with red cell transfusions and 0.004% with platelet transfusions. Other recurrent events included transfusion associated dyspnea (n = 2), circulatory overload (n = 2) and TRALI (n = 2). The least frequent reactions observed in only one patient each included anaphylaxis and AHTR.

The frequency of transfusion reactions was highest with red cells (2/1000) followed by platelets (0.4/1000) and plasma (0.3/1000).
3.2. *ABO* mis-match transfusions and root cause analysis

During 2006–2012 period, 142,066 red cell units were transfused to 90,750 patients. Nine *ABO*-mismatch transfusions were reported. The computed incidence of ABO-mismatch transfusion was 1 in 15,785 units. The most common cause of *ABO*-mismatch transfusion accounting for 56% (n = 5) of cases was an error in the final bedside check. In three cases (33.3%), blood bank was implicated due to testing on wrong blood tube (n = 1) and dispensing wrong blood bags (n = 2). Additionally, failure to perform the final bed side check before transfusion led to wrong blood transfusion. Mislabeled sample tube for grouping was observed in one case. Root cause analysis showed usage of a pre-labeled tube for sample collection (Table 3).

Majority (6/9) of the mismatch transfusions were picked up when patient developed signs and symptoms of transfusion reaction specifically fever and hypotension. In two cases, the error was identified by the blood bank personnel and transfusion was stopped promptly. In one case, patient’s son recognized the error as he knew his father’s blood group and identified that wrong transfusion was being given.

3.3. Transfusion associated mortality

The mortality associated with ABO-mismatch transfusion was 2/142,066 red cells transfused with a calculated risk of one death in 71,033 transfused units.

In one of these cases, the patient was a 25 year old male admitted with dengue haemorrhagic fever who required packed red cell transfusion. After receiving 200 ml of blood he developed fever, hypotension and became anuric. It was identified that he was receiving wrong blood transfusion. Patient was A+ve and he received AB+ve blood. In this case, the error was in the final bed side check. Though patient had serious morbidities but we assumed that wrong blood transfusion led to the early demise of this patient.

The second case in which ABO-mismatch transfusion led to death of the patient was that of a 65 year old male. This man was seriously ill and was admitted with complaints of drowsiness, slurring of speech and difficulty in breathing. Patient was also hypotensive. He was diagnosed to have acute renal failure and septic shock. He was intubated and shifted to ICU. Due to low hemoglobin he required red cell transfusion. He was typed as A+ve. One unit (250 ml) of compatible A+ve blood was transfused. A second sample of patient was sent to blood bank on the same day for arranging more packed red cells. The group could not be identified on that sample because of mixed field reaction. Finally, it was identified that the patient was B+ve and the initial sample sent to the blood bank for grouping was mislabeled by the nursing staff. Transfusion reaction was not identified by the nursing staff as patient was already febrile and hypotensive due to septic shock and on inotropic support. Although physicians believed that patient died because of his underlying pathology and several co-morbidities but we assumed that wrong blood mismatch transfusion would have played a role in his early demise.

4. Discussion

We observed 1.16 adverse reactions for every 1000 blood units transfused. This incidence seems low when compared to reports from countries like Brazil, France...
and Netherlands which are respectively 2.6, 2.8 and 2.9 per 10^5 transfused products. In UK, the rate of serious reactions and IBCT is 0.20/1000 units [14]. This contrast reflects the possibility of under reporting of transfusion reactions in our institute.

Non-hemolytic transfusion reactions are usually reported as the most frequent events [15]. Reported incidence for allergic reactions varies from 0.1% to 2% [16] while for pyrexia it is 4% to 30% after platelets and 0.5% with red cells transfusions [17]. On the contrary, we observed 0.06% of allergic reactions from transfusion of various blood products. The incidence of FNHTR with red cell transfusions in our study was 0.08% and with platelet transfusions it was only 0.004%, both of which are almost unacceptable. Since we used non-leuco reduced blood products, the expected febrile reactions should have been higher raising the possibility of underreporting in our setting.

The estimated reported frequency of TRALI is one in 5000 transfusions [16]. The frequency of TRALI found in our study was 1 in 59,960 transfusions. The incidence of TAD and TACO each was also found to be low and similar to the incidence of TRALI. Low incidences of these transfusion reactions at our institution show that there is less awareness among physicians and nursing staff about these reactions. Hence insufficient patient identification prior to transfusion was the sole reason in majority of the cases. Besides, mislabeled tube was identified as the main cause of dispensing wrong unit from blood bank. This error has been highlighted by many and frequency varies from 1:467 to 1:5555 [24,25]. We observed that an error in final bedside check due to human error [22,23]. We observed that an error in final bedside check was exclusive reason in 5/9 and additional factor in 3/9 ABO mismatched transfusions. Hence insufficient patient identification prior to transfusion was the sole reason in majority of the cases. Besides, mislabeled tube was identified as the main cause of dispensing wrong unit from blood bank.

Precise patient identification is a very critical step in blood transfusion. By no surprise, most of mismatched transfusions results from failure of correctly identifying the intended recipient [21]. Single most important factor is error in final bedside check due to human error [22,23]. We observed that an error in final bedside check was exclusive reason in 5/9 and additional factor in 3/9 ABO mismatched transfusions. Hence insufficient patient identification prior to transfusion was the sole reason in majority of the cases. Besides, mislabeled tube was identified as the main cause of dispensing wrong unit from blood bank. This error has been highlighted by many and frequency varies from 1:467 to 1:5555 [24,25] SHOT reported 29% incorrect blood component transfusion due to laboratory errors including testing on wrong blood sample or technical errors in blood grouping [20,26]. In our setting, only one case was identified where blood typing and cross-matching was done on a wrong tube.

With nine recognized ABO mismatched transfusions at our institution, the computed fatality rate was 1 in 71,033 red cell units transfused. This estimate is high when compared to mortality rate of 1:1800,000 reported by French hemovigilance system [27] and 1:1500,000 units by SHOT [14].

### 4.1. Lessons learnt and initiatives taken

Reporting of transfusion reactions is essential for any health care organization as it contributes to analysis of transfusion hazards and improves transfusion safety. Analysis of transfusion reactions by hospital transfusion committee at our institution helped in identifying the root causes and resulted in development and implementation of strategies from time to time in order to enhance transfusion safety. There was reinforcement through existing guidelines and In-service training through intranet and lectures under the supervision of blood utilization committee (BUC). As bed side check error was the commonest error leading to wrong transfusion, various steps were taken to minimize it. Importance of correct patient identification using two identifiers was enforced. Emphasis was laid on proper sample collection, labeling the sample at bed side and avoiding use of pre-labeled tubes. A policy was

<table>
<thead>
<tr>
<th>Year</th>
<th>Red cell transfusions (n)</th>
<th>ABO mismatch transfusion (n)</th>
<th>Volume transfused (ml)</th>
<th>Location</th>
<th>Primary root cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006</td>
<td>12,850</td>
<td>1</td>
<td>30</td>
<td>Floor</td>
<td>Bed side check error</td>
</tr>
<tr>
<td>2007</td>
<td>20,539</td>
<td>1</td>
<td>200</td>
<td>ICU</td>
<td>Bed side check error</td>
</tr>
<tr>
<td>2008</td>
<td>21,273</td>
<td>1</td>
<td>20</td>
<td>ER</td>
<td>Blood bank error</td>
</tr>
<tr>
<td>2009</td>
<td>21,034</td>
<td>1</td>
<td>30</td>
<td>OR</td>
<td>Bed side check error</td>
</tr>
<tr>
<td>2010</td>
<td>21,500</td>
<td>1</td>
<td>25</td>
<td>ER</td>
<td>Blood bank error</td>
</tr>
<tr>
<td>2011</td>
<td>22,339</td>
<td>1</td>
<td>250</td>
<td>ICU</td>
<td>Mislabeled sample tube</td>
</tr>
<tr>
<td>2012</td>
<td>22,531</td>
<td>0</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

CCU, cardiac care unit; ICU, intensive care unit; OR, operating room; and ER, emergency room.

Table 3 Evaluation of ABO incompatible transfusion reactions (2006–2012).

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implemented according to which two nurses instead of one will check the blood component against patient’s identity and will sign the form before transfusing blood/blood component. Flyers were designed with diagrammatic representation of various steps of sample labeling, proper identification and blood collection. These flyers were distributed in all the hospital units. Implementation of bar-code technology for correct patient and sample identification was one of the major initiatives to improve transfusion safety and minimize wrong transfusion. The bar-code system that links patients’ bar-coded wristbands with bar-coded labels on blood sample tubes and blood component bags has finally been implemented at our institute. Training of residents and nurses was done with regard to identification and management of transfusion reactions. Orientation and training of staff of timely communication and incident reporting was done. In order to improve reporting of transfusion reactions, on-line incident reporting was also started. The nursing staff can timely fill the transfusion reaction form using this facility.

To reduce blood bank errors, a policy has been implemented that a blood group performed by one technologist is confirmed by another technologist so as to minimize clerical errors. Similarly, two technologists verify the identification on blood bag and request slip before releasing the product. Despite all this, if there is wrong blood in tube, it can lead to wrong transfusion. To handle this issue, it has been proposed that if a historic record of patient’s blood group is not available in the blood bank then the group should be done on two samples sent at different time for confirmation. In emergency situation, O-ve blood is released until group has been confirmed on two samples.

To further improve our existing system and to ensure that complete information about the transfusion is sent to the blood bank, an online transfusion form is also formulated and piloted in certain units. This form will be filled online by the nursing staff for each transfusion and will be mandatory. The form will contain information about type of component and volume transfused as well as recipients’ vitals and any reaction during transfusion. This information will be stored in blood bank information system and routine audits will be done to assess the completeness of transfusion reaction reporting.

Good transfusion practice can be promoted by sharing experiences. Understanding of the cause of errors and the lessons learnt from each transfusion reaction helps in improving transfusion safety and these experiences are of benefit not only for the institution itself but everyone involved in transfusion medicine.

4.2. Strengths and limitations

This is the first comprehensive report of transfusion reactions from Pakistan. The limitation of the study is that this is a retrospective review. There is missing data. We do not have information about the different types of transfusion reactions and reactions according to the type of blood component administered prior to January 2011. This study was completed by the time bar code technology was implemented at the institution. Therefore, further follow-up studies are needed to see the impact of implementation of various policies including bar code technology to minimize wrong transfusion events.

5. Conclusions

We observed urticaria and fever as the most frequent adverse events following transfusion. ABO incompatible transfusions were less frequent and resulted mostly from clerical errors. Regular audit of transfusion reactions as a quality indicator helped our institute in developing concrete preventive strategies.

References


