ARTICLE
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Frequency of acute transfusion incidents in recipients of blood-based products

Frequência dos incidentes transfusionais imediatos em receptores de hemocomponentes

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ABSTRACT

Objectives: to identify the frequency and severity of the most common Adverse Reactions (ARs) related to acute transfusion reactions. **Method:** a retrospective cross-sectional study of ARs notified to the National Hemovigilance System from May 2002 to May 2016 was done in a high complexity Teaching Hospital with 862 beds. The study was preceded by approval of the Ethics Committee of the institution, on October 26, 2016. **Results:** we analyzed 1,462 notification forms reporting transfusion reactions. The profile found was mostly of acute events associated to the transfusion of red blood cells, being Febrile Nonhemolytic Transfusion and Allergic Reaction the most frequent ARs. As for the severity, the ARs were considered mild. Among the cases considered severe, these two types of ARs occurred in 13 (62%) of the cases. **Conclusion:** the study enabled a better evaluation and understanding of transfusion reactions, which, in turn, allows for the improvement of the quality of the blood cycle and greater safety of patients undergoing transfusion therapy.

KEYWORDS: Transfusion reaction; Adverse effects; Blood safety; Patient safety; Health surveillance

RESUMO

Objectives: to identify the frequency and severity of the most common Adverse Reactions (ARs) related to acute transfusion reactions. **Method:** a retrospective cross-sectional study of ARs notified to the National Hemovigilance System from May 2002 to May 2016 was done in a high complexity Teaching Hospital with 862 beds. The study was preceded by approval of the Ethics Committee of the institution, on October 26, 2016. **Results:** we analyzed 1,462 notification forms reporting transfusion reactions. The profile found was mostly of acute events associated to the transfusion of red blood cells, being Febrile Nonhemolytic Transfusion and Allergic Reaction the most frequent ARs. As for the severity, the ARs were considered mild. Among the cases considered severe, these two types of ARs occurred in 13 (62%) of the cases. **Conclusion:** the study enabled a better evaluation and understanding of transfusion reactions, which, in turn, allows for the improvement of the quality of the blood cycle and greater safety of patients undergoing transfusion therapy.

PALAVRAS-CHAVE: Transfusion reaction; Adverse effects; Blood safety; Patient safety; Health surveillance

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INTRODUCTION

Blood and blood-based product transfusions are usually effective manners of temporarily correcting deficiencies of erythrocytes, platelets and coagulation factors[1]. However, in the history of medicine, transfusion therapy is a rather recent option that developed only in the mid-twentieth century. Furthermore, despite all technological advances, even today we have not yet discovered anything that can replace human blood.

Transfusions are widely used in healthcare. Blood transfusions are irreversible events with undeniable benefits, but they also pose risks to the recipient. Since these are biological products of human origin, the risks can be severe and put the patient's life at risk[3]. Even with accurate indication and correct administration, blood transfusions can lead to adverse reactions. A transfusion adverse reaction is defined as an undesirable effect or response, temporally associated with the administration of blood or blood-based products[4].

Transfusion reactions can be classified according to their severity, the time it takes them to appear and their cause. Severe acute life-threatening complications are rarer, whereas mild reactions are more common. They occur as a consequence of the transfusion of blood or blood-based products during or after the administration and are reported in routine clinical practice. They can thus be classified as immediate (acute) when they occur within 24 hours of the transfusion, or late, when they occur after this period[3].

Transfusion reactions may be represented by any sign or symptom caused by the transfusion therapy or by other non-conformities in hemotherapy procedures throughout the blood cycle. These can be elevation of basal temperature to values equal to or higher than 1° C after the beginning of the transfusion, chills, pain in the chest, abdomen or lower back, changes in blood pressure, respiratory discomfort, nausea with or without vomiting, hemoglobinuria, shock, among others[5,6]. However, transfusion therapy is essential for the continuity of some treatments, and hemovigilance (blood surveillance) is capable of identifying risks related to blood use, especially those related to process failures. The final goal is to implement corrective and preventive measures that may contribute to transfusion safety[7].

In a research project conducted in Brazil, we noticed that most of the studies that address blood transfusion involved oncology patients. This fact may be associated with the peculiarities of cancer patients regarding their immune and hematological condition and their need for many blood transfusions during the treatment[1,8,9].

In a review of the literature[10], 29 articles were analyzed and grouped into two themes: those that dealt with the types of acute transfusion incidents and those that addressed hemovigilance actions, from 1980 to 2009. Only two publications used Brazilian data[1,11].

Blood transfusion policies began to be effectively implemented in Brazil in the year 2000. Monitoring, detection, screening and treatment of transfusion reactions, as well as preventive measures to avoid recurrence, became mandatory in Brazil in 2004[3,4,12].

In view of the above and the lack of literature on the occurrence of transfusion reactions among patients in a general hospital of high complexity, we were motivated to investigate the most frequent adverse events related to transfusion reactions. Therefore, the present study aims to identify the most frequent adverse events related to transfusion reactions among patients receiving blood-based products that were notified to the Health Surveillance Notification System (Notivisa).

METHOD

Ethical aspects

This study was preceded by the approval of the Research Ethics Committee of Hospital São Paulo, University Hospital of the Federal University of São Paulo, under n. 1.794.086, on October 26, 2016.

Design, period and place of study

This is a retrospective study, carried out from May 2002 to May 2016. The research was done in a high complexity university hospital, of philanthropic nature, with 862 beds, located in the city of São Paulo. This hospital is a national and international reference for teaching and research. It is a member of the Brazilian Network of Sentinel Hospitals. Through the Hospital Health Risk Management, it has been carrying out Hemovigilance actions since 2002. The data collection involved all Transfusion Incident Report Cards of all the patients who presented transfusion reactions after receiving blood and blood-related products. The data was stored and tabulated in *Microsoft Excel* 2010. The full sample consisted of 1,462 records reporting acute transfusion reactions. The classification of the transfusion reactions and their diagnosis followed the recommendations of the National Agency of Health Surveillance (Anvisa) published in 2015[4].

Inclusion criteria

Duly filled out notification form with the diagnosis of Immediate Acute Incident, done by a hemotherapist physician.

Exclusion criteria

Late incidents or reporting forms whose signs and symptoms were not correlated with the transfusion reaction. Of 1,468 all-cause reports, 1,462 were included for data analysis and only six were excluded.

Study protocol

After the receipt of the reporting forms prepared and validated by the institution itself, with the following variables: age, gender, diagnostic hypothesis, unit of occurrence, type of

blood-based product, confirmation of transfusion reaction by a transfusion specialist, reactions were filed in a database for further analysis. All the transfusion reactions that occurred during the period of this study were entered into the Anvisa National Hemovigilance System through the Notivisa system.

Analysis of results and statistics

The data stored in Excel spreadsheets in a database of Hospital São Paulo's Health Risk Management was analyzed through descriptive statistics, frequency distribution techniques and mean variables. The results were presented in the form of charts for analysis and discussed according to the existing literature.

RESULTS

From May 2002 to May 2016, 1,462 transfusion reactions were reported, initially at an incipient frequency, with only 33 (2.40%) of total notifications in 2002, with a monthly average of 74 notifications between 2003 and 2009, and then doubling to 142 as of 2010. There was a substantial increase in 2014, the year in which the nurses began to be trained to notify the 1° C rise in temperature after the start of blood transfusions.

When the incidence of transfusion reactions was verified, in the second half of 2014, of the 15,915 transfusions performed, a transfusion reaction rate of 0.60% per thousand was obtained. In the second half of 2015, this rate was of 0.64%.

Figure 1 shows the curve with the frequency of transfusion reaction notifications received by the Risk Management and entered into Notivisa.

Regarding the notifying units, we observed that the highest number of notifications occurred among cancer treatment units, with 451 (30.80%) of the total notifications, followed by clinical units, with 352 (24.10%). Emergency and urgency units account for 16.30% (239) of the total notifications. Among the lowest percentage of notifications, there are the surgical units (8.40%) and the pediatric units, with only 2.20% of the total.

In our study of cases, no gender differences were observed. Transfusion reactions were found in 745 (51.00%) men and 717 (49.00%) women. In our sample, special highlights to the distribution of age groups, in which a slight difference between men and women was observed. In the age group of 70+, 115 reactions were reported in men (54.20%), while in the age group 60-69, 106 reactions were reported in women (44.80%). In other age groups, the distribution is fairly the same between the two genders. The lowest percentages of transfusion incidents were observed among children and adolescents, with 12%, and among adults (40 to 49 years), with 14% of the total reactions.

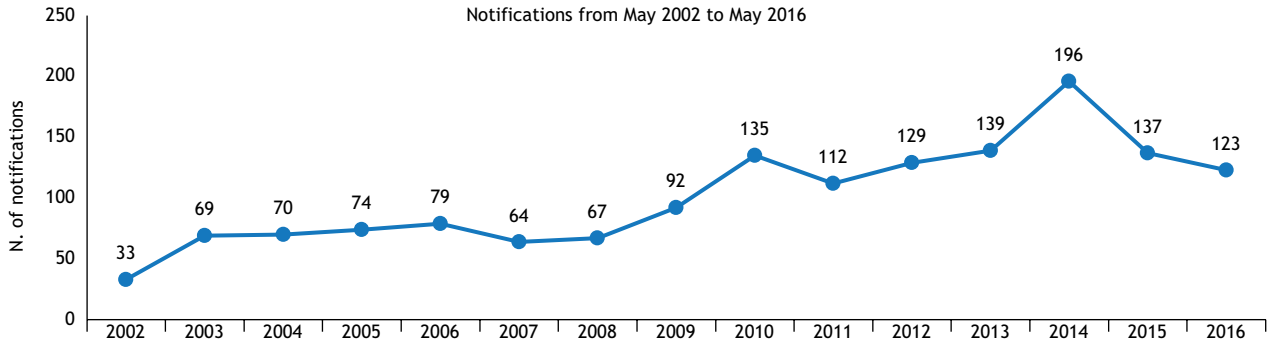
In Figure 2 we present the distribution of the transfusion reactions according to gender and age.

Regarding the clinical diagnosis of patients who received transfusion of blood or blood-based products and presented transfusion reactions, we observed that carcinomas stood out with 195 cases (13.30%), followed by acute myeloid leukemia (AML), with 178 (12.20%) and acute lymphoid leukemia (ALL), with 53 (3.60%). Another finding corroborates the researched literature, which points out a greater number of transfusion incidents in cancer patients. The cases reported during surgeries, as well as those occurred in the surgical center, accounted for 12.10% of the total reported incidents and were not treated in this study as clinical diagnosis, but as perioperative transfusions.

Table 1 shows the frequency of adverse reactions related to the type of blood-based product used in blood transfusion.

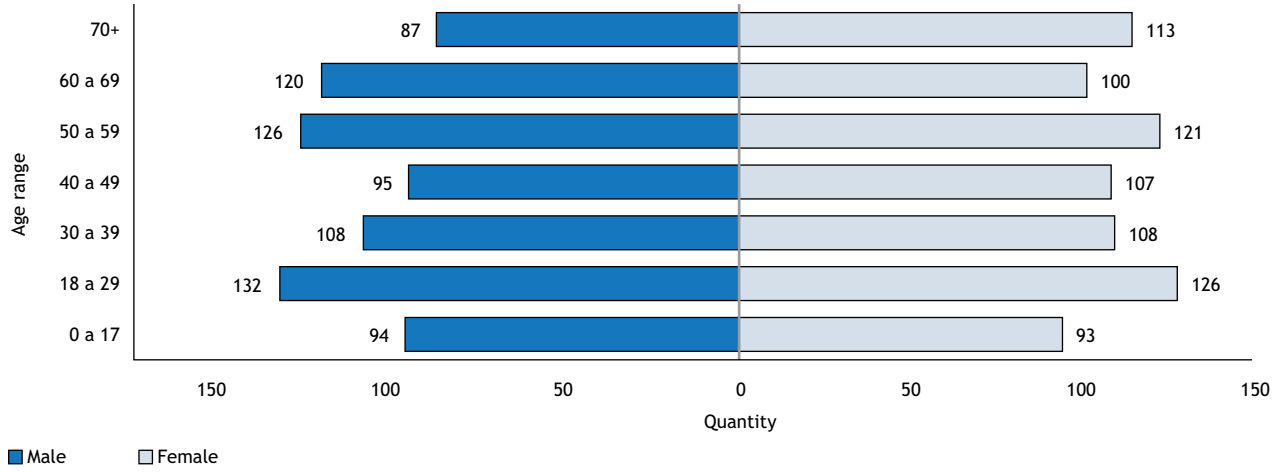
Regarding the type of blood-based product used in blood transfusion, we observed that the highest number of reactions was related to the therapeutic use of packed red blood cells, with 71.8% of the total reactions, followed by the platelet concentrate, with 17.4% of the total reactions, and 10.6% related to the use of fresh frozen plasma (FFP). Other types of blood-based products appear with less than 1% and were related to one case of granulocytes and another to cryoprecipitate.

As shown in Table 2, the highest rates of acute reactions were from febrile non-hemolytic transfusion reaction (FNHTR), with 814 (55.7%) of all cases reported, followed by allergic



Risk Management at Hospital São Paulo, 2002-2016.
N. = number of notifications received in the Risk Management and notified in the National Hemovigilance System.

Figure 1. Distribution of notifications received by the Risk Management and reported to the National Hemovigilance System, 2002-2016.



Risk Management at Hospital São Paulo, 2002-16.

Figure 2. Distribution of the age of the patients who presented transfusion reactions, 2002-2016.

Table 1. Distribution of type of blood-based products associated with transfusion reactions, 2002-2016.

Type of blood-based product	n	%
Packed red blood cells	1,050	71.8
Platelet concentrate	255	17.4
Fresh frozen plasma	155	10.6
Others	2	0.2
Total	1,462	100

Risk Management at Hospital São Paulo, 2002-16.

reactions (ALG), with 39.3%. However, when we observed the acute reactions of moderate or severe intensity, we verified the inversion of this data: moderate cases became more common and severe ones were mainly ALG (128 cases). At the same time, absolute values decrease precipitously for the cases of moderate and severe FNHTR (37 cases). Although there was greater morbidity, severe reactions were almost never reported in our study.

It can be seen in Table 2 that almost all reported transfusion reactions were mild (86.8%), followed by moderate and severe reactions, with 13.2% of the total. The severe reactions were mostly ALG (57.1%) followed by circulatory overload (TACO), with 23.8% of the total reactions entered into Notivisa.

DISCUSSION

The present study aimed to identify the most frequent adverse events related to the transfusion reactions that were entered into the Anvisa National Hemovigilance System. Data from the Notivisa system was used for insertion.

Hemovigilance at the researched institution was officially incorporated into Risk Management in 2002, when it began to report cases to Notivisa. We can emphasize that there was an upward curve of notification in the period between 2002 to 2015, and in the last five years, the notification increased by 100% (Figure 1). When analyzing our case series, between 2002 and 2009, we verified that we reported 4.65% of the total number of cases received by Notivisa from all institutions in the Network of Sentinel Hospitals in Brazil from 2002 to 2009[13,14].

Regarding the incidence of adverse events, we observed that this data differs from that reported in the European literature[12], which indicates the expected incidence of three reactions per thousand transfusions. In our series, when we analyzed the incidence rate per thousand transfusions, we observed values of 0.6% for the second half of 2014 and 0.64% for the same period of 2015. This data is quite close to that found in a study carried out in Iran, with a rate of 0.4%[15] and lower than that reported in Northwest India, of 0.92%[16].

In the present study, the highest number of reports occurred among the cancer treatment units, followed by the Clinical and Urgency and Emergency units. This data corroborates the literature, which evidences the highest number of incidents in cancer patients[1,8,9,17] and in Clinical Medical Units[12,13].

We noticed no difference in the gender of the patients who presented transfusion reactions. In our study, the mean age was 43.9 years. In a study conducted in Northwest India, it was 43.7 years, with a significant predominance of transfusion reactions among women, with 59.40% of the total reactions[16]. In other studies, a slight difference was observed between men and women: 47.9% and 45.7%[15]and 52.1% and 48.5%[18], respectively, and no differences were found between the two groups of men and women. In another cohort study, carried out in 21 centers in 11 countries, the predominance for males was 60%[17].

Regarding the type of blood-based products used, we verified that the highest number of reactions was related to the therapeutic use of packed red blood cells, with 71.8% of the total blood-based products, followed by the platelet concentrate, with 17.4%, and the FFP, with 10.6%.

Table 2. Distribution of the type of transfusion reaction according to the severity of the reaction, 2002-2016.

Reaction Type/Severity	Mild		Moderate		Severe		Total	
	n	%	n	%	n	%	n	%
Febrile non-hemolytic transfusion reaction (FNHTR)	777	61.2	36	20.9	1	4.8	814	55.7
Allergic reaction (ALG)	447	35.2	116	67.4	12	57.10	575	39.3
Circulatory overload (TACO)	19	1.5	10	5.8	5	23.8	34	2.3
Transfusion-related acute lung injury (TRALI)	5	0.4	6	3.5	2	9.5	13	0.9
Acute immunological hemolytic reaction (AIHR)	12	1	2	1.20	1	4.8	15	1
Hypotensive transfusion reaction (HIPOT)	6	0.5	2	1.2	-	-	8	0.6
Bacterial contamination (BC)	3	0.2	-	-	-	-	3	0.2
Total	1,269	100	2	100	21	100	1,462	100

Risk Management at Hospital São Paulo, 2002-16.

Regarding the type of reaction, we can highlight the FNHTR, data aligned with the national literature and Notivisa data, which reports 51.6% and 51.1% of the total cases diagnosed with FNHTR reported by all federated units in 2008[12] and 2010[13] respectively. In contrast to this data, a study with children indicated ALG as the main reaction, with 69.8%, followed by FNHTR, with 27.2% of the cases[9].

In our study of cases, concerning the severity of the reactions, we verified that, for the most part, those of greater severity were associated with ALG. This is corroborated by the national literature, which points out ALG as the main reaction reported to Notivisa by the Hospitals of the Sentinel Network[12,13,14].

Although the highest frequency reactions were mild, there was a 13.2% rate of moderate and severe clinical reactions. Among those considered severe, 57.1% were allergic and 23.8% were TACO. This data is corroborated by the literature[12,17,19].

We can point out as limitations to the study the possibility of a few records in the phase that preceded the orientation of reporting incidents from the identification of the increase of at least 1° C of elevation of body temperature in relation to the pre-transfusional value, which may have favored underreporting in the period prior to these recommendations.

Nevertheless, we reckon this study brings important contributions to clinical practice, both regarding the importance of reports of adverse events related to transfusion safety, and the presentation of the most frequent reactions and types of reported incidents. This scenario will enable preventive interventions of healthcare professionals to increase quality throughout the blood cycle, resulting in greater safety for patients and hemotherapy assistance.

CONCLUSIONS

The data on transfusion reactions at Hospital São Paulo, presented in this study, reported a growing average in recent years, with an average of 142 notifications/month after 2010. No differences were observed between the gender and age of blood and blood-based products recipients who had acute reactions. The most common reactions are FNHTR, mainly reported among cancer patients. Those that presented greater morbidity and mortality rates were the severe reactions, both ALG and TACO and transfusion-related acute lung injury (TRALI).

Through the critical analysis of this study we expect that the data can contribute to the improvement of hemovigilance services, in addition to having contributed to the feedback of Anvisa's Notivisa System. However, future studies that can evaluate more deeply the risk factors of these reactions should be encouraged in order to improve hemotherapy services and increase the safety of patients undergoing blood transfusion.

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Conflict of Interest

Authors have no potential conflict of interest to declare, related to this study's political or financial peers and institutions.