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Implementation of technical supervision of the public blood management agencies of Federal District and its effects on hemovigilance activities

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Abstract

Objective: To analyze the impact of the implementation of technical supervision in the Transfusion Agencies (TAs) of the public blood network hospitals of Federal District (DF) on hemovigilance activities, from 2009 to 2019.

Methods: Retrospective descriptive cross-sectional study with a quantitative approach. Two secondary databases were used: one with information on Transfusion Reactions (TRs) registered in the System of Notifications in Health Surveillance (Notivisa) and another with information on the number of transfusions performed, reported in the Hemotherapy Production Information System (Hemoprod). The information from each TA was separated into two periods: "without a supervisor" and "with a supervisor".

Results: 1,096 TRs were reported and 574,708 transfusions were performed. Considering only confirmed, probable and possible TRs, the number of TRs increased to 981, of which 85.43% were immediate, Allergic (37.92%) and Febrile non-hemolytic reaction (33.74%). More than 80% were mild, however, 2 deaths were attributed to transfusion (0.21%). They occurred predominantly in women (56.27%) and between 25 and 35 years (16.50%). The Transfusion Outpatient (22.43%) was the hospital sector with the highest occurrence of TRs, with Concentrated Red Blood Cells being the blood component most involved in these records (68.40%). In the "no supervisor" period, the notification rate was 0.220 and the underreporting was 92.666%, using the French parameter for comparison (3 TRs/1,000 transfusions). In the "with supervisor" period, the notification rate was 2.297 and the underreporting was 23.417%, showing that the inclusion of supervisors had an impact on the hemovigilance scenario in the TAs of the hospitals in the public blood network of the DF, reducing underreporting by 74.78%.

Keywords: Hemovigilance; Blood Transfusion; Transfusion Reaction; Transfusion Agency; Hemotherapy

1. Introduction

Blood transfusion consists of the intravenous infusion of blood components, which can be red blood cells (erythrocytes), white blood cells (leukocytes), platelets and/or plasma. It is used to reestablish or stabilize a -patient's clinical condition, and may even be the only treatment capable of saving the individual's life at that moment [1].

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As established by the Ministry of Health (MH) [2] and the National Health Regulatory Agency (ANVISA) [3] blood transfusion is proven to be effective, but it must be evaluated and indicated carefully, since every transfusion brings with it a risk to the recipient, whether immediate or late called Transfusion Reaction (TR). These can be classified according to the time of onset of the clinical and/or laboratory condition, severity, correlation with transfusion and diagnosis [3].

In Brazil, the National Hemovigilance System (NHS) began in 2001, when ANVISA identified the need for a program to assess the safety of blood transfusions, based on notifications of immediate or late transfusion incidents. In the same year, the first version of the Technical Manual of Hemovigilance was launched [4] and the Resolution of the Collegiate Board of Directors (RDC) n°149 was published, which regulated the structuring of the National System of Information on Hemotherapy Production [5].

In 2002, the NHS was implemented in a sentinel network of 100 hospitals, with the proposal to gradually reach the country's health services that performed any procedure included in the blood cycle [4]. However, in 2004, aiming at improving hemotherapy practice, RDC nº 153 [6] was published, which established the mandatory constitution of a multidisciplinary Transfusion Committee (TC) by health services that had a Hemotherapy Service (HS).

The Notivisa information system in force today, is a web system that can be accessed by health services and professionals and allows for the notification of adverse events and technical complaints about products and services under sanitary surveillance. Until 2010, TRs in Brazil were reported spontaneously, with the publication of RDC nº 57 [7], replaced by RDC nº 34/2014 [8] these notifications became compulsory.

In 2015, the NSH was revised, with the publication of the Conceptual and Operational Framework for Hemovigilance: Guide to Hemovigilance in Brazil, which expanded the scope of hemovigilance in the country, including donor, recipient and retrosurveillance hemovigilance. Thus, in addition to reporting all adverse reactions, it becomes mandatory to report serious near misses and incidents to which adverse reactions were not attributed [3].

In view of the above, the present study aimed to analyze the impact of the implementation of technical supervision in the Transfusion Agencies (TAs) of the public blood network hospitals of a federal unit in Brazil.

2. Material and methods

This is a descriptive, retrospective cross-sectional study with a quantitative approach. Two databases were used with information from public TAs with capacity for FHB (Fundação Hemocentro de Brasília) supervisors from 2009 to 2019. The first of the databanks brought information recorded in ANVISA's Notivisa System while the second one contained information on the total amount of transfusions performed by the TAs during the study period. Due to the lack of information on the number of transfusions performed, statistical corrections were necessary in 80 months, of the 1,584 analyzed in the study.

This information on the number of reactions and transfusions was used to calculate the incidence rate of each type of reaction for 1,000 transfusions performed, aiming at comparison with the national and world scenarios.

The TR notification rate by TA was calculated after differentiating the periods “with” and “without” a supervisor, using the following algorithm: the number of TRs that occurred for each year was linearly interpolated in relation to the month of entry or exit from the supervisor for each TA; the estimated TRs for each period (without supervisor and with supervisor) were added up; the number of transfusions performed during each period (without supervisor and with supervisor) was calculated; the TR results were divided by the number of transfusions and multiplied by 1,000.

Finally, for the execution of the comparative study, the French parameter was used, which estimates 3 TRs (confirmed, probable or possible) for every 1,000 transfusions, to find the expected reactions considering the defined intervals. Then, the difference between the number of expected reactions and the number of reactions that actually happened was calculated, which indicates whether there was possible underreporting or if there were more notifications of reactions than expected. It was divided by the number of expected reactions to make the comparison and transform this value into a percentage, always differentiating the periods without a supervisor and with a supervisor.

Information on notifications and the number of transfusions were stored in a Microsoft Excel® software spreadsheet (Microsoft Corp., USA), separated by TA and year, using the R statistical software for statistical analysis. Data were analyzed using simple descriptive statistics, using absolute and relative frequency.

To access the Notivisa data, authorization was requested from ANVISA through the ANVISA service channel (http://portal.anvisa.gov.br/contato). Regarding the information on the number of transfusions, authorization was requested from the FHB, through a letter of consent.

3. Results

In the period outlined for the study, 1,096 TRs were reported in the Notivisa System by the TAs of the public blood network hospitals that had the capacity of supervisors and 574,708 transfusions took place, according to information contained in the Hemoprod and after the statistical corrections performed.

The TRs only started to have records from 2011 onwards, with 2012 as the year with the highest number of notifications (19.07%). Of the 1,096 TRs notified in the analyzed period, only 981 met the imputability criterion defined for comparative analysis (confirmed, probable, possible).

As for the time of onset of the clinical and/or laboratory condition, 835 immediate reactions (85.12%), 143 delayed reactions (14.57%) and 3 without information (0.31%) were recorded. Only the Anaphylactic reaction did not present information about the reaction time, however, it is known that this is an immediate allergic reaction. Among the delayed reactions, the Alloimmunization/Positive irregular antibody screening (ALLO/PAI) type reaction was the only one that showed an increase in the number of notifications in recent years, from 10 records in 2016 to 50 in 2019.

The period between 2011 and 2019 showed predominance of Allergic reaction (ALG), with 372 records, followed by Febrile non-hemolytic reaction (FNHTR) with 331 records, in both, more than 80% were classified as mild. Despite the absence of any serious reaction in Acute non-immune hemolytic reaction (ANIHR) there was one confirmed death attributed to this reaction. The other death identified in the analyzed period was classified as possible, in the Transfusion-associated circulatory overload (TACO) reaction. The Anaphylactic reaction had only three occurrence records, being predominantly moderate (66.67%). In 2015, with the publication of the Conceptual and Operational Framework for Hemovigilance: Guide to Hemovigilance in Brazil, the Anaphylactic classification was excluded [3].

In the analyzed period, there was no occurrence of TR of the Infectious disease transmission type (IDT), Transfusion-associated graft-versus-host disease (TA-GVHD), Post-transfusional purpura (PTP), Hemosiderosis with organ involvement (HEMOS) and Metabolic disturbances (MD).

In this group of analyzed TRs, only 4 had the gender item as ignored, being 2 ALG and 2 FNHTR, corresponding to 0.41% of the total. There was a predominance of the occurrence of reactions in females, with 552 records of the 981 occurrences, corresponding to 56.27% of this total.

Regarding age, this was grouped into 5-year interval groups, with the exception of the interval between 0 and 1 year, 1 year and 5 years and 85 and 100 years. The age group with the highest number of TRs was between 25 and 35 years old, with 162 records (16.50%) and the lowest number of TRs was identified in the 85-100 age group, with only 15 TRs (1.54 %).

Regarding the hospital sector where the reactions occurred, it was found that most of the reactions occurred in the Transfusion Outpatient (220 records) and in the Medical Clinic (214 records), corresponding, respectively, to 22.43% and 21.81% of the total of reactions occurred. The Bone Marrow Transplant sector registered the lowest number of reactions, only 3, which corresponds to 0.32% of the total reactions. In the ICU/ICU, it was the place where the only Bacterial infection (TTBI)occurred. In the Emergency/PS of the 141 occurrences, 49 were ALG (34.75%) and 46 FNHTR (32.62%). The only confirmed death occurred at the Gyneco-Obstetric Clinic.

Regarding the identification of blood components involved in TRs, 68.40% occurred in the exclusive transfusion of Red Blood Cells Concentrated (RBCC), while 19.70% occurred exclusively in the transfusion of Concentrated Platelets (PC) and 6.32% occurred exclusively in Fresh Frozen Plasma (FFP) transfusion. All reactions were predominant in RBCC transfusions, with the exception of ALG, which totaled 45.43% when PC was transfused.

3.1. Analysis of rates: incidence and under notification

If we consider all reactions, regardless of imputability and transfusions performed by public TAs with supervisors, we find a TR rate of 1.91/1,000 transfusions. In an analysis considering only the TRs in the confirmed, probable and possible imputability, this rate becomes 1.71/1,000 transfusions in the studied period.

Analyzing Table 1, which deals with the incidence rate of each type of reaction, it is possible to identify the TRs ALG and FNHTR were the ones with the highest incidence.

Table 1 Rate of TRs per 1000 transfusions, Brasília, DF, 2009-2019

Total reaction type	**Total (confirmed, probable, possible)**	**Rate**
Allergic - ALG	372	0,647
Anaphylactic	3	0,005
Alloimmunization/Positive irregular antibody screening - ALLO/PAI	138	0,240
Transfusion transmitted bacterial infection - TTBI	1	0,002
Transfusion-associated dyspnea - TAD	8	0,014
Acute pain transfusion reaction – APTR	1	0,002
Transfusion-associated acute lung injury - TRALI	10	0,017
Febrile non-hemolytic reaction - FNHTR	331	0,576
Acute non-immune hemolytic reaction - ANIHR	2	0,003
Acute immune hemolytic reaction - AHTR	13	0,023
Delayed hemolytic reaction - DHTR	3	0,005
Hypotensive transfusion reaction – HTR	11	0,019
Other immediate reactions - OI	47	0,082
Other delayed reactions - OD	2	0,003
Transfusion-associated circulatory overload - TACO	39	0,068
TOTAL	981	

Source: author's elaboration based on ANVISA data.

In terms of the impact of technical supervision on hemovigilance, according to the records analyzed, the date of occurrence of some TRs is not consistent with the year in which they were notified. In addition, it is possible to verify that in the presence of the supervisor most of the reactions show agreement between the record of the year of occurrence and the year of notification. Those represented as discordant evidence that the TR had been identified at the time, but had not been registered in Notivisa or even that the TR was identified by the supervisor in a retrospective analysis, based on the information recorded in the medical records. It is noted that in the interval in which there was no supervisors' presence, many TAs did not notify the TRs and even though those TAs did register, many reactions occurred in the period prior to the notified one.

In raw data, when using the French parameter of 3 TRs per 1,000 transfusions, for the 574,708 transfusions, 1,724.12 TRs would be expected in public TAs with supervisors. As only 981 TRs actually took place, we found a global underreporting of 43.10% in the analyzed period. However, as observed in Table 2, with the number of supervisors, the rates of notifications increased, highlighting the TA of hospital 2, which had a rate in the period with a supervisor that was 22 times higher than that recorded in the period without a supervisor.

The comparison used was the division between the rate after the supervisor entered by the rate before the supervisor entered. The symbol "-" indicates division, meaning that values divided by 0 are undetermined. For the other values, it is noted that the inclusion of supervisors increased the number of TRs notified in all TAs.

Analyzing the general data in the pre-supervision period, of the total notified, 36 reactions in 163,389 transfusions actually occurred. The expected, according to the French parameter, would be 490.167 TRs, which shows an underreporting of 92.666%. After the supervisors were hired, there were 944,997 reactions in 411,319 transfusions. In

this case, taking into account the same parameter, 1,233,957 reactions would be expected, which shows an underreporting of only 23.417%. Therefore, it is demonstrated that the inclusion of supervisors had an impact on the hemovigilance scenario in the TAs of the public blood network hospitals, since there was a 74.78% reduction in underreporting, indicating an increase in the number of notifications of TRs in Notivisa.

Table 2 Rate of TRs according to period with absence and presence of supervisors in each TA, Brasília, DF, 2009-2019

TA - Hospital	Period without Supervisor	Rate	Period with supervisor	Rate	Ratio among rates
1	Until Nov. 2010	0,000	Nov. 2010 – Dec. 2019	2,254	-
2	Until Feb. 2012	0,131	Feb. 2012 – Dec. 2019	2,906	22,184
3	Until Feb. 2011	0,509	Feb. 2011– Nov. 2011	2,758	5,418
	Dec. 2011 – Sept. 2012		Oct. 2012 – Dec. 2019		
4	Until Oct. 2010	0,154	Oct. 2010 – Dec. 2010	2,772	18
	Jan. 2011 – Feb. 2011		March. 2011 – Apr. 2014		
	May/2014		Jun. 2014 – Dec. 2019		
5	Until April. 2013	0,706	Apr. 2013 – Aug. 2013	4,106	5,816
	Sept. 2013 – Jan. 2018		Feb. 2018 – Dec. 2019		
6	Until Feb. 2011	0,000	Feb. 2011 – Dec. 2019	2,737	-
7	Until April. 2013	0,189	April. 2013 – Dec. 2019	1,788	9,460
8	Until Oct. 2010	0,280	Oct. 2010 – Dec. 2014	1,935	6,911
	Jan. 2015 – Jan. 2018		Feb. 2018 – Dec. 2019		
9	Until March. 2011	0,000	March. 2011 – Dec. 2019	1,920	-
10	Until Feb. 2011	0,000	Feb. 2011 – Dec. 2019	1,417	-
11	Until Oct/2012	0,846	Oct. 2012 – Oct. 2016	1,011	1,195
	Nov. 2016 – Jan. 2018		Feb. 2018 – Dec. 2019		
12	Until dec. 2010	0,000	Dec. 2010 – Dec. 2019	2,821	
Blood bank rate without supervisor		0,220	Blood bank rate without	2,297	10,441

Source: author's elaboration based on data from ANVISA, Blood Management Section (SEHEMO) and Planning Section (SEPLAN). Note: Rate - ratio between the number of transfusion reactions and the number of transfusions performed for every 1000 transfusions.

4. Discussion

Although it is necessary, the transfusion process involves the risk of transfusion incidents that can generate additional costs for the health system and in some cases it might lead to death [9]. Transfusion safety is the main objective of recipient hemovigilance and it depends on the various actors involved in the hemotherapy process [10].

Due to the fact that many reactions start with non-specific symptoms such as fever or chills and occur in patients who have complex underlying clinical conditions, many TRs go unnoticed by the care team or are identified at a more advanced stage, impacting the patient's clinical condition [11]. Therefore, knowledge and training of professionals in topics related to hemovigilance is essential, thus building more and more evidence that corroborates safety in clinical practice [12].

From 1,096 TRs notified in the period from 2009 to 2019 in patients transfused in public TAs with supervisors, most were registered in 2012, when training was carried out for professionals involved in hemovigilance. At that time, many supervisors reported reactions that had already occurred in previous years, contributing to a high number of notifications.

Considering (n=1,096, all notified TRs), the percentage of immediate transfusions was 85.95% and that of late transfusions was 14.05%. According to the Hemovigilance Report – Consolidated Data from 2007-2015, immediate TRs predominate in Brazil, reaching a percentage higher than 97% [13]. In the international scenario, although immediate TRs also predominate, the percentage is lower than in Brazil, which can be explained by the adoption of conducts in the hemotherapy routine, such as the universal filtration of blood components. In this study, there was no universal filtration of blood components and it was not possible to identify which TRs occurred with filtered blood components, since this information is not available in the database used.

The ALLO/PAI type reaction was the only late one that showed an increase in the number of notifications in the last four years. This exponential growth of ALLO/PAI type reactions may be related to the gradual implementation of the gel methodology in TAs, which began in 2013 and ended in 2014. The gel technique, when compared to the methodology for carrying out immuno- hematological tests in tubes, is faster and safer, since it is a more sensitive technique, which allows the identification and accurate reading of the results.

In the analysis (n=981, confirmed, probable and possible TRs), the reactions that occurred most in the study were ALG and FNHTR, corresponding, respectively, to 37.92% and 33.74% of the total. When we analyze (n=1,096), this percentage increases to 34.49% in ALG reactions and 35.31% in FNHTR, coming closer to the scenario set out in the Consolidated Report 2007-2015 Hemovigilance in Brazil, which concluded that the reactions more frequently reported in the country were FNHTR, (49%) and ALG (37%) [13]. Therefore, this result allows us to conclude that the percentage of these reactions is below the national value, which can infer that many reactions may have gone unnoticed, both by patients and by the team, and it is extremely important to clarify the patient about the possible adverse effects of transfusion. and the intensification of the training of professionals.

In terms of severity classification, analyzed (n=1,096), 78.92% were mild, 14.96% moderate, 5.75% severe and 0.36% died. The Hemovigilance Report – Consolidated Data 2007-2015 identified an average frequency of approximately 83% of mild TRs in Brazil [13] and the Hemovigilance Bulletin nº 7 October 2015 [14], in the analysis of reaction notifications by type of severity for 2014, it was found that moderate severity corresponded to 14.3%; severe severity 2.8% and death 0.3% of the year's notifications. It is noted that what was found in the study was higher than that found in Brazil in 2014, which suggests a probable underreporting of severe reactions in Brazil or even a deficit in hemotherapy care in the DF.

Of the 2 records of deaths caused by TR, only 1 was confirmed at the end of the investigation, being attributed to ANIHR, which is considered a rare reaction and would hardly require a more rigorous intervention [4]. The other death was classified as possible in the TACO reaction and occurred in a 68-year-old patient, corroborating the concern about the severity of TACO described in the summarized annual report of the SHOT Report 2016, which recommends the application of a previous checklist in elderly patients aiming at the evaluation of the receptor and the prevention of the risk of developing this reaction [15].

The occurrence of these 2 deaths generated an incidence rate of 0.35 deaths per 100,000 blood components transfused. As stated in the Consolidated Report 2007-2015 Hemovigilance in Brazil, in 2015 the French system presented the frequency of occurrence of severity IV - death attributed to transfusion (n=981) of 0.2/10,000 transfused patients or 0.32 deaths per 100,000 grants released [13], similar to the results found in this study. However, this comparability proves to be unreliable, given the divergence between the denominators of the French hemovigilance system, which uses transfused patients or released bags, and the Brazilian system, which uses transfused bags/units [13], in compliance with the provisions of RDC nº 149 of august 14, 2001 [5].

As foreseen in the Consolidated Report 2007-2015 Hemovigilance in Brazil [13] there was a small predominance of females, with 56.39% (n=1,096) and 56.27% (n=981). Regarding age, the age group with the highest number of notifications of TRs was between 25 and 35 years old, with 181 records (16.50%), which differs from that found in this same report, in which the greater participation of the older age groups was evident high in the occurrence of TRs [13]. This higher concentration of TRs in the age group between 25 and 35 years (16.50%) may only reflect the fact that in this age group, the occurrence of reactions is more frequent than in the smaller or older groups.

In the analysis (n=1,096), the Medical Clinic (21.99%) and the Transfusion Outpatient (21.08%) were the places with the highest occurrence of TRs. In the analysis (n=981), the sector with the highest occurrence of TRs became the Transfusion Outpatient (22.43%), followed by the Medical Clinic (21.81%). In the Consolidated Report 2007-2015 Hemovigilance in Brazil, the sector with the highest prevalence of reported TRs is Medical Clinic, followed by ICU/ICU and Transfusion Outpatient [13]. In this study, the ICU/ICU site appeared in fourth place, with 10.77% of notifications. The prevalence of notifications of TRs in these sectors may be due to the more intense action of supervisors in these

places due to the ease of access; the greater number of professionals trained in hemovigilance actions; the lower turnover of care teams; or even, due to the better clinical condition of the patients, since the patients of the transfusion clinic and the medical clinic are not as severe as the patients in the ICU/ICU or operating room, which allows the symptoms of TRs to become more evident for team identification.

Most of the TRs (68.40%) occurred in the exclusive transfusion of RBCC, while 19.70% occurred exclusively in the transfusion of PC. As described in the Consolidated Report 2007-2015 [13] RBCC was the blood component most associated with reported TRs, which is consistent with the literature, since approximately 85 million RBCC are transfused annually worldwide [16]. In this study, all types of reactions were predominant in RBCC transfusions, with the exception of ALG, which totaled 45.43% when PC was transfused, meeting the expectation described in the literature.

Unlike what is predicted in the literature, which reports a higher prevalence of FNHTR in PC transfusions [17], in this study, FNHTR occurred predominantly in RBCC transfusions. The divergence could also be observed in the TRALI-type reaction, whose literature predicts a higher occurrence in FFP transfusions [4] and in this study it was in RBCC transfusions. This higher occurrence of TRALI in RBCC transfusion is similar to the result found in the study developed in São Paulo (SP), which identified 87 TRALI-type reactions in RBCC transfusions, 23 in PC transfusions and 9 in FFP transfusions [10].

Regarding the calculation of incidences by type of reaction, three questions need to be clarified. First, the incidences of the French, American and other countries' hemovigilance systems consider only the TRs that had a confirmed, probable or possible association with transfusion [10]. On the other hand, the Brazilian hemovigilance system only started to work with this same analysis in 2015, when the Conceptual and Operational Framework for Hemovigilance: Guide to Hemovigilance in Brazil was published [3]. Second, that there may be divergence in the numerator and denominator. In this study, to calculate the incidence, the number of TRs in the numerator and the number of blood components transfused in the denominator, which are most commonly used, were used [10, 13]. And third, that the incidence of certain reactions may have been influenced by notifications in OI (0.082/1,000) and OD (0.003/1,000) classifications, in which reactions not listed in the list defined by Notivisa or even those that care professionals had some difficulty in defining, leading to a wrong classification.

The incidence rate of ALG reactions (n=981) was 0.647/1,000 transfusions, which is consistent with the frequency observed in New Zealand in 2015, which identified an incidence of 0.67/1,000 for ALG reactions [18]. As mentioned above, 45.43% of ALG reactions occurred during PC transfusion, which is consistent with the study by Hirayama [19] which states that the occurrence of ALG reaction is apparently associated with a higher risk in PC transfusion. Regarding the occurrence of Anaphylactic reactions, we can say that it is a rare reaction and varies from 3.33 to 8/100,000 transfusions [9, 20]. In this study, the incidence found was 2.61/100,000 transfusions, inferring, therefore, an underreporting of this type of reaction, making it necessary to reinforce the training actions of the teams.

The incidence of FNHTR varies from 0.01 to 3/100 transfused units [9, 21]. Therefore, the incidence found in this study of 0.06/100 transfusions is consistent with that described in the literature. Savage [21] states that the occurrence of FNHTR increases with the storage time of the blood component and decreases with the use of a filter to remove leukocytes. In addition to these factors, the use of antipyretics prior to transfusions interferes with the incidence of FNHTR. In this study, the storage time of the blood component, the use of filters and the previous use of antipyretics by the patients were not subject to analysis.

The third highest incidence found in the study was the ALLO/PAI reaction (0.240/1,000). The frequency of this reaction in this study corresponded to 14.07% of the reactions that occurred, being higher than that found in the study carried out in 25 countries from 2006 to 2012, which found a frequency of 12.1% in ALLO/PAI reactions [22]. The incidence of this reaction is directly proportional to the number of transfusions, being higher in chronic patients who receive frequent transfusions (up to 60%) [23]. In the study carried out, it was not possible to analyze this information on transfusion in groups of chronic patients and their respective allo-immunization rates.

TTBI is considered a serious TR and its incidence rate may vary depending on the use of technologies to reduce pathogens [24]. Regarding the rate of bacterial infection by transfusion, according to the Consolidated Report 2007-2015 Hemovigilance in Brazil, in 2015 the French system presented a rate of 0.16 for every 100,000 blood components released [13]. In this study, the rate found was 0.17 per 100,000 transfused blood components. However, as already discussed in the discussion of the frequency of occurrence of severity IV – death attributed to transfusion, this comparability is shown to be unreliable, due to the divergence of denominators of the French and Brazilian hemovigilance systems [13].

The same also occurs with the incidence rate of TRALI, which in the French system was 0.6/100,000 blood components released and in this study it was 1.74/100,000 blood components transfused (n=981). In the United States, where TRALI prevention measures are most effective, this rate was 1.1/100,000 transfused units in the period from 2010 to 2012 [25]. In the analysis (n=1,096), the incidence of TRALI increased to 2.96/100,000 transfusions, higher than the Brazilian rate found in the Consolidated Report 2007-2015 Hemovigilance in Brazil, which was 1.98/100,000 transfusions [13].

The incidence of TAD found was 0.014/1,000 transfusions and corresponded to 0.82% of the TRs that occurred, being almost 3 times lower than the result found in the study carried out in 25 countries from 2006 to 2012, which found a frequency of 2, 2% of TAD-type reactions [22]. Therefore, this result shows an underreporting of TAD in this study, which may be due to the difficulty in characterizing this reaction, since respiratory distress should not meet the criteria for TRALI, circulatory overload associated with transfusion and allergic reaction [3].

According to Brasil [4] the incidence of APTR is 1 in every 4,500 units transfused, however, in this study the incidence found in the analysis of all reported TRs was 0.003/1,000 transfusions, much lower than predicted in the literature, showing underreporting. Despite the low incidence of ANIHR in the study (0.003/1,000 transfusions), one death was attributed to this reaction. In the study carried out by Fernandes, the maximum incidence of ANIHR was 0.02/1,000 tranfusions [10].

In Brazil, for 2015, the Consolidated Report 2007-2015 Hemovigilance in Brazil [13] showed a percentage of occurrence of AHTR of 0.43% among all reported reactions, maintaining the same percentages as in 2014. In 2015, France found a incidence of AHTR of 0.4/100,000 units delivered [26] and the United States, in the period from 2010 to 2012, identified a frequency of AHTR of 1.1/100,000 units transfused [25]. In this study, the percentage of occurrence of this reaction was 1.33% (2.3/100,000 transfused blood components) when considered (n=981) and 1.19% if considered (n=1,096), evidencing a higher percentage than described in the hemovigilance systems mentioned above. This result reflects that it will still be necessary to go a long and continuous way to improve the quality of hemotherapy care in public TAs that had the capacity of supervisors. Once again, it is necessary to talk about the need for the TC to act and for periodic training of those involved in the transfusion process, since this is a preventable reaction, from the point of view of the execution of the process, since its main cause is linked to human failures, such as errors in the identification of the recipient or the samples collected for pre-transfusion tests. It is noteworthy that the severity of this reaction is directly associated with the amount of incompatible blood transfused. Therefore, if there is any suspicion, it is recommended to suspend the transfusion immediately and collect new samples to repeat the pre-transfusion tests.

The occurrence of DHTR was 0.52/100,000 transfusions, a value well below the incidence found in the study carried out in the United States from 2010 to 2012 (4.2/100,000) [25]. The underreporting of this reaction may be related to its late occurrence, which varies between 24 hours and 28 days after transfusion, making its correlation with transfusion difficult.

Another uncommon reaction is HTR in this study its incidence was 1.91/100,000 transfusions, 3.3 times lower than in the United States (6.3/100,000), pointed out by Harvey et al [25]. The difficulty in characterizing this reaction may be the main cause of this underreporting, since its etiology is not yet well established [4].

The occurrence of TACO is directly associated with the excessive amount and rapid rate of infusion of the blood component. It occurs more frequently in the elderly and patients with renal or heart failure [9]. The incidence of TACO found in the study was 0.068/1,000 transfusions (0.68/10,000 or 6.79/100,000), which is very close to the rate in Portugal from 2007 to 2015, which was 0.5/10,000 transfusions. [27].

The general rate of notified TRs (n=981) in public TAs with supervisors in the analyzed period was 1.71 per 1,000 transfused blood components and 1.91 per 1,000 transfused blood components, if all reactions reported in this period are considered (n =1,096). The result found (1.91/1,000) is lower than the Brazilian average, which corresponded to 2.8/1,000 in the period from 2011 to 2014 [28] and is also lower (1.71/1,000) than the result of a study carried out in United States, in which reactions reported from 2010 to 2012 in the Hemovigilance Module of the National Healthcare Safety Network (NHSN) resulted in a reporting rate of 2.39/1,000 [25]. Although the difference between the rates observed in public TAs with supervisors and in Brazil is not large, it may have been biased by the statistical corrections made to the missing information on the number of transfusions performed.

Despite the incidence of TRs in the study being lower than expected, the results before and after the inclusion of supervisors in the TAs of the public blood network allow us to affirm that the presence of the supervisor contributed to the hemovigilance activities, since it increased from 36 to 944,997 the number of notifications of TRs occurred. As a

result, the TRs rate went from 0.220 in the period of the "without a supervisor" to 2.297 in the period "with a supervisor", evidencing an increase of more than 10 times in this rate and approaching the French parameter of 3/1,000, in addition to reducing underreporting by 74.727%.

This rate of TRs of public TAs with supervisory capacity of 2,297 reactions per 1,000 transfusions contradicts the expectation provided for in the Consolidated Report 2007-2015 Hemovigilance in Brazil, that the rate of TRs in the country should be closer to 5 TRs/1,000 transfusions [13]. Therefore, even with the evident improvement in hemovigilance actions in the face of the capacity of supervisors, there is still much to be done, as this underreporting is a risk not only for patients, but also for care teams and hemotherapy managers.

Limitations of the study

The results of this study are subject to the following limitations: first, it was necessary to correct the missing data regarding the number of blood components transfused in 80 months, using the average and median. In addition, despite the current legislation defining that the hemoprod field must be filled in with the number of blood components transfused, there are reports of filling errors, where information on the number of transfused patients is considered. Finally, the manual filling of the hemoprod information may have caused transcription errors and loss of information. Therefore, all these intercurrences may have influenced the denominator used to calculate the rates.

5. Conclusion

Hemovigilance is essential for greater patient safety, with the reduction and prevention of transfusion risks, since its information contributes to the adequate monitoring and improvement of activities related to the transfusion act.

This study allowed the consolidation of the hemovigilance scenario in the TAs of the public blood network hospitals, making it possible to carry out a deeper analysis of the notifications of TRs and also to make some recommendations, namely:

- The inclusion of more supervisors or the extension of the period of work of these professionals in the TAs of the hospitals of the public blood network can further reduce the underreporting of TRs and qualify their records;
- It is necessary to invest in the continuing education of health professionals who work in the transfusion process, including those responsible for technicians and prescribing doctors, so that the transfusion is strictly indicated and monitored;
- Also related to the training of teams, they should be made aware of the importance of early identification of signs and symptoms of TRs, management and notification. The need for complete records should be reinforced, allowing the identification of the main risk factors and the establishment of preventive measures against future incidents, increasing the safety of patients undergoing transfusion therapy;
- The creation and dissemination of subjects related to hemovigilance in posters, folders, applications and the computerization of this post-use process, with the design of the TR notification form, can contribute to increasing the adherence of teams in the monitoring of adverse events;
- The role of the TC must be intensified in hospitals, as it is essential to improve the quality of transfusion processes and mitigate the underreporting of TRs;
- The strengthening of the TC team is essential to expand the active search for TRs and their notification in the Notivisa System. In this process, it is important to include other health professionals working in each TA or in the Patient Safety Center (NSP) of the hospital, in the respective TC, aiming at the formation of an active multidisciplinary team;
- For the management of the transfusion process, the creation of an indicator related to the occurrence of TRs is considerable, allowing quick and satisfactory interventions,
- The evaluation of the hemovigilance process will be more reliable with the availability of a computerized tool or with the strengthening of existing tools for collecting the number of transfusions;
- The creation of the Hemovigilance and Good Transfusion Practices Subsection in the organizational structure of the FHB will contribute to the evolution of activities related to the topic, requiring the establishment of flows and a routine of data collection and analysis of the TRs notified by the hospitals of the public blood network, in order to a reduction in TRs related to the production process of blood components;
- Efforts to establish benchmarking with other regional, national and international institutions may allow the standardization of methodologies for the characterization and measurement of TRs and consequently a more valid comparison between the systems.

Therefore, future studies in the area of hemovigilance should focus on prevention, adequate management, treatment and standardization of notification of transfusion incidents. This expansion and consolidation of information will contribute to the strengthening of scientific evidence and consequently to the safety of the transfusion act, offering quality care and new knowledge in this area.

Compliance with ethical standards

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No conflict of interest.

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