THE INCIDENCE OF ADVERSE REACTIONS AMONG VOLUNTARY WHOLE BLOOD DONORS IN VOJVODINA: A FIVE YEAR CROSS-SECTIONAL STUDY

Bežanović Milomir (1), Gulan Zdravko (1), Budakov Obradović Zorana (1,2), Grujić Jasmina (1,2)

(1) BLOOD TRANSFUSION INSTITUTE OF VOJVODINA, HAJDUK VELJKOVA 9A, NOVI SAD.
(2) DEPARTMENT OF INTERNAL MEDICINE, FACULTY OF MEDICINE IN NOVI SAD, HAJDUK VELJKOVA 3, NOVI SAD, UNIVERSITY OF NOVI SAD.

Abstract: Introduction: Blood donors (BDs), in most cases, tolerate the whole blood donation procedure well. However, occasionally adverse reactions (ARs) may occur. ARs often have a negative impact on donors return. Therefore, the staff of transfusion institutions must be educated and properly trained to recognize and take care of BDs who experience ARs before, during or after the procedure. The incidence of ARs is about 1,4%. Aim: To determine the frequency and severity of ARs that occurred among BDs on the territory of Vojvodina, analyze the age and profile of donors in whom they were recognized, indicate possible prevention of ARs. Material and methods: In a retrospective study, the records of ARs among whole BDs at the Blood Transfusion Institute Vojvodina, from January 1 2017, until December 31, 2021 were analyzed. Demographic data of the donors were obtained from the Institute's information system. The data were analyzed according to the time and manner of occurrence and the severity of ARs. Results: During the study period there were 194 425 blood donations. The ARs were identified in 2722 (1,4%) donations. The incidence was 14 in every 1000 donations. BDs who suffered ARs were 28,0 ± 8,3 years old, 1881 (69,1%) were male, 841 (30,9%) were female, while 1908 (70,1%) donated blood for the first time. In 2396 (88,03%) BDs vasovagal reaction occurred, 737 (27,08%) experienced nausea, 363 (13,33%) suffered syncope, 221 (8,13%) developed hyperventilation, 64 (2,34%) gained hematoma. Severe ARs in the form of collapse with convulsions were experienced by 12 (0.44%) donors. In multiple BDs, ARs were significantly less frequent ($p<0,05$). Conclusion: Although the number of donors with ARs in institution is low, it is necessary to monitor them, react promptly in case of their occurrence and minimize the risks of occurrence, primarily through education and preparation of donors for the whole blood donation procedure.

Key words: Blood donors, haemovigilance, fainting, adverse reactions/incidences, vasovagal reaction

INTRODUCTION

Continuous supply of health institutions with sufficient amounts of blood and blood products represents the main task of every transfusion institution. Blood transfusion is one of the most common interventions in medical practice since there is no effective substitute for human blood. Having in mind that blood collection is limited to healthy individuals, ensuring donor's safety without adverse reactions (ARs) is an essential factor that will encourage them to donate blood and come back again in the near future. Blood donation is voluntary, non-remunerated and anonymous. On the territory of Serbia, all needs for blood and blood components are met from one's own sources [1]. In order to ensure sufficient amounts of blood, it is necessary to take measures to retain the old voluntary blood donors (BDs) and recruit new ones. With that in mind, it's important to implement a series of activities to motivate the population and promote blood donation. Although blood donation is considered a safe procedure with low risk rates, every potential BD is thoroughly screened to ensure the safety of both the donor and the recipient. Based on the Ordinance on donors of blood or blood components (Službeni glasnik RS, No. 6/2019-132), any healthy person aged from 18 to 65 years who fulfills the following criteria can be a donor of blood or blood components:

a) good general condition and good venous access;
b) body weight of at least 50 kilograms;
c) adequate hemoglobin and hematocrit values (above 125 g/L and 0,38 L/L for a female; above 135 g/L and 0,40 L/L for a male);
d) body temperature less than 37 °C, pulse 50-100 heartbeats per minute;

e) blood pressure not higher than 180/100 mmHg and not lower than 100/60 mmHg.

After selection and examination of the BDs, blood for transfusion is taken from the cubital vein into disposable bags of 450 mL so that the amount of blood taken is up to 13% of the total volume of the donor's blood. Adverse reactions (ARs) in BDs are defined as any adverse response associated with the collection of blood or blood components and they occurred in about 1% to 5% of blood donations [2]. They must be documented in the donor's records, but also in the records of the quality control system. Analysis of donor adverse reaction reports will definitely help developing approaches to the improvement of the overall safety of blood collection. According to the recommendations of the Council of Europe and the Guide for the preparation, use and quality assurance of blood components, 20th edition, from 2020, a classification of complications related to blood donation was performed [3].

ARs can be classified as:

a) Local complications: hematoma, arterial puncture, nerve injury or compression, tendon injury, thrombophlebitis, local allergic reaction, infection;

b) General complications: vasovagal reaction (VVR) (immediate or delayed; at the venipuncture site or outside);

c) Other complications: generalized allergic reactions, cardiovascular reactions (cardiac arrest, angina pectoris, cerebral ischemia), accident or injury.

According to the severity, ARs can be divided into:

a) ARs which are not significant, classified as mild and moderate:

Hematoma: - local discomfort only during phlebotomy, minor pain or functional impairment (mild)

local discomfort during phlebotomy, but also after the procedure, when performing daily activities (moderate)

Arterial puncture: - without symptoms or local discomfort during venipuncture, without hematoma (mild)

local discomfort that persists after blood collection is completed (moderate)

Pain in the arm: - symptoms lasting less than 2 weeks (mild)

symptoms lasting more than 2 weeks but less than 1 year (moderate)

Vasovagal reactions: - subjective symptoms only (mild)

objective symptoms (moderate)

b) Adverse reactions associated with blood collection that could lead to incapacitation of the donor and result in hospitalization and morbidity are defined as severe reactions such as delayed syncope, cardiac arrest, collapse with convulsions, cerebral ischemia.

AIM

The aim of this study was to determine the frequency and severity of ARs that occurred among BDs on the territory of Vojvodina by analyzing the age and profile of donors in whom they were recognized but also to indicate possible prevention of ARs.

MATERIAL AND METHODS

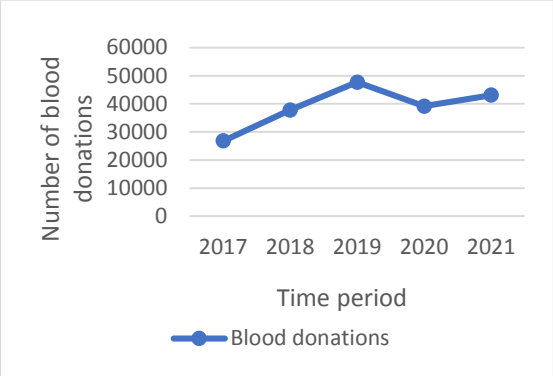
In a retrospective study, the records of ARs among whole BDs at the Blood Transfusion Institute Vojvodina, from January 1, 2017, until December 31, 202 were analyzed. Depending on the number of blood donations, donors are categorized into first-time and multiple donors. Demographic data of the donors related to age, gender, number of donations and place of donation were obtained from the Institute's information system. Depending on the time of occurrence, a classification and analysis of ARs were performed on those that occurred before the beginning of the blood donation procedure, during the procedure and after the procedure is completed. According to the type of occurrence, ARs were divided into local and systemic reactions, while, according to the severity, they were classified and analyzed into mild, moderate, and severe.

The data were analyzed and processed using the methods of descriptive statistics in the Minitab 16 software program. The following descriptive statistical parameters were used: arithmetic mean, standard deviation and median. ANOVA was used to assess the statistical significance of the obtained results with a significance level of less than 0.05. The findings are presented in tabular and graphical form.

RESULTS

During the study period, 194,425 donations were collected and analyzed, in which 108,014 voluntary donors of whole blood participated (Graph 1). Among the blood donors, there were 83.678 (77.47%) men and 24,336 (22.53%) women (the male/female ratio was 3:1). There were 99,524 (92.14%) multiple donors and 8,490 (7.86%) first-time donors.

Graph 1. Number of blood donations in the period from 2017 to 2021



Based on the total number of donations, adverse reactions occurred during 2722 procedures (1.4%). The number of incidence was 14 in every 1000 donations. BDs who experienced ARs were 28,0 ± 8,3 years old, 1881 (69.1%) were male and 841 (30.9%) were female. People who donated blood for the first time were at a higher risk of experiencing an adverse reaction, which happened to 1908 people (70.1%), while multiple donors were less represented, merely 814 of them (29.9%). Donors from urban regions were more represented, 2,349 of them (86.3%), while there were 373 (13.7%) from rural regions.

The chi-square test was used to analyze the occurrence of adverse reactions in men 1811/83678 (2.16%) in regards to women 841/24336 (3.45%) and a highly significant statistical difference was determined ($p<0.001$). Also, the chi-square test was used to analyze the occurrence of adverse reactions in first-time BDs 1908/8490 (22.5%) compared to 814/99524 (0.82%) multiple ones and a statistically significant difference was also determined ($p<0.001$). According to the time of occurrence of the adverse reaction, it was observed that the most ARs occurred during blood donation procedure, 1717 (63.1%). After the blood donation procedure was completed, 893 (32.8%) ARs were identified, while112 ARs (4.1%) were identified before the procedure.

In relation to localization, systemic reactions predominated in 2619 (96.2%) donors, while local reactions occurred in 103 (3.8%). BDs who were younger than 30 years and weighed less than 60 kg had vasovagal reactions, nausea and syncope more often ($p<0.005$). The occurrence of local and systemic ARs in BDs in relation to their donor status is shown in Table 1.

Table 1. Types of adverse reactions during whole blood donation procedure

Adverse reactions		BDs with ARs		Total
		First-time	Multiple	N (%)
Local - associated with venipuncture	Pain, hyperemia and swelling at the puncture site Hematoma	16 28	15 36	31 (1.13%) 64 (2,34%)
	Local phlebitis and thrombophlebitis	14	10	24 (0,89%)
Systemic	Vasovagal reaction	1715	681	2396 (88.02%)
	Syncope	196	167	363 (13.33%)
	Nausea Hyperventilation	553 166	184 55	737 (27,08%) 221 (8,12%)

In relation to the severity of the ARs, 64 (2.34%) BDs had mild reactions in the form of hematoma, and 2396 (88.03%) of them experienced weakness and fainting. Moderate ARs in the form of nausea and sweating occurred in 737 (27.08%) donors. Severe ARs in the form of collapse with convulsions were experienced by 12 (0.44%) donors. Adverse reactions were mostly mild and moderate ($p<0.05$).

DISCUSSION

Caring for donors primarily means protecting their own health. In addition, any inconvenience associated with blood donation procedure may

result in refusing BDs to come again. Conversely, the safe and pleasant experience that BDs have when donating blood can encourage them to come again and be recruited and motivated to become regular blood donors, which consequently leads to a satisfactory supply of blood units. France et al. indicate that donors give up further blood donation after experiencing an adverse reaction [4]. It is very important to analyze ARs related to blood donation, to consider what affects their occurrence so that preventive measures and adequate care can be taken. Several authors dealt with the consideration of the factors that influence the emergence of ARs and the question of which the weakest links in the chain of work processes with BDs are, in order, first of all, to correct them and thereby increase the satisfaction of DDK [5,6]. In case of occurrence of ARs, the most important thing is to provide adequate professional help in a timely manner, determine the cause of the occurrence, and, after analysis, implement corrective and preventive measures. Each adverse reaction with all the measures taken is recorded in the donor's file, while it is a legal obligation to report severe ARs to the hemovigilance system at the national level.

The frequency of ARs certainly depends on several factors, from the preparation of the BD for the blood donation procedure, his/her general condition and hydration, venipuncture, conversation with him/her during the procedure, as well as the provision of post-donation information about behavior after donating blood. In our population of whole blood donors, the incidence of total ARs is 1.4%, while according to published data it ranges from 0.03% to 6% [7,8]. The difference in the mentioned data may be due to the wide range of ARs that were analyzed, as well as the size of the population that was the subject of the research.

On the other hand, most reported ARs are systemic, but even here there are significant differences. While in our study systemic adverse reactions in relation to the total number of donations occurs with an incidence of about 1%, in Greece the frequency is 0.88%, and in Japan 6% [9,10]. Systemic reactions are influenced by many factors, in which the most important are age, gender, stress, fluid intake, proper diet and adequate sleep before donating blood.

Vasovagal reaction is the most common type of AR in our population with a share of about 88% in relation to all other reactions and 1,23% in relation to the total number of donations. The incidence of VVR varies among different populations. Agnihotri et al. published the data that among whole blood donors, 1.6% have VVR, and these are, above all, younger women donating blood for the first time [11]. Dogra et al. came to a similar conclusion, although the incidence was much lower and amounted to 0.365% [12]. VVR represents the reaction of the neurovegetative system to stress, which can also have a cause in acute blood loss. Although it has a low incidence, it can have a long-term negative impact on the return rate of BDs and is often the main reason donors refrain from coming back. The most vulnerable group of BDs for the occurrence of ARs are high school students weighing up to 55 kg who are donating blood for the first time. Since VVR are the most represented, a seasonal variation in their manifestation was also observed because it correlated with periods when there was a higher representation of high school students in organized blood donation actions. Sultan et al. and Tondon et al. indicated a positive correlation between the increase in the age categories of BDs with a decrease in the risk of VVR [10,13]. The reason for this correlation lies in the fact that younger people have a greater sensitivity of the carotid-aortic baroreceptor, which can be the cause of VVR if the receptor is stimulated during or after the donation process. As the age of DDK increases, baroreceptor sensitivity decreases, which explains the decrease in VVR incidence in older age groups. Many studies have indicated that female gender is more associated with the occurrence of ARs, primarily due to the difference in blood pressure. It has been proven that there are gender differences in the renin-angiotensin system and the effects of the bound angiotensin II type 2 receptor on renal vascular resistance, whereby renal sympathetic nervous activity affects the value of blood pressure [14]. The data of our study indicate that in relation to the majority of ARs, the predominant clinical form are mild and moderate adverse reactions, while severe forms occur very rarely. These findings are consistent with data from many other studies, which indicate the fact that blood donation is a safe procedure, mostly without complications [15-17].

It is important to implement all mechanisms that could prevent ARs, especially when it comes to

BDs who are donating blood for the first time. These procedures include: the shortest possible waiting time for BDs, from arrival to the venipuncture itself, in a pleasant environment, good psychological preparation for BDs, pre-donation hydration, performing muscle tension exercises, hiring experienced staff and good puncturers [4,18-20]. Communication with blood donors is extremely important and it is considered that no other prevention measure can replace it.

CONCLUSION

Continuous attention and monitoring of donors during the entire blood donation procedure contribute to a low incidence of adverse reactions. Education of the medical personnel to identify risk factors contributes to the prevention of adverse reactions. Prevention measures of adverse reactions, as well as their quick treatment, are important because of the preservation of donor's health and the negative effects they have on the motivation of the donors and their return.

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