

USE OF BLOOD PRODUCTS IN ONCOLOGICAL PATIENTS TREATED WITH RADIO AND CHEMOTHERAPY

Ana Antic, Sladjana Filipovic, Ivica Pejic and Svetislav Vrbic

Retrospectively, we analyzed the use of blood products in the Oncology Clinic of the Clinical Centre Nis in the period November 1st 2007-November 1st 2008, and also the influence of the treatment on degree of anemia and thrombocytopenia and use of blood products. None of the patients received the whole blood. In this period, 324 patients received the transfusion of blood components, 302 patients received 983 units of red cells (red blood cell concentrate, resuspended, washed, filtered), 17 patients received 5050 ml of platelets (single-donor concentrate or pooled platelet concentrate) and 5 patients 2200 ml of fresh frozen plasma. An average use of red cell transfusion is 3,26 units, platelet concentrate 5,54, fresh frozen plasma 2 units per oncological patient who receives transfusion. The use of red cell units and platelet concentrate transfusion was adequate (91,85% of patients received transfusion of red cells when Hgb<70g/l, 89,2% of patients received platelet concentrate transfusion when platelet count was less than $20 \times 10^9/l$). During radio and chemotherapy we noticed a decrease of hematological parameters' values, whereas the experimental group of patients were dependent on blood product transfusion. Statistically, a significant decrease of hemoglobin level and platelet count was observed in the patients treated only with radiotherapy who are the greatest consumers of blood products. *Acta Medica Medianae 2008;47(4):13-18.*

Key words: radiotherapy, chemotherapy, anemia, thrombocytopenia, component transfusion therapy

Blood Transfusion Centre Nis, Serbia¹
Oncology Clinic, Clinical Centre Nis, Serbia²

Kontakt: Ana Antic
Blood Transfusion Centre Nis
48 Dr Zoran Djindjic Blvd.
18000 Nis, Serbia
Phone: 038118 533-260
E-mail: anaantic@transfuzijanis.rs

Introduction

Blood and blood component therapy represent the application of cell and plasmatic blood components in order to correct anemia, thrombocytopenia and stop bleeding. The aim of chemotherapy is to reconstitute and maintain homeostasis in circulation of the blood using specific chemoproducts, thus influencing the volume of circulating blood and capacity for binding and transportation of the oxygen, chemostatic function of blood and activity of the mediator of immune response (1). By allogeneic transfusion, in the circulation of the recipient different cells are introduced, of which mononuclear cells - T and B lymphocytes, dendritic cells, chemotaxis and other cells can survive longer and are able to be functional in circulation. Interaction of some of the mononuclear cells with immune system of the receiver and clinical consequences of those reactions depend on the degree of histocompatibility between donor and recipient, the period of time and way of

storing blood, number and type of mononuclear cells, as well as the condition of patient's immune system (2,3).

For years, transfusion of blood and blood products has been very important in supportive medical treatment of oncological patients. In that way, we have significantly reduced the mortality of patients with malignant diseases and decreased unwanted chemobiological disturbances occurring because of radio- and chemotherapy (4,5).

In spite of a positive therapy effect, transfusion can be joined with numerous unwanted effects, the reason of which the use of transfusion is not without risks for patients (2). Therefore, before making a decision whether the patients should receive transfusion or not, it is very important to estimate all the damages and benefits. In the contemporary therapy, we use direct chemotherapy, the so-called selective transfusion which means selection of the specific component of blood that is the most suitable for correction of present deficit in patient, which reduces the risk of potential complications to minimal. By direct chemotherapy, a patient receives just the part of blood which he needs and there is no danger of overloading the blood circulation; sensibilisation to antigens of blood cells and plasma proteins is avoided, and transfusions are shorter and do not confine the patients to bed for a long period of time (3).

Oncological patients are the patients who experience transfusion treatment with difficulties (5). Most of the patients belong to the group of polytransfused patients bearing the greater risk of post-transfusion reactions, and some of them are sensibilised to received blood-group antigens, which leads to problems in finding out compatible blood units. In some of the patients there occur disturbances of the immune system in the sense of the appearance of autoantibodies, paraproteins and forming rulox formation red cells, which leads to difficulties in laboratory analyses during determining blood groups and compatibility tests (3,4).

Aims

The aim of this work was:

- to establish an average use of blood components by malignant patients (number of red cells units, number of thrombocyte doses and number of units of fresh frozen plasma),
- to determine the level of hemoglobin and number of platelets which represented the indications for transfusion,
- to estimate the influence of the type of therapy on the levels of anemia and thrombocytopenia, as well as the difference in consumption of blood in comparison with other therapies,
- to define the number and the type of complications occurring because of receiving transfusion.

Material and methods

Retrospectively, we analyzed the use of blood products in the Oncology Clinic of the Clinical Centre Nis in the period November 1st 2007-November 1st 2008. Patients who received transfusion were treated at the Clinic or in the Daily Hospital Centre. Patients received: red cells resuspended in additive solution (SAGM), red cell resuspended in SAGM reduced in leucocytes and trombocytes, deplasmated red cells, deplasmated red cells reduced in leucocytes and trombocytes, washed red cells, filtered red cells, single-donor concentrate of platelets, pooled platelet concentrates and fresh frozen plasma.

Patients who received blood components were divided into three groups, according to the therapy treatment:

- I. Patients treated only with radiotherapy
- II. Patients treated only with chemotherapy
- III. Patients treated with radio and chemotherapy.

Control group comprised 200 patients who did not receive blood components in therapy.

We used ABO and Rh(D) reagents Seralone anti-A, anti-B and anti-D(RH1)332 (Biotest, Germany) for determination of blood groups in tubes, own-produced phenotyped screening red cells for antibody screening in tubes and red cells DiaMed, ID-DiaCell I, II for gel-filtration method of antibody screening (DiaMed, Switzerland), panel of red cells DiaMed, ID-DiaPanel for antibody identification using gel filtration method (DiaMed, Switzerland) and Seralone Anti Human-Globulin

monoclonal anti-IgG, anti-C3c, anti-C3d d for Coombs AHG test (Biotest, Germany).

We determined a count of platelets, leucocytes and hemoglobin level at the beginning and during the therapy.

Post-ransfusion reactions were recorded in a special form; one copy with fulfilled results was returned to the Oncology Clinic, the other one remained in the Protocol in BTI.

Obtained data were statistically processed using following the following tests: Shapiro-Wilk, χ^2 , t-test, ANOVA test and Tukey post hoc test.

Results

In the period of investigation, 324 patients received the transfusion of different blood components. Average age of patients was 54,77±9,95 years. The youngest patient was 28, the oldest one was 83 years old. The analysis of the presence of malignant diseases in this investigation showed that the most frequent diagnosis was Ca mammae and Ca cervicis uteri for women, and Ca pulmonum and Ca prostatae for men, which is in accordance with the data published by the World Health Organization.

Distribution of blood groups of patients showed that the most frequent blood group was O Rh(D) positive, then A Rh(D) positive. This distribution is shown in Table 1.

Table 1. Distrubution of blood groups of patients who received transfusion of blood products in the period of examination

Blood group	Number of patients	Percentage (%)
A+	94	29%
A-	13	4%
O+	116	36%
O-	19	6%
B+	45	14%
B-	6	2%
AB+	19	6%
AB-	10	3%
Total	324	100%

Use of blood components (red cells, platelets, fresh frozen plasma) during the period of investigation is shown in Table 2.

Table 2. Use of blood components (red cells, platelets, FFP) in period of investigation

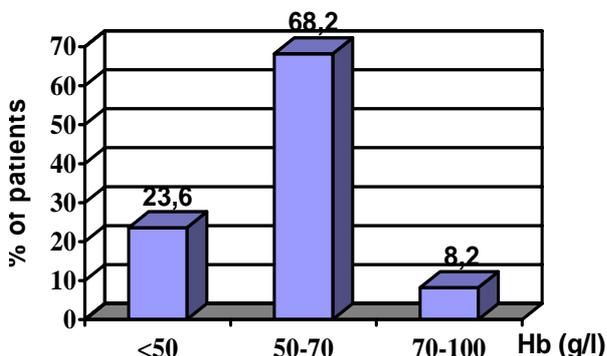
Blood component	Number od doses/units	Number of patients
Red cells (resusp.i depl)	920	302
Red cells (washed,filtered)	63	
Platelets	18 pul.(5050m)	17
FFP	2200ml	5

An average use of red cells (red blood cell concentrate, resuspended, washed, filtered) is 3,26 units per oncological patient who received transfusion, range from 1 to 9 units. Patients received 983 units, which is 4,87% of total units in that period in the Blood Transfusion Institute Nis (20514 units).

An average use of platelet concentrates is 5,94 single-donor concentrates or approximately one pooled platelet concentrate (it consists of 6 single-donor concentrates) per oncological patient who received transfusion, range was from 4 to 12 concentrates. Out of 17 patients who received platelet concentrations, nine of them had hemorrhagic syndrome.

An average use of fresh frozen plasma (FFP) was 440 ml- 2 units per oncological patient who received transfusion, range was from 220 ml to 1000 ml (1-5 units). Out of five patients who received FFP, four of them had a disturbance of coagulation system.

We checked hemoglobin concentration (g/l) which was the indication for red cell transfusion, and platelet count ($\times 10^9 / l$) which was the indication for transfusion of platelets. 91,85% of patients received transfusion of red cells when Hgb was less then 70 g/l, 23,6% of patients had difficult form of anemia (Hgb<50g/l). Hemoglobine concentration as an indication for transfusion of red cells is shown on Graph 1.



*p<0,01 vs other groups

Graph 1. Concentration of hemoglobin (g/l) in patients as indication for red cells transfusion

Analysing the patients divided according to the type of therapy, we noticed a decrease of hemoglobin concentration after therapy, which was 19,83 g/l (z=4,18 and p>0,001). If we analyse each group, this value is different:

- Group I- 24,81g/l (z=3,09, p<0,01)
- Group II -17,82g/l (z=1,60, p>0,05)
- Group III- 11,23g/l (z=3,20, p<0,01).

In control group, hemoglobin concentration after therapy was by 10,73 g/l I less than the initial value (z=3,78, p<0,001), which was statistically significant decrease. The analysis of the obtained results showed that decrease of hemoglobin concentration was statistically significantly higher in experimental group than in the control one (t-test=2,61, p<0,01), and also, that decrease of hemoglobin concentration was higher in the group I than in groups II and III (ANOVA and Tukey post hoc test, p<0,05).

Patients from all the groups received different types of red cells in order to correct anemia, but the number of units the patients received differed between them. Total of 302 patients received red cells transfusion: 151 patient from group I, 32 from group II and 119 patients from group III. Use of red cell components according to therapy type is shown in Table 3.

Tab.3. Use of red cell units according to type of applicated therapy in experimental group

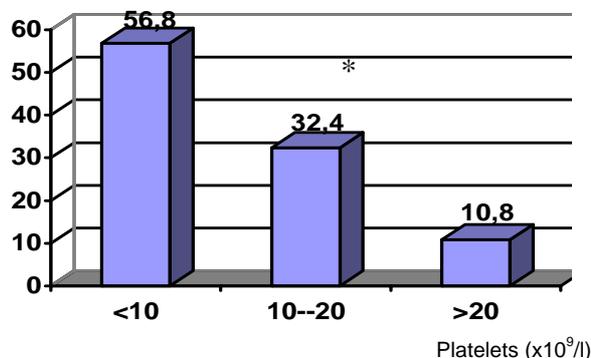
Statistical parameter	Group I	Group II	Group III
X _{sr}	3,54	1,36	1,17
SD	1,40	0,57	0,72
X _{min}	1	1	1
X _{max}	7	3	4

Group I - patients received radiotherapy
 Group II - patients received chemotherapy
 Group III - patients received radio and chemotherapy

An average use of red cell transfusion was 2,04±1,32 units, the least in group III, and the most in group I. ANOVA and Tukey post hoc test showed that the number of units the patients received treated only by radiotherapy was statistically larger than in other groups of patients, and also that difference between group I and II was not statistically significant.

89,2% of patients received transfusion of platelets when the platelet count was less than $20 \times 10^9 / l$; 56,8% of patients had difficult form of thrombocytopenia ($<10 \times 10^9 / l$). Platelet count as an indication for transfusion of platelets is shown on Graph 2.

Graph 2. Platelet number as indication for transfusion of platelet concentrates



*p<0,01 vs other groups

An average platelet count in patients in experimental group was lower by 78,80 after the tretament (z=4,83, p<0,001), and differed according to the type of therapy:

- Group I - 84,60 (z=3,38, p<0,01)
- Group II -98,72 (z=1,90, p>0,05)
- Group III- 51,24 (z=3,02, p<0,01).

In control group, platelet account after the therapy decreased approximately by $19,75 \times 10^9/l$ ($z=3,62$, $p<0,001$), which was statistically significant decrease.

Decrease of platelet account is statistically significant greater in experimental group then in control one ($t\text{-test}=3,78$, $p<0,001$).

In order to correct the platelet count we used transfusion of platelet concentrates (single-donor or pooled concentrate, which consists of six single-donor concentrates). Out of 17 patients who received platelet concentrates, seven patients were from group I, eight from group II and two patients from group III. The analysis of using platelet concentrates showed that patients in group II received statistically significantly more concentrates than patients from groups I and III. Use of platelet concentrates according to therapy type is shown on Chart 4.

Table 4. Use of platelets according to type of therapy in experimental group

Statistical parameter	Group I	Group II	Group III
Xsr	6,10	7,18	3,04
SD	2,38	4,11	1,21
Xmin	3	4	3
Xmax	6	12	6

Group I - patients received radiotherapy

Group II - patients received chemotherapy

Group III - patients received radio and chemotherapy

Transfusion can be joined with numerous unwanted effects, especially in polytransfused patients. In the period of investigation, two transfusion reactions were registered. After analyzing the pre-transfusion sample and post-transfusion sample of patients, and samples of the units patients received, we concluded there were not any immunohematological disagreements. We supposed that it was febrile non-hemolytic transfusion reaction in both cases. In the further treatment, the patients received leukoreduced red cells components (washed, filtered).

Red blood cell antibodies were identified in four patients, one of them had positive DAT. That patient had auto antibodies in his serum. Identification of antibodies in sera of other patients showed different specificity: anti-Kell, anti-D and anti C+D.

Discussion

Even in the 21st century, malignant diseases still remain the great enigma. They show constant and apparent trend of increasing, influencing thus population mortality (5). The frequency of occurrence of some of malignant diseases is in conformity with the data of the World Health Organization (in women, firstly, breast carcinoma, in men, lung carcinoma).

The results of this investigation showed that the principle of the component transfusion therapy was fully obeyed, because none of the patients received whole blood (whole blood is not used in the Blood Transfusion Institute Nis; all of the units of fresh blood are separated during six hours from taking the blood).

Malignant patients usually have normocite-normochrom anemia (6). Sera iron and total capacity of binding iron are usually low, and sera feritin is high, pointing to blockade in transfer of iron from depo in progenitors of erythrocytes (6,7,8). In some patients we noticed anemia of higher degree because of blood loss, infiltration of bone marrow malignant cells or the effects of some additional factor (9,10). In the treatment of anemia in our oncological patients, we prepared red cell preparations: red cells resuspended in SAGM, red cell resuspended in SAGM reduced in leucocytes and trombocytes, deplasmated red cells, deplasmated red cells reduced in leucocytes and trombocytes, washed red cells, filtered red cells. The indication for transfusion of red cells was adequate in 91,85% of the patients as they received transfusion of red cells with Hgb<70 g/l. In elderly patients suffering from cardiorespiratory diseases, transfusion was administered with Hgb<85 g/l, which is in line with the attitudes of Balint's (11) and Turek attitude. The patients who received transfusion of deleucocyte red cells, had shorter hematological recovery, lower rate of infections and longer period without relapse of disease. Generally, each unit of red cells, transfused to average adult person, can lead to growth of haematocrit by 0,03 and at the same time increasing the concentration of hemoglobin by 10 g/l, approximately (1,2).

For curing thrombocytopenia, we use transfusion of platelet concentrates, the indication for which was also adequate (89,2% transfusion of platelets were received by patients with the number of platelets less than $20 \times 10^9/l$). There are different attitudes concerning the application of platelet transfusion in reference to when the therapy should be implicated with review to degree of thrombocytopenia. Almost all clinicians agree that platelet transfusions bear high risk of bacterial infection occurrence (trombocyte concentrates are stored at $22 \pm 2^\circ C$) and alloimmunisation (12,13). Therefore, the number of transfusions of platelet concentrates should be reduced, that is, we should direct them to the application of platelets from separator from one single donor with lower contents of leukocytes, which reduces the risk of alloimmunisation of patients, with the prevention of transmission of intracellular pathogens such as CMV, HTLV-1 as well as the cause of the new variant Creutzfeldt-Jacobs disease. With this type of platelets, it is possible to achieve the amount of about $2-4 \times 10^{11}$ platelets per unit of concentrate (1,3). Transfusions of platelets should be limited also for the occurrence of refractoriness to platelets which appear in 10-15% patients who received large number of platelet transfusions (14,15).

There is a common attitude that transfusions of platelet concentrates should be given when the number of platelets is $10 \times 10^9/l$ if the patient has no sepsis or coagulopathy, and for invasive processes it is necessary to achieve the number of platelets up to $50 \times 10^9/l$ (15,16).

The use of fresh frozen plasma (FFP) was reduced to a minimum in five patients, which confirms the fact that FFP is no longer used as a replacement for albumin in order to correct hypoproteinemia. Indications for its use are very strict: congenital or acquired coagulopathy, overdosed therapy with oral anticoagulants, massive transfusion with haemostatic deficit, thrombotic thrombocytopenic purpura and hard liver diseases with active bleeding (17).

Unwanted effects of transfusion therapy have been followed in the Haemovigilance system since 1997. Two registered posttransfusion reactions in oncological patients in the period of monitoring represent 15,85% of all reported reactions in the Blood transfusion Institute Nis in the research period.

The percent of alloimmunised patients is less than 1% (0,6%), which is in line with data from literature (1,2); also, the highest frequency of antibodies is from Rh and Kell systems.

The results of examination of patients that underwent the treatment by radio and chemotherapy show that there is a significant decrease of hemoglobin volume after the use of therapy in experimental rather than control group, significantly greater in the group of patients treated only by radiotherapy. All the patients from this group received red cells, so the consumption of blood units was statistically greater in that group than in other groups. Other authors report that average level of hemoglobin concentration is lower by 46 g/l 30 days after chemotherapy (18,19).

Reduction in the number of platelets was registered in all groups, but it was statistically higher in experimental group compared to control one. The greatest consumption of concentrated platelets was shown by the patients from the group treated only by radiotherapy. Average number of platelets after the application of therapy shows a decrease by $78,30 \times 10^9/l$. Having compared the obtained results with the results of other authors on the changes in the number of

trombocytes after the use of chemotherapy, we could conclude that the average number of trombocytes was lower by $35 \times 10^9/l$ in the examined group (19).

Specificity of the patients with malignant diseases and necessity of long and frequent transfusion therapy in these patients requires the introduction of preventive measures in blood transfusion therapy (20,21). That is, first of all, reduction of the application of blood transfusion (patients frequently adapt to lower values of hemoglobin, so there is no need to insist on complete correction of parameters of erythrocyte group to normal values). During treatments with radio and chemotherapy, patients need blood transfusion of different products, so it is necessary to provide for the patients only the deficient components. (22). In polytransfused patients, transfusion of deleukocytized (filtered) erythrocytes is necessary (23). In order to correct the number of trombocytes, the use of platelets obtained on separator of blood cells is suggested (20).

During transfusion, it is necessary to follow up the patients all the time, and to look for clinical, hematological and serological signs of posttransfusion reaction (24).

Conclusion

The principle of component transfusion therapy was completely obeyed in all the patients. None of the patients received the whole blood. An average use of red cell transfusion was 3,26 units, platelet concentrate 5,54, fresh frozen plasma 2 units per oncological patient who received transfusion. During radio and chemotherapy we noticed a decrease of hematological parameters' values, whereas the experimental group of patients were dependent on blood product transfusion. Statistically, a significant decrease of hemoglobin level and platelet count was observed in the patients treated only with radiotherapy; therefore, these patients are the greatest consumers of blood products.

In order to conduct an efficient transfusion management in the patients with malignant diseases, we have to be up-to-date with the latest knowledge and attitudes about clinical use of blood products.

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PRIMENA PRODUKATA OD KRVI KOD ONKOLOŠKIH BOLESNIKA LEČENIH RADIO I HEMIOTERAPIJOM

Ana Antić¹, Slađana Filipović², Ivica Pejčić² i Svetislav Vrbić²

Retrospektivnom analizom procenjena je primena transfuzija na Klinici za onkologiju Kliničkog centra u Nišu u periodu 01.11.2007 - 01.11.2008. godine, kao i uticaj vrste terapije na stepen anemije i trombocitopenije, odnosno potrošnju produkata od krvi. Kod svih bolesnika obolelih od malignih bolesti ispoštovan je princip komponentne transfuzijske terapije. U praćenom periodu, 324 bolesnika primilo je krvne komponente, i to 302 bolesnika 983 jedinice eritrocita (deplazmatisani, resuspendovani, isprani, filtrirani), 17 je primilo 5050 ml trombocita (koncentrati, pul trombociti) i 5 bolesnika 2200 ml zamrznute sveže plazme (ZSP). Prosečna potrošnja eritrocita po onkološkom bolesniku koji prima transfuziju iznosi 3,26 jedinica, trombocita 5,94 doza, a zamrznute sveže plazme 2 jedinice. Indikovanje transfuzija i eritrocita i trombocita bilo je adekvatno (91,85% bolesnika dobilo je transfuziju eritrocita pri Hb<70g/l, 89,2% primilo je transfuziju trombocita kad je broj trombocita bio niži od 20 x10⁹/l). Tokom lečenja radio i hemioterapijom došlo je do umanjenja hematoloških parametara, pri čemu su bolesnici eksperimentalne grupe bili zavisni od primene transfuzije krvi i nastavak njihove radio i hemioterapije bio je uslovljen primenom transfuzije eritrocita i trombocita. Statistički značajnije umanjenje koncentracije hemoglobina i broja trombocita registrovano je kod bolesnika koji su lečeni samo zračnom terapijom, te su oni ujedno i najveći potrošači produkata od krvi. *Acta Medica Medianae* 2008;47(4):13-18.

Ključne reči: radioterapija, hemioterapija, anemija, trombocitopenija, komponentna transfuzijska terapija