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Research Article

Evaluation of a two-year period of irradiated blood products administration in Khorasan Razavi province blood transfusion center.

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ABSTRACT

Introduction: The common method of preventing Graft Versus Host Disease is irradiation of blood products which deactivates the T lymphocytes of the donor. In the present study, irradiated blood products of KhorasanRazavi province blood transfusion center were studied.

Methods: In this review, 619 requests of irradiated products were analyzed in terms of the number and type of the irradiated product, patient's age and irradiation indication. The analysis of the data was performed using T-test and SPSS version 18.

Findings: Irradiated products included:356concentrate platelet (57.5%), 230 Packed-RBCs (37.1%), 21 leukocyte reducedPacked-RBCs (3.4%), 5 washed RBCs (0.8%), 4 whole bloods (0.6%), and 3 pediatric blood bags (0.5%). Patients included children (65.8%), adults (33.1%), new-borns (0.6%), and infants (0.5%). Requests were for as follows; 535 transplantations (86.5%), 55 leukemia's and lymphomas (8.9%), 11 anemia's (1.8%), 7 intrauterine transfusions(1.2%), 7 suppressive treatments (1.2%) and 4 immunodeficiency's(0.1%).

Conclusion: Since the irradiation of blood products is remarkably less associated with complications, it is strongly suggested to inform the centers and train clinical staff to use irradiated blood products properly.

Keywords: Irradiated blood products, Graft Versus Host Disease, blood transfusion reactions

INTRODUCTION:

Irradiation of whole blood and blood Components before transfusion is currently the only accepted method to prevent TA-GVHD. In case of occurrence of this complication, there is no particular treatment and in many cases it leads to fatalities.GVHD is one of the common compli

cations of bone marrow transplantation but a rare one for blood transfusion. This disease happens when the T lymphocytes of the immunocompetenton or are transplanted into the immunocmpromised recipient's body which is not able to reject these T lymphocytes.(1)GVHD was initially discovered in humans in late 1950s, however, a similar syndrome was reported in 1916 by Murphy and Danchakoff in chick fetus by stimulating the chorioallantoic membrane, which was associated with the recipient splenomegaly(1,2).

A similar syndrome has been reported in humans after firstcases of bone marrow transplantation. (3)The first TA-GVHD was reported in 1982 soon after it was detected in immunocmpromised newborns who had been administered blood transfusions (4,5). TA-GVHD symptoms are malfunctions of skin, liver, digestive system and bone marrow including high fever, erythematous macolopapular rash, anorexia,nausea, pain in the upper-right quarter of the abdomen, severe diarrhea (up to 9 liters per day). The laboratory findings include increased level of liver enzymes, bilirubin, ALP and pancytopenia. The initial symptoms are fever 3 to 39 days after the transfusion and rashes are observed within 2 to 5 days after theonset of fever and finally severe bone marrow hyperplasia whose mortality rate is above 90% (6.7).

TA-GVHD follows administration of non-irradiated blood products such as whole blood, Packed-RBC, platelet, granulocyte products, fresh plasma, though it has not been reported following administration of frozen and diglycerol RBC, FFP, cryoprecipitate unless they havebeen accompanied by other products.

Risk of incidence of GVHD is directly associated with cellular immunodeficiency's, particularly if the donor is homozygous for a specific HLA haplotype for which the recipient is haploidentical(8). HLA typing has proven that in many cases of GVHD, the donor is homozygous for an HLA haplotype for which the recipient is heterozygous. This incident usually occurs among immediate family members. However there have been reported cases in Japan and Israel where the donor had not been a relative of the recipient(9-11). A fatal TA-GVHD was reported in a 22-year old pregnant mother without any diagnosed risk factors who had received 2 units of 5-day PRBC from a non-relative donor, at the time of giving birth because of mild pre-eclampsia(12).Another case of fatal TA-GVHD after cholecystectomy and receiving 3 non-irradiated units of PRBC from a non-relative donor was reported in Japan. (9)Many cases of TA-GVHD in immunocompetent recipients follow open heart surgery. Since treatment of TA-GVHD is not effective, the focus is on prevention and lowering the risk. Deactivating the lymphocytes by irradiation of the components prior to transfusion is considered one of the best ways to lower the risk of TA-GVHD incidence (12). It has been observed in previous studies that irradiation of the lymphocytes of a normal donor with a dose of 15Gy and 50Gy can reduce myogenic response by 90% and 97% respectively (13). 5 to 6 logarithms of myogenic responses have been observed in components irradiated with doses of 15 to 20Gy in comparison with non-irrDieted ones(14). Mature RBCs are remarkably resistant to irradiation(15,16). Damaging the function of platelets and granulocytes depends on the dose. There have not been any reported cases of complications regarding storage of irradiated platelet products. However, caution must be exercised in newborns and in cases where the potassium is increased following the administration of irradiated RBC.(17)

Currently the common way of preventing TA-GVHD is irradiation of whole blood and other blood products with gamma-ray (cesium 137 or cobalt 60) or x-ray of which both have yielded satisfactory results in deactivating T lymphocytes.(18)

The minimum dose of irradiation delivered to the central portion of the container must be 20Gy, though in no point the dose should exceed 50 Gy with a minimum dose at any point in the component being at least 15Gy.(19)

There is disagreement about the time of the irradiation and the time at which the irradiated products could be used. AABB standards accept irradiation of the products at any point before its expiry date. The expiry date would be either 28 days after the irradiation or the

normal expiry date (whichever is earlier).(19) Whereas according to England's standards irradiation could only be done within 14 days of donation and it could be used for 14 days from the time of irradiation(20). Platelets are not affected with doses of up to 50Gy and they could be irradiated at any point before their expiry date and after their irradiation they could be used until their expiry date.(19,20)

Granulocytes must be irradiated prior to triggering and should be administered within the least time possible after irradiation. When administering irradiated components, the policies of the respective center and the clinical condition of the recipient must be taken into account. In an AABB study in 1990, only 12.3% of 1444 institutes (including 21.7% blood transfusion centers and 11.7% hospitals) had on-site gamma irradiation facilities. Cases routinely receiving irradiated products are bone marrow transplantation recipients, autologous bone marrow transplantation, patients with congenital immunodeficiencies, premature newborns and leukemia patients.(17)

This study reviews the cases of request, their indications and recipients to draw an outline of the current situation.

METHODS AND MATERIALS:

This retrospective study was based on available cases in irradiation department. Samples included 619 units of irradiated blood products requested for clinical centers of KhorasanRazavi province in 2012-2013, of which all were entered into the study by statistics. Irradiation was performed on demand of hospitals by using Biobeam-800 device with gamma source and cesium137 source. Gathering information was carried out by request forms for blood products of distribution department of KhorasanRazavi blood transfusion center. Data concerning the number and types of units being irradiated, patients age, indications and hospitals demanding the units were put into SPSS version 18 and analysis was performed using descriptive statistics and T-test with $p<0.05$.

Findings: During a 2-year time period of using irradiated blood products in headquarters of blood transfusion of KhorasanRazavi in 2012-2014, 619 bags of irradiated blood products were provided and distributed which included 356concentrate platelet (57.5%), 230 Packed-RBCs (37.1%), 21 leukocyte reducedPacked-RBCs (3.4%), 5 washed RBCs (0.8%), 4 whole bloods (0.6%), and 3 pediatric blood bags (0.5%).(Table 1)

Patients included children (65.8%), adults (33.1%), newborns (0.6%), and infants (0.5%). In some cases overlap was observed for reasons of requests.(Table 2)

Reasons of request in order of abundance were; 535 transplantation(86.5%) of which 503 were bone marrow transplantation, 55 leukemia and lymphomas (8.9%), 11 anemia's (1.8%), 7 intrauterine transfusions(1.2%), 7 suppressive treatments (1.2%) and 4 immunodeficiency's (0.1%).(Table 3)

Table 1-Frequency of irradiated products

Product	Frequency	Percent of all products	Percent of all RBC s
Packed RBC	230	37.1%	87.3%
Reduced-leukocyte RBC	21	3.4%	8.1%
Washed RBC	5	0.8%	1.9%
Whole Blood	4	0.6%	1.5%
Pediatric blood bag	3	0.5%	1.3%
Platelet concentrate	356	57.5%	

Table 2-Age range frequency of studied patients

Age range	Number of all patients	Percent of all patients
Children	407	65.8%
Adults	205	33.1%
Newborns	4	0.6%
Infants	3	0.5%

Table 3-Indications for irradiated blood transfusion

Indication	All products (RBC+Plt)		RBC		Platelet	
Transplantation	535 (86.5%)	BMT 503 (81.3%)	210 (79.8%)	BMT 190 (72.2%)	325 (91.3%)	BMT 313 (96.4%)
		Others 32 (5.2%)		OTHERS 20 (7.6%)		OTHERS 12 (3.6%)
Leukemia/Lymphoma	55 (8.9%)		24 (9.3%)		31 (8.7%)	
Intrauterine transfusion	7 (1.2%)		7 (2.8%)			
Immunodeficiency	4 (0.7%)		4 (1.54%)			
Anemia	11 (1.8%)	Aplastic 5 (0.8%)		Aplastic 5 (1.9%)		
		Sickel cell 6 (1%)		Sickel cell 6 (2.2%)		
Suppressive treatment	7 (1.1%)		7 (2.6%)			

DISCUSSION:

Blood transfusion is a potentially dangerous treatment and if proper precautions are not taken, consequent complications could be lethal. Administration of blood and its components, while being beneficial, has the potential of bringing about detrimental reactions to blood transfusion(21). 13 million units of blood are taken and administered to 4 million patients annually. Among these recipients 10% experience a harmful reaction. These blood transfusion complications could be acute or chronic. In acute complications symptoms appear within 1 to 2 hours after the administration which includes hemolytic (1 in 25000), feverish (1 in 200) and allergic (1% to 3%) complications plus bacterial infection and circulation overload. Chronic complications, on the other hand, are prone to occur within days, weeks or even months after administration. They include GVHD, delayed hemolytic reaction, purpura, hemosidrosis, etc. each of which has its own specific symptoms that are helpful in diagnosis and prevention. In the United States, cases of blood transfusion reactions must he reported to FDA within 24 hours. If the physician or nurse carefully monitors the patient, with immediate and proper actions, lethal complications could be prevented.(22)In a study carried out in pediatric hospitals and thalassemia centers of Tehran in 2007-2008, which had reviewed complications of blood transfusion, 3 cases of GVHD were observed all of whose transfusions had been at the end of the week when providing irradiated blood had not been possible. After reported cases of GVHD, irradiation unit of Tehran blood transfusion center was established. Previously, limited irradiation of blood units was done on working days of the week at Shariati hospital of Tehran. Irradiation with doses of around 25Gy causes lymphocytes to lose their ability to proliferate, therefore GVHD is prevented. In this method either X or gamma-ray could be used and there is not a noticeable difference between them.(18) GVHD is a rare lethal chronic complication of blood transfusion whose symptoms include fever, macolopapular cutaneous rashes, nausea, vomiting, diarrhea, hepatitis, pancytopenia following bone marrow hyperplasia. TA-GVHD is usually a result of transplantation of the donor T cells in cellular components to a recipient who is incapable of either detecting or destroying them. According to the reports, of the 38 consequent deaths of blood transfusion during 1995-1996 and 2000-2001, 12 have been because of TA-GVHD.

Patients with B cell neoplasms are particularly at risk. The greatest number of TA-GVHD reported in immunocompetent patients have been in Japan where HLA hemogenousity is

prevalent(9). Fatality of TA-GVHD is over 90% which is because of involvement of bone marrow and consequently pancytopenia and ulti mately death occurs as a result of hemorrhagic and/or infection. In communities su ch as in Japan where HLA is homogenous all the products are irradiated.Findings of a study on a dministration of irradiated components, carried out by Maryam Zadsar et al in 2008, were as foll ows; concentrateplatelet (71.3), Packed-RBC (2 8.1%), FFP (0.4%), pediatric blood bag (0.2%) a nd whole blood (0.1%).Finally it should be emp hasized that since lymphocytes and platelets are both located in the buffy coat during the compon ents separation process, platelet products have th e most contamination with lymphocytes.(23)

CONCLUSION:

Despite the increasing number of requests for irr adiated components, they still make up a small portion of the products. Although they are neces sary for patients with leukemia, lymphoma or bo ne marrow transplantation, platelet components are not being irradiated and requests for irradiate d Packed-RBC is less than expected. Informing t he staff regarding the benefits of irradiation and training them for its proper administration is recommended. It is also vital to have the staff of the irradiation department undergo comet assay test every 6 months at most to check them for any DNA breaks in CBC blood samples.

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