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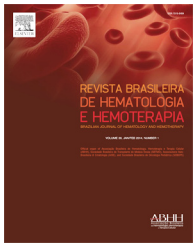

Original article

Evaluation of the effectiveness of packed red blood cell irradiation by a linear accelerator

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ABSTRACT

Irradiation of blood components with ionizing radiation generated by a specific device is recommended to prevent transfusion-associated graft-versus-host disease. However, a linear accelerator can also be used in the absence of such a device, which is the case of the blood bank facility studied herein. In order to evaluate the quality of the irradiated packed red blood cells, this study aimed to determine whether the procedure currently employed in the facility is effective in inhibiting the proliferation of T lymphocytes without damaging blood components.

The proliferation of T lymphocytes, plasma potassium levels, and the degree of hemolysis were evaluated and compared to blood bags that received no irradiation. Packed red blood cell bags were irradiated at a dose of 25 Gy in a linear accelerator. For this purpose, a container was designed to hold the bags and to ensure even distribution of irradiation as evaluated by computed tomography and dose-volume histogram.

Irradiation was observed to inhibit the proliferation of lymphocytes. The percentage of hemolysis in irradiated bags was slightly higher than in non-irradiated bags (p-value >0.05), but it was always less than 0.4% of the red cell mass. Although potassium increased in both groups, it was more pronounced in irradiated red blood cells, especially after seven days of storage, with a linear increase over storage time.

The findings showed that, at an appropriate dosage and under validated conditions, the irradiation of packed red blood cells in a linear accelerator is effective, inhibiting lymphocyte proliferation but without compromising the viability of the red cells.

Introduction

Transfusion-associated graft-versus-host disease (TA-GvHD) is a rare and acute delayed transfusion reaction which occurs after the transfusion of blood components; this complication is correlated to a high mortality rate. The main mechanism for the occurrence of TA-GVHD is the transfer of T lymphocytes from the blood donor that damage and promote a response in the tissues of the recipient. After recognizing

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host tissues as foreign, the cytokines released by transfused T lymphocytes, such as interleukin-1 (IL-1) and tumor necrosis factor (TNF), drive an inflammatory response. These cytokines activate inflammatory cells, including natural killer (NK) cells, macrophages, and other T lymphocytes, resulting in the destruction of host tissues thereby causing TA-GVHD.[1,2] Another mechanism for the occurrence of TA-GVHD occurs through donor-recipient HLA incompatibility.[3] The development of this transfusion reaction appears to relate to the number and viability of T lymphocytes transfused in blood components (although this number is not yet known), to the level of immunosuppression of the patient, and to the extent that antigens of the HLA system are common to both the donor and recipient.[4,5] Therefore, the greater the number of blood components received, the greater the chance of TA-GVHD occurring in at-risk patients.

In susceptible patients, TA-GVHD occurs when the number of viable transfused lymphocytes is more than 1×10^4 cells/kg of body weight.[3,5] It is known that non-leukodepleted packed red blood cell (PRBC) bags have approximately 2–3 $\times 10^9$ leukocytes, whereas leukodepleted PRBC bags have from 2–3 $\times 10^6$ leukocytes. Therefore, even leukodepletion is not able to protect these patients from TA-GVHD.[3,6] In situations in which the patient has a healthy immune system, lymphocytes are destroyed. However, in immunosuppressed patients, these cells are not destroyed by the recipient's immune system and so after proliferation and producing cytokines, the lymphocytes may cause a TA-GvHD-related inflammatory response. Thus, the only effective method to prevent this disease completely is to inactivate donor lymphocytes by irradiating blood components.

Determination No. 34 of the Ministry of Health of Brazil/National Health Surveillance Agency (ANVISA) states that the irradiation of blood and blood components should be performed in a specific cell irradiator, and that when this equipment is not available, irradiation can be carried out in a linear accelerator used for radiation therapy.[7] Using linear accelerators instead of cell irradiators has been the subject of discussion among authors. Although Vetter and Dodd consider the performance of both methods to be similar,[8] dose uniformity may fail to meet the quality standards in linear accelerators if the method is not standardized. This was also reported by Janatpour et al. on comparing the irradiation of blood components with X-rays and gamma-rays.[9] Bashir et al. demonstrated similar effects in the dosage of potassium and in the degree of hemolysis in red blood cells subjected to X-rays and gamma radiation, and suggested employing linear accelerators in the place of radioactive equipment due to the lower maintenance cost and personnel training, and the dangers of the inappropriate use of cesium.[10]

Radiation protocols for linear accelerators describe a wide range of types and sizes of containers to be used during radiation. Protocols also differ in respect to the distance between the container and the radiation source, the quantity of bags to be irradiated by each procedure, and the range of results.[11,12] Proper irradiation should provide homogeneous distribution of radiation inside the container used, resulting in inhibition of lymphocyte proliferation and lower levels of hemolysis than established by regulatory bodies.[13] The PRBC units produced in the Regional Blood Center of Uberaba (HRU) are irradiated in a clinical linear accelerator in the Radiotherapy Department of the Hospital de Clínicas of the Universidade Federal do Triângulo Mineiro (UFTM). This study aimed to evaluate the efficiency of irradiation of PRBCs and possible damage to red blood cells using this method.

Methods

Standardization of the method and irradiation of packed red blood cells

A 30 cm × 30 cm × 15 cm polycarbonate container was designed with a 0.5 cm wall thickness big enough to hold up to 18 PRBC bags (Figure 1). When fewer than 18 bags are being processed, a special lid was created to reduce the size inside the container in order to better control irradiation. A 0.6-mL TN30013 waterproof Farmer ionization chamber coupled to a T10010 Unidos E electrometer (PTW Freiburg) jointly calibrated by the Brazilian Institute of Energy and Nuclear Research (*IPEN*) were used to measure the dose in the middle of the container. A computed tomography (CT) of the container was performed to provide images for the Eclipse three-dimensional treatment planning system. The analytical anisotropic algorithm (AAA) was used to calculate dose distribution in the irradiated material including identifying regions of uneven irradiation. Radiation indicators (RadTag® RTG 15, RadTag Technologies, Alberta, Canada) were placed on each bag to detect irradiation doses of from 15 to 50 Gy.

Four irradiation procedures involving ten or 12 PRBC bags each were performed at a total dose of 25 Gy in the parallel opposed fields of a Clinac 600™ linear accelerator (Varian) with a nominal power of 6 MV.

Upon confirmation of the irradiation of the bags by the radiation indicators, ten bags from the total of 42 irradiated PRBC

Figure 1 – Polycarbonate container designed to irradiate packed red blood cell bags.