GUIDELINES ON THE INDICATIONS FOR IRRADIATED CELLULAR BLOOD PRODUCTS

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DR. QHASMIRA BINTI ABU HAZIR
MMC: 65110
Ketua Unit Tabung Darah
Jabatan Perkhidmatan Makmal Diagnostik
Hospital Canselor Tuanku Muhriz/ PPUKM

Editor

1. Dr. Qhasmira Abu Hazir
2. Dr. Rabeya Yousuf
3. Dr. Nur Afifah Suhemi
4. Dr. Kaalpana A/P Jayakumar

Reviewed by:

A. HOSPITAL TRANSFUSION COMMITTEE (HTC)

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15. Dr. Qhasmira Abu Hazir
16. Dr. Rabeya Yousuf
17. Dr. Nur Afifah Suhemi
18. Dr. Kaalpana A/P Jayakumar
19. En. Mohd Herman Mobin
20. Pn. Paizah Paijan
21. Pn. Maryana Razali

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1.0 INTRODUCTION

Transfusion of blood and blood components is not without risk. One of the serious effects following blood transfusion is transfusion-associated graft versus host disease (TA-GvHD). This TA-GvHD is a rare, usually fatal, complication of transfusion of blood components containing lymphocytes. It is indeed a major and serious risk for certain severely immunosuppressed or immunodeficient patients or even immunocompetent recipients who have received HLA-matched components or blood from an individual with a similar HLA haplotype, such as a close relative.

The pathogenesis of TA-GvHD is caused by engrafted donor lymphocytes in the immunosuppressed patients where the host immune mechanism was unable to eliminate the foreign donor lymphocytes and allowed them to be engrafted in the host; whereas in the immunocompetent recipient that received the homozygous HLA matched blood, the donor lymphocytes of similar HLA type are not perceived as foreign and therefore not destroyed by the recipient's immune system and thus engrafted in the host. With the proliferation of the engrafted donor lymphocytes which subsequently identify that the tissues of the host are different from itself, it started attacking the host tissues causing an almost invariably fatal syndrome. Features of TA-GvHD noted in the Kopolovic *et al*[1] review include:rash (80.2%), fever (67.5%), diarrhea (43.1%), bone marrow aplasia (22.7%) or hypocellularity (17.2%) and hepatomegaly (13.5%). These symptoms arise within 1-6 weeks after transfusion, and death usually ensues within the first month after symptoms. The disease cannot be treated effectively. Occasionally, chronic GVHD may appear some 100 days after transfusion, producing a scleroderma like syndrome.

Lymphocytes viability is retained in stored red cells for at least 3 weeks, TA-GvHD has developed following the transfusion of red cells, platelets and granulocytes. Leukoreduction does not adequately reduce the risk of GVHD. The mainstay of prevention of TA-GvHD is by gamma irradiation of blood products to prevent lymphocytes proliferation. The recommended minimal dose achieved in the irradiation field should be 25Gy, with no part receiving >50Gy[2].

Irradiation with 25Gy has not been demonstrated to significantly alter the lifespan or function of platelets or polymorphonuclear leukocytes. Irradiation does reduce red blood cell (RBC) viability. It is recommended that red cells may be irradiated at any time up to 14 days after collection, and the expiration date for irradiated RBCs is 14 days from the irradiation or up to the expiry date of the bag, whichever is earlier. The platelet concentrates can be irradiated at any

stage of their 5-days storage and can thereafter be stored up to their normal shelf life of 5 days after collection. As for the granulocytes products, they should be irradiated as soon as possible after production and thereafter transfuse with minimal delay.

At present, no data are available to support the speculation that administration of irradiated blood components carries any immediate or long-term risks other than those associated with similar non-irradiated components.

Irradiated units are not radioactive and require no special handling. Irradiated units may be used for patients other than the intended patient. There is no evidence that this practice is harmful.

2.0 Clinical indications for irradiated cellular blood products

2.1 Absolute indication

2.1.1 General

1. Transfusion of blood or blood products donated by 1st or 2nd degree relatives or HLA-selected/matched donors.
2. Granulocyte transfusions – should be transfused as soon as possible after irradiation.

2.1.2 Paediatric :

1. Intrauterine transfusion (IUT) – red cells and / or platelets
2. Exchange transfusion (ET)
    a. neonate with previous history of IUT
    b. neonate receiving products from 1st or 2nd degree relatives
    c. other ET cases where irradiation does not delay the transfusion

    (for both the IUT and ET, blood should be transfused within 24 hours of irradiation)
3. Top-up red cell or platelet transfusion in term and pre-term infant with previous history of IUT up to 6 months after the expected delivery date
4. Top-up red cell or platelet transfusion in pre-term infant < 32 weeks of gestation or body weight <1.5kg
5. Transfusion of blood or blood products donated by 1st or 2nd degree relatives.
6. All severe congenital T lymphocyte immunodeficiency syndromes with significant qualitative or quantitative T lymphocytes deficiency (diagnosed / suspected till diagnosis confirmed).

2.1.3 Haematological diseases :

1. All recipients (paediatric and adult) of allogeneic haemopoietic stem cell transplantation (HSCT)–
    - From time of initiation of conditioning radio-chemotherapy until all these criteria are met: 6 months post transplant ,lymphocytes > 1.0 $x10^9$/L, free of active chronic GvHD and off all immunosuppression.
    - Chronic GvHD patient on continued immunosuppressive treatment.
    - Based on transplant conditioning, underlying disease or previous treatment e.g previous diagnosis of Hodgkin Lymphoma (HL) or previous purine analogue treatment, the treatment with irradiated blood components should continue indefinitely.
2. Allogeneic cellular blood components transfused to bone marrow or peripheral blood stem cells donor of HSCT of all ages within 7 days prior to or during harvest.
3. Recipients (adult and paediatric) of autologous haemopoietic stem cell transplantation (ASCT)-
    - 7 days prior to and during the harvesting.
    - Initiation of conditioning chemo/radiotherapy until 3 months post-transplant (6 months if total body irradiation was used in conditioning) unless conditioning, disease or previous treatment determine indefinite duration, e.g previous diagnosis of HL or purine analogue treatment.
4. All patients with Hodgkin Lymphoma (adult and paediatric) at any stage of the disease.

2.1.4 Other patient group

1. Patients treated with purine analogues drugs (eg: fludarabine, cladribine, bendamustine, pentostatin) deoxycoformicin) regardless of the underlying condition.
2. Patients with CLL or other haematological diagnosis treated with anti-thymocytes globulin (ATG) or alemtuzumab.
3. Patients receiving ATG or other T-lymphoycytes- depleting serotherapy for rare types of immune dysfunction conditions.

4. Patients with aplastic anemia undergoing treatment with ATG or alemtuzumab .
5. Patients undergoing peripheral blood lymphocyte collections for future CAR-T cell re-infusion
    1. 7 days prior to and during the harvest.
    2. Until 3 months following CAR-T cell infusion (unless conditioning, disease or previous treatment determine indefinite duration)

2.2 No indication/ no recommendation unless falls into above category

1. Patients with acute leukemia
2. Patients with non-Hodgkin lymphoma
3. Patients with HIV antibody positive or who have AIDS.
4. Patients undergoing cardiac surgery
5. Patients undergoing routine surgery
6. Patients with solid tumors, autoimmune disorders, acquired immunodeficiency
7. Patients post solid organ transplantation (including who have received alemtuzumab or ATG as induction therapy or for treatment of graft rejection)
8. Patients with aplastic anemia except for HLA-selected platelets, transfusion of granulocytes, donation from first- or second- degree relatives, or planned relevant treatment (e.g ATG, alemtuzumab,HSCT)
9. Patients on rituximab (anti-CD20)
10. Following treatment of alemtuzumab using schedule currently recommended for multiple sclerosis or vasculitis
11. Infants or children with temporary defects of T-lymphocytes function as the result of viral infection.
12. Adults, and children aged > 2 years without a significant history of infection, referred for elective cardiac surgery for problems associated with DiGeorge syndrome, such as aortic arch anomalies and pulmonary artery stenosis, or in whom DiGeorge anomaly is suspected, unless there is a significant history consistent with severe T-lymphocyte-associated immunodeficiency

3.0 Blood components that require irradiation:

Only **cellular blood components** need to be irradiated:

a) Red cells – whole blood, packed cells, leukocyte poor packed cells
b) Platelets – random unit or apheresis platelets
c) Granulocytes

Fresh frozen plasma (FFP), cryoprecipitate and other fractionated plasma products (e.g clotting factor concentrates, albumin, IVIG) is not necessary need to be irradiated as the lymphocytes will not, or are extremely unlikely to survive the freezing or fractionation process. Cryopreserved red cells after deglycerolisation does not need to be irradiated as the leukocytes are thoroughly washed free after thawing.

Fresh plasma (not previously frozen) transfusion from first or second-degree relatives should be irradiated even if the patient is immunocompetent.

4.0 Other specific requirements for irradiation of blood components

4.1 Red cells for intrauterine or exchange transfusion

- fresh (preferably less than 5 days old)
- recommended to transfuse within 24 hours of irradiation to ensure optimal red cell function and low potassium levels

4.2 Red cells for other patient groups

- preferable less that 14 days old when irradiated (will expire 14 days after irradiation or up to the expiry date of the bag, whichever is earlier)

4.3 Platelets can be irradiated at any stage in their 5 day storage and thereafter can be stored up to their normal shelf life of 5 days after collection.

4.4 Granulocytes for all recipients should be irradiated as soon as possible after production and thereafter transfused with minimal delay.

5.0 Blood prescription and administration

- If patients require irradiated cellular blood components, components must be requested and clearly prescribed as irradiated.
- Specific requirements of irradiated blood components must be part of bedside checking prior to administration of blood components and it should be clearly documented in patient case notes.

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