

Uctioleuco Reduction of Blood Products- A Rising Essentiality in Transfusion Medicine

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Abstract: Blood and blood component transfusions have become integral part in day- to- day practice but are associated with higher incidence of complications such as FNHTR, CMV transmission, HLA allo- immunization and platelet refractoriness which are usually due to WBCs in transfused blood, fragmentation of WBCs and release of cytokines on storage. This can be overcome by pre- storage leuco- reduction using 4th generation leucocyte filters in which WBCs are reduced to $> 5 \times 10^6$ cells/ unit. The outcome is enhanced patient safety, decreased transfusion requirements, decreased hospitalization and reduction in the incidence of FNHTR, allo-immunization in patients with aplastic anemia, MDS with myelofibrosis and Thalassemia. Thus, leuco-reduction of blood product serves as an effective tool in the reduction of post- transfusion complications, cost of hospitalization and mortality.

I. Introduction:

Blood and blood components are considered drugs because of their use in treating diseases. In day- to – day health care practice, each doctor inclusive of both surgeons and physicians face circumstances in which blood transfusion will be the ‘Saviour’. As like drugs, adverse effects may occur, necessitating careful monitoring and therapy.

Transfusion risks¹:

1. Increased post operative infections
2. Increased severity of existing infections
3. Bacterial contamination of platelets
4. Increased injury to the pulmones
5. Multi- organ failure in surgery/ critical care
6. Increased incidence of thrombosis
7. Increased tumor recurrence
8. Transmission blood- borne infections
9. ABO incompatibility

Owing to the complication and risks of transfusion, whole blood concept has been replaced with blood component therapy, where the specific deficient component in the patient is replaced.

II. Background and Rationale:

WBCs are responsible for many of the complications associated with blood transfusion. Leucocytes on storage undergo cytolysis and fragmentation releasing cell membrane debris and cytokines into the blood product which are responsible for the post-transfusion immunological reactions.

There are paring transmitted to immunocompromised recipients like thalassemia and hemato- oncology patients who require frequent blood transfusions. Very often they become allo- immunized to RBC, patelet and HLA antigens during the course of transfusion, which further causes sensitization leading to various immune-hematological problems and platelet refractoriness.

Leukotropic viruses such as Cytomegalovirus, Human T Lymphotropic virus reside inside the WBCs of a patient or a carrier. It should also be taken under consideration that, according to the available protocols, in the present scenario of practice, no donor is being screened for these viral infections due to which transfusion of blood products still remain the main mode of transmission of these viruses. Leuco reduction helps eliminating the above risks enabling a comparatively safer transfusion.

Procedure of LR:

The donors initially undergo physical examination by a qualified physician followed by routine screening investigations for blood grouping, Rh typing, hemoglobin levels, HIV (ELISA) and HBV

(HepatELISA). After screening, if the donor is found to be fit with optimum hemoglobin levels, seronegativity for HIV and HBV, blood will be collected by peripheral venepuncture (usually median cubital vein) according to institutional protocols and convenience. Fresh blood contains 10^9 leucocytes. Prior to storage, obtained blood will undergo pre- storage filtration using 4th generation leucofilters². This process of pre- storage filtration will eliminate almost 99.99% of the leucocytes. The residual leucocyte count will be $< 5 \times 10^6$ WBCs/ unit. Thus, it helps in reduction of transfusion- associated risks.

III. Proven benefits of Leuco- Reduction:

Reduction of Febrile Non- Hemolytic Transfusion reaction (FNHTR):

FNHTR is one of the most commonly encountered post- transfusion sequelae. It is defined as a temperature rise of $> 1^\circ \text{C}$, associated with or without chills and rigors following transfusion. Febrile reactions complicate 0.5- 6% red cell transfusion and 1- 38% of platelet transfusions. The pathogenesis underlying this febrile reaction is the immune reaction that occurs between the antibodies in the recipient plasma with antigens present on the transfused lymphocytes, granulocytes and platelets. This can also be attributed to the infusion of cytokines that have accumulated in the blood bag following storage. Hence, pre- storage leuco- reduction reduces the incidence of FNHTR to about 50% and 30% in red cell and platelet transfusions respectively³.

Reduction of Cytomegalovirus (CMV) transmission:

Cytomegalovirus is known to reside inside the leucocytes but does not possess much virulence in immune competent patients. Transfusion acquired CMV infection particularly occurs in immune- compromised individuals such as low birth weight infants, solid and allogenic bone marrow transplant recipients⁴. Pre- storage leuco reduction can be considered to equivalent to serologically negative allogenic blood transfusion.

Clinically it is recommended for:

- CMV seronegative pregnant women.
- CMV seronegative recipients of solid organ and allogenic bone marrow transplant recipients.
- Premature infants born to CMV seronegative mother.
- Low birth weight infants born to CMV seronegative mothers.
- Patient with previously diagnosed HIV/ AIDS who remain seronegative for CMV.

Reduction in HLA Allo- immunization and platelet refractoriness:

HLA class I (A, B and C) and HLA class II (DR, DQ, DPA and DPB) molecules are expressed on the surfaces of B lymphocytes, T lymphocytes, monocytes, dendritic cells and granulocytes. The HLAs present antigens to T lymphocytes, especially CD4⁺ T helper cells. There exists a phenomenon termed *allorecognition*, where the HLA molecules of the recipient are recognized foreign by the host T cells which in turn lodge an immune response. HLA antigens form a major barrier to the success of solid organ and bone marrow transplantation where they produce strong alloimmunisation. HLA antibodies are responsible for platelet refractoriness. In severe aplastic anemia, there is increased risk of graft rejection due to sensitization of transfused antigens in potential transplant recipients. It is recommended that patients with severe aplastic anemia and HSCT recipients should receive leuco reduced blood⁴.

Neonatal/ Fetal transfusion:

Fresh blood has leucocytes capable of transmitting CMV and producing Transfusion associated Graft versus Host disease (TAGVHD). LR can be considered for infants < 1 year of age and for intra- uterine transfusions.

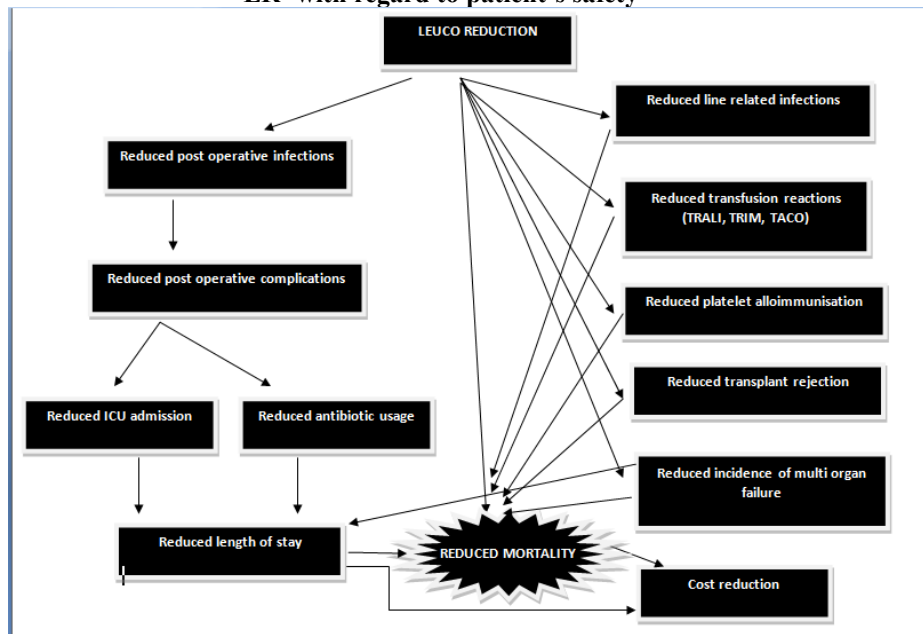
Role in Cardiac Surgeries:

During CABG, blood is exposed to extra corporeal circuit, hypothermia and ischemia- reperfusion injury, generating products of degraded tissue leading to release of stress hormones, inflammatory cytokines and chemokines. CABG leads to Severe Inflammatory Response Syndrome (SIRS) presenting as a cytokine storm with abnormal regulation of cytokines and is immediately counteracted by Compensatory Anti- inflammatory Response Syndrome (CARS). SIRS usually resolves with supportive therapy. If overwhelming, SIRS can dominate CARS progressing to MODS which leads to increased mortality.

Patient Friendliness:

LR serves in reduction of post operative infections following surgery for colorectal carcinoma and GI diseases. It reduces the risk of post operative mortality and multi organ failure. In acute leukemia, it reduces blood use, infections, hospital cost and mortality. In case of bone marrow transplantation for lymphoma, LR reduces blood loss, infections and costs.

LR- with regard to patient's safety



TRALI- Transfusion related acute lung injury
 TRIM- Transfusion related Immuno- modulation
 TACO- Transfusion associated cardiac overload

IV. Conclusion:

In view of SIRS and prolonged hospitalization, utilization of pre- storage leuco- reduced red cells, filtered with 4th generation leuco- filters is recommended for CABG. The outcome is decreased transfusion requirements and reduced length of hospitalization. LR red cells have a great potency in the prevention of FNHTR, allo- immunization in patients with aplastic anemia, Myelodysplastic syndrome (MDS) with myelofibrosis and thalassemia (both alpha and beta).

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