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Original Research Paper

Prevention of transfusion reactions and in post transfusion reactions, promoting patient safety [3P's]

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ABSTRACT:
Background: Blood transfusion is a natural lifesaving medicine which has a significant role in treating the patients. However this can also be associated with transfusion reactions as well. Presenting from mild reaction to fatal consequences. In this view the appropriate usage of blood and blood components and careful monitoring for early diagnosis and management of transfusion reactions are essential for patient safety**. Materials and Methods**: Retrospective observational analysis done from January 2023 – August 2024 in Blood centre, Apollo hospitals, health city, Visakhapatnam. The leukodepleted blood components utilized to minimize transfusion reactions. **Results:** Total number of buffy coat removal blood and blood components issued is 8083 out of which 11 (0.13%) cases reported transfusion reaction. Combination of washed RBC and followed by leukodepleted filter transfused in these 11 patients and in 57cases for the clinically indicated patients. These patients had successful transfusion. On further evaluation of these patients, adverse reaction rate was 0% .And proactively prevented adverse reaction in multiple transfusions of 910 cases by utilizing leucodepleted blood components**. Conclusion: "PPPP" the** blood components therapy ensures **the** right **p**roduct is administered to the - right **p**atient at the right time for the appropriate indication- which is crucial in preventing transfusion reactions and promoting patient safety. The use of Leucodepleted blood components helps in reducing the risk of blood transfusion reactions. When combined with washed packed red blood cells, it provides an additional layer of safety in preventing reactions in post transfusion reactions. The combination of washed RBC and leucodepleted filter has clinical benefit by preventing any obstacles for treating clinicians and surgeons allowing for improvedpatient care.

Keywords: Transfusion reactions, leukodepleted packed red cells,washed red blood cells.

INTRODUCTION:

A blood transfusion is considered as a liquid organ transplant because it replenishes blood loss through trauma, surgery and illness (1).Blood transfusion therapy is a natural life saving medicine as it is used to treat people with anemia, blood disorders and those undergoing chemotherapy. However blood transfusion has risk of adverse reaction. The antigenic heterogeneity of plasma proteins and antibodies make the blood responsible for a plethora of adverse effects (2) all the blood and blood components should be safely administered to the patient. World Health Organization (WHO) (3) defines patient safety as the absence of preventable harm to a patient during the process of health care and reduction of risk of unnecessary harm associated with health care to an acceptable minimum. The discovery of blood groups by Karl Landsteiner in 1901has made modern-day blood transfusion therapy a relatively safe procedure but still observe adverse reactions due to blood transfusion (4). Blood transfusion adverse reaction define as: An undesirable response or effect in a patient temporally associated with the administration of blood or blood component (5). Presentation of transfusion reactions: (6) Transfusion reactions are usually classified on the basis of time of onset and the mechanisms (immune or non-immune) leading to the reaction. Observation and monitoring of the patient is required throughout the transfusion episode, more so for within first 15 min is most important. Reactions occurring within 24 hours of transfusion are termed acute(Table 1) and delayed (Table 2)

Table 1:

Immune-mediated	Non-Immune mediated
• Haemolytic transfusion reactions(HTR) • Febrile non-haemolytic transfusionreactions (FNHTR) • Allergic reactionsAnaphylaxis • Transfusion related acute lung injury(TRALI)	• Transfusion associated circulatoryoverload (TACO) • Transfusion associated dyspnoea(TAD) • Transfusion associatedhypotension (TAH) • Metabolic complications Transfusion transmitted bacterialinfections (TTBI)

Table 2:

Immune mediated	Non-Immune mediated
• Delayed haemolytic transfusionreactions (DHTR) • Delayed serological transfusionreaction (DSTR) • Post-transfusion purpura (PTP) • Transfusion associated graft vs.host disease (TA-GvHD) • Transfusion related immunomodulation (TRIM)	• Transfusion transmitted viralinfection • Transfusion transmittedmalaria • Transfusion transmitted priondisease • Iron overload

Transfusion reactions should be investigated by correlating with clinical signs and symptoms with work up of post transfusion laboratory tests. Corrective and preventive action is to be done and documented .These transfusion reactions must be reported to hemovigilance. Haemovigilance(7) is an important tool for blood safety. It is defined as "a set of surveillance procedures covering the whole transfusion chain from the collection of blood and its components to the follow-up of its recipients, intended to collect and assess information on unexpected or undesirable effects resulting from the therapeutic use of labile blood products and to prevent their occurrence and recurrence".

Prevention of adverse reaction due to blood and its components is a challenging task for any blood centre.It is difficult to predict transfusion reaction occurrence especially in multiple transfusion due to develop antibodies reacts with antigens causes' adverse effect. To address this issue in our blood centre efforts made to mitigate transfusion reactions which are crucial for patient safety and treatment efficacy.

AIM:

To study on utilization of combination of washed RBC followed by leukodepleted filter. Overall there is a limited data on utilization of both washed PRBC and leucodepleted filter.

Objective:

1. To prevent transfusion reactions in multiple blood transfusion
2. To prevent reactions in post transfusion reaction

MATERIALSA AND METHODS:

Retrospective Observational study done in Apollo hospitals,Visakhapatnam.

Highest number of blood and its component requirement is from oncology department followed by cardiac thoracic department.

The utilization of Leucodepleted blood components and safetymeasures as follows:

1. Buffy coat removal of blood bags
2. Leukodepleted packed red blood cells (LDPRBC)
3. Washed red blood cells
4. Washed red blood cells and followed by Leukodepleted filter (Washed leukodepleted red blood cells)
5. Specific aphaeresis devices
6. For safe transfusion of blood and blood components precautionary measures taken from the donor counselling, proper collection, proper storage, use of quality products, properly calibrated equipments, quality reagents and kits, continuous temperature monitoring systems. We are also ensuring quality assurance at every stage with well-trained technical personnel and maintaining proper documentation.
7. And in preventing errors we maintained multiple check points in administration of blood and blood component. Observation is done by our trained nursing staff starting from preadministration check, administration of blood and blood components, monitoring of recipient during transfusion and recording the transfusion.

RESULTS:

Retrospective observational analysis data as Described Below:

Table 3:showing total number of blood and blood components utilized.

• Total number of months for the study	20 months
• Total number of multiple transfusion (more than two • transfusion of PRBC'sand including components • aphaeresis)	910
• Total number of transfusion reaction	11
• Total number of washed red blood cells	57
• Total number of leukodepleted red blood (more than two • transfusion of PRBC's)	580
• Total number of bloodand blood componentsissued(buffy coat • removal)	8083

Table4: showing patients transfused with both washed PRBC andfollowed by leukodepleted filter.

• Oncology patients onchemotherapy	12
• Transfusion reaction	11
• Coronary heart disease	09
• Relapsed multiple myeloma	07
• Sepsis	06
• Haemoglobinopathies (sickle celldisease)	05
• Autoimmune disorder	04
• Acute febrile illness	04
• Transplant	03
• Low birth neonates	02
• Acute haemolytic reaction	02
• Jaundice with acute kidneydisease	02
• Post partum haemorrhage	01
Total	68

Review of data analysis showed in table 1 as total number of blood and blood components issued (buffy coat removal) is 8083 out of which 11 (0.1%) cases reported transfusion reaction. For the patients experienced transfusion reaction and has requirement of blood transfusion we recommend washed PRBC and leucodepleted filter.Table4 shows list of patients transfused with both washed PRBC and leukodepleted filter. Review of data analysis showed Males slight predominance than females with ratio 37:31.Maximum age is 86years, male, case of coronary heart disease. Minimum age is 7 months, male, low birth infant with sepsis. There was no transfusion reaction (0%) observed in further evaluation of the patient.

DISCUSSION:

Blood transfusion is the one of the essential drug in treating the patient. Of which blood components preparation is an essential part, which can serve the needs of the four patients at a time with one unit of blood. Thus component separation helps in rationalizing use of the blood. This should be use judiciously; to prevent transfusion reaction (8).In our blood centre all blood components are available and usage is 100%.

In multiple blood transfusion can lead to a variety of different immunologic consequences which expose the patient to a plethora of foreign antigens and may stimulate the immune system to develop antibodies against the donor's antigens (alloantibody) and/or the patient's antigens (auto antibodies). Antibodies may develop against all types of blood cells (9).

Francesco Bennardello at el (10) states it is not always possible to predict the evolution of transfusion reaction and not possible to distinguish symptoms of mild reactions from more serious problems, such as sepsis, haemolytic reactions or anaphylaxis. This is also noticed in patients under general anaesthesia may mask the symptoms of both haemolytic and nonhemolytic transfusion reactions (11).We also encountered this challenge for two cases. Studies have shown transfusion reaction can be prevented by usage ofleucodepleted blood components (12) (13).

In this view we approached proactively towards prevention of transfusion reaction by utilizing leucodepleted blood components. Method followed for leucodepleted preparation asfollows:

Buffy coat removal packed red blood cell:

In Buffy coat removal packed red blood cell contains most leucocytes, <1·2 × 109.These blood components are called leukocyte reduced but not leukocyte depleted. Leucocyte depletion is obtained only by filtration. The main advantages of Buffy coat removal are micro aggregate formation during storage and febrile non-haemolytic transfusion reactions (FNHTR) are greatly reduced (14). And also PRBC can be stored for 42 days due to additive solutions (AS)/ saline, adenine, glucose and mannitol solution (SAGM). To prevent FNHTR, recommend to use Buffy-coat-depleted RBC in multiple transfusions and in low risk patients while leucoreduction by filtration is restricted to patients with the well-known indications, in view of safety and cost effectiveness. (15)

Our centre is multispecialty hospital comprising of patients mostly from oncology, transplant unit, trauma unit, dialysis unit, cardiology, and other general departments. Recommend Buffy coat removal RBCs suspended in additive solution (AS) which are prepared from top and top quadruple blood bags. These blood bags consist of a primary collection bag containing an anticoagulant preservative with CPD and SAGM, with three integrally attached satellite bags with one containing an AS. We have issued 8083 Buffy coat removal PRBC out of which 11cases observed transfusion reaction such as rashes, itching, mild fever with chills, allergic reaction all over the body, chills & rigors and shortness of breath. All of them were treated symptomatically and prevented post transfusion reaction on further blood transfusion.

Saline washed red cells:

Aaron A R Tobian et.al(16) study describes about washing transfusion products can decrease the incidence of transfusion reaction .The utilization of washed packed red blood cells (PRBC) is not contemporary in transfusion medicine. Washed PRBCs are used commonly used for patients with history of recurring and/or severe allergic transfusion reactions refractory to medical management, because studies have shown that washing PRBCs markedly decreases the incidence of allergic transfusion reactions.

Washed RBC used in patients complaining of allergic reaction, in haemoglobinopathies (17) (18).It can be used in drug interference incompatibility such as daratumumab interference inducing blood incompatibity in multiple myeloma patients. Dr. Westhoff(19) States “Monoclonal antibodies used for treatment are becoming much more prevalent, and many of the target antigens are also expressed on red cells.

Harold C. Sullivan et.al (20) study observed anti-CD38 monoclonal antibody daratumumab (DARA) produce reactive indirect antibody test (IAT) results in pretransfusion testing. In our blood centre successful blood transfusion done without any adverse reaction by using washed leucodepleted packed red blood cells for two myelomapatients who had multiple transfusion.

Schmidt A et.al(21), study recommends washed PRBCs is to discard the units after 24 hours due to increased risk for bacterial contamination which is a limitation for future implementation of this strategy. As washing red blood cells removes electrolytes and 99% of plasma proteins from the supernatant due to the storage lesion.

In our blood centre washed packed red blood cells indicated in 68 cases such as sickle cell anemia, relapsed multiple myeloma, sepsis ,preterm babies, dialysis, leukemia, lymphoma, exchange transfusion, positive antiglobulin test(DAT)of low grade, and post transfusionreaction.

Saline washed red cells preparation: Red cells are washed with 1/2 litre sterile normal saline (0.9% NaCl) which is stored at 2-80 C, by centrifugation at 40 C .The supernatant is discarded. This is prepared in open system.

Leukodepletion filters Bordin, J.O et.al (22) explains the biologic effects of leucocytes in blood components, is responsible for many of the complications associated with blood transfusion.

Kumar.H et.al (23) defines, the total content of leucocytes in a unit of red cells should be less than 5 × 106 per unit (99.9 percent or a log 3 leucoreduction) which helps in prevention of primary alloimmunisation against the histocompatability antigens.

Dzik S et.al(24) study specifies about specifically designed filters which permits leukocyte removal of cellular blood components.The leucodepleted filters contain multiple layers of synthetic polyester non-woven fibres which will retain white cells such as Lymphocytes and monocytes and granulocytes are trapped by adhesion while allowing red cells or platelets to flow through.

Tayler VV et al. (25) determines the advances in filtration techniques and type of filters have resulted in reducing white blood cells (WBC) in red cell and platelet concentrates to 99.9 percent (less than 5×10^6 WBC per unit) and *Buchholz DH et al (26)* elucidates WBC reduction by filtration reduce significant bacterial proliferation, possibly by removal of microorganisms along with white blood cells.

Recommended indications for leukoreduction (27)

- Patients needing transfusion and had at least two episodes FNHTRin previous transfusion
- In haematopoietic stem cell transplant recipients requiringtransfusions
- To avoid post transfusion CMV infection in immunocompromised patients
- All neonatal and paediatric transfusions for children less than ayear.

A. R. Thomson et.al (28) also explains about beneficial effects of leucoreduced RBCs: prevent febrile non-haemolytic transfusion reactions (FNHTR), human leukocyte antigen (HLA) alloimmunization in multi-transfused patients, and transmission of leucotropic viruses, especially cytomegalovirus (CMV). To avoid

immunomodulation in recipients and prospective recipients of solid organ (kidney), haematopoietic stem cell transplant and patients with malignancies.

In view of precautionary measures in our blood centre we recommend leukodepleted packed red blood cell (LDPRBC) for the patients who had multiple transfusion (more than 2 units of blood or blood components utilized) , in post transfusion reaction and in preterm neonates. The PRBC dose for neonates and infants is 10-15 ml/kg and may also require multiple transfusions. This is achieved by aliquoting one PRBC unit into Pedi-packs (from 50 -150 ml). This will avoid multiple donor exposures to the patient and also helps to maintain an inventory.

Third and fourth generation of leucofilters used in our blood centre, done at post processing (within the blood bank)and few at bed side. On quality of the LDPRBC the leukocyte count is less than less than 5 × 106 WBC per unit.

Specific aphaeresis devices:

Miyamoto M et al (29) study shows leucodepletion filters for platelets show the loss of platelets during this procedure, has been reported as 9 to 35 percent. This increased requirement of transfusions. Whereas Dzik S et.al (30) reveals current generation of aphaeresis machines and disposable sets used are capable of achieving a 3 log leucodepletion, obviating the need for filtration. Which is correlating in our study showing 3 log reductions of leucocytes (99.9%). All the leucodepleted blood components are beneficial towards the patient safety. Blood is precious and unique biological resource which should have limiting wastage. There is an evolving trend in medicine and patient blood management (PBM) that places greater emphasis on an individual patient-centred approach (31).

CONCLUSION:

Studies have elucidated that leucodepleted blood components has a significant role in minimizing transfusion adverse effects. This cost effectiveness can override the expense when compared to post transfusion complications, especially in high risk patient. Conservative approach to transfusion is recommended.

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