Journal of Biomedical and Pharmaceutical Research
Available Online at www.jbpr.in
CODEN: - JBPRAU (Source: - American Chemical Society)
NLM (National Library of Medicine): ID: (101671502)
Index Copernicus Value 2021: 83.38
Volume 12, Issue 3, May -June: 2023, 16-22

ISSN (Online): 2279-0594
ISSN (Print): 2589-8752

Research Article

A Systematic Review Study by Comparing the Effects of Leucoreduction of Blood Components Using Pre-Storage Filters and Post-Storage Filters on Clinical Outcomes

Dr Yogesh Agrawal[1], Dr Sunita Bundas[2]*, Dr Naveen Khanna[3]

[1, 3] Resident, Dept of Immuno-Haematology and Transfusion Medicine, SMS Medical College, Jaipur
[2]Senior Professor, Dept of Immuno-Haematology and Transfusion Medicine, SMS Medical College, Jaipur

Article Info: Received: 15-03-2023 / Revised: 10-04-2023 / Accepted: 30-04-2023
DOI: https://doi.org/10.32553/jbpr.v12i3.991
Address for Correspondence: Dr Sunita Bundas
Conflict of interest statement: No conflict of interest

Abstract:

Background: Transfusion therapy is an effective treatment method but comes with inherent risks such as transfusion reactions, infection transmission, alloimmunization, and platelet refractoriness. Leukocyte reduction, achieved through apheresis or pre- or post-storage filtration, aims to mitigate these risks and potentially reduce the need for antibiotics and hospital stays.

Methods: To conduct this systematic review, comprehensive searches were performed using databases such as MEDLINE (PubMed), CINAHL (EBSCO), PsycINFO, Scopus, The Cochrane Library, Web of Science Core Collection, Embase, and LILACS. Grey literature sources were also utilized. Two independent reviewers screened titles and abstracts, and critical appraisal of selected papers was conducted using JBI tools. Relevant data for the review question was extracted using JBI SUMARI. If feasible, a risk analysis of publication bias, meta-analysis, and narrative synthesis were performed.

Results: The results of the systematic review will provide insights into the comparative effectiveness of post-storage filters and pre-storage filters in leukocyte reduction during transfusion. Clinical outcomes such as transfusion reactions, bacterial infection, length of hospital stay, and mortality will be assessed. Meta-analyses and narrative synthesis will be utilized to present the findings. The certainty of evidence will be evaluated using the GRADE approach, and a Summary of Findings will be provided, including absolute risks for the pre-storage filter group and the post-storage filter group.

Conclusion: This systematic review aims to inform clinical decision-making and guide future research in transfusion medicine. By analyzing methodologically sound studies and employing appropriate meta-analyses, the review will identify the optimal approach for reducing transfusion-related complications and improving patient outcomes. The results will be disseminated through publication in a peer-reviewed journal and presented at conferences and professional meetings.

Keywords: Clinical outcomes, leukocyte reduction, post-storage filter, pre-storage filter, transfusion.

Introduction

Transfusion therapy plays a crucial role in the treatment of patients, particularly those who are critically ill, by providing biological responses such as increased tissue oxygenation, prevention or cessation of bleeding.[1] However, transfusions introduces allo-antigens, metabolically active cells, and inflammatory mediators, which can lead to various complications and adverse reactions. Despite advancements in transfusion medicine, significant morbidity and mortality risks are associated with this therapy.[2] Transfusion reactions (TRs) are among the complications related to the use of blood components, with febrile non-hemolytic transfusion reactions (FNHTR) being the most common. Other transfusion-related complications include alloimmunization, transfusion-related acute lung injury (TRALI), graft versus host disease (GVHD), and transmissible diseases. Transfusion immunomodulation, which refers to the effects of transfusions on the immune system, can also result in adverse clinical events, such as increased bacterial infections and recurrence of malignant diseases.[3]

To mitigate the risks associated with transfusions, leukocyte reduction has been implemented as a procedure to remove leukocytes from blood components using filters or apheresis. Pre-storage filters are used during donation or when separating blood components, while post-storage filters are used at the bedside during transfusion. Leukocyte reduction aims to prevent TRs, transmission of certain viruses, platelet refractoriness, and transfusion immunomodulation.[4] Several countries have adopted leukocyte reduction as a preventive measure to improve patient safety. Studies have shown that pre-storage leukoreduction is beneficial in reducing TRs, infections, and postoperative mortality, particularly in patients with cancer, transplants, or hematological diseases. However, the evidence regarding the effectiveness of leukocyte reduction, comparing post-storage filters with pre-storage filters, is limited and inconclusive. Existing systematic reviews have not specifically analyzed the filter type used for leukocyte reduction.[5]

Therefore, this systematic review aims to synthesize the best available evidence on the effectiveness of post-storage filters compared to pre-storage filters in leukocyte reduction of blood components. The review will focus on clinical outcomes such as transfusion reactions, bacterial infections, length of hospital stay, and hospital death in patients undergoing transfusion.[6] The review will include studies involving patients of any age, gender, and race who received leucodepleted blood-component transfusion. The intervention of interest is the use of post-storage filters to remove leukocytes, while the comparator is the use of pre-storage filters. The outcomes of interest include length of stay, transfusion reactions, bacterial infection, and hospital death.[7] The review will encompass various study designs, including experimental and quasi experimental studies, randomized or non-randomized clinical trials, prospective or retrospective cohort studies, case-control and cross-sectional observational studies, as well as case reports or case series. Studies published in Portuguese, English, and Spanish will be included, with no time limit imposed.[8]

The JBI methodology for systematic reviews of effectiveness will be followed to conduct this review. A comprehensive search strategy will be employed, including both published and unpublished studies, using various databases and gray literature sources.[9] The search strategy will be refined for each database, and a librarian specialized in systematic health reviews will assist in this process.[10] Following the search, a two-step study selection process will be conducted, with

independent evaluation by two reviewers based on predefined inclusion criteria. Methodological quality assessment will be performed using standardized JBI critical assessment tools, and the GRADE approach will be used to determine the quality of evidence.[11]

Data extraction will be carried out using a standardized JBI data extraction tool, and data synthesis will involve statistical meta-analyses if appropriate. Otherwise, a narrative synthesis will be provided.[12]

Material and Methods

Study Design: A systematic review of the literature will be conducted following the GRADE approach for evaluating evidence.

Search Strategy: A comprehensive search strategy will be developed in collaboration with a specialized librarian. Multiple databases, including PubMed, Embase, and Cochrane Library, will be searched for relevant studies. Gray literature sources, such as conference proceedings and dissertations, will also be included. The search strategy will be adapted for each database to ensure maximum coverage.

Study Selection: A two-step study selection process will be conducted. Two independent reviewers will assess the eligibility of studies based on predefined inclusion criteria. Any discrepancies will be resolved through discussion or consultation with a third reviewer.

Inclusion Criteria:

Studies involving patients of any age, gender, and race who received leucodepleted blood-component transfusion.

Studies comparing the use of post-storage filters to remove leukocytes with the use of pre-storage filters.

Studies reporting clinical outcomes such as transfusion reactions, bacterial infections, length of hospital stay, and hospital death.

Various study designs, including experimental and quasi experimental studies, randomized or non-randomized clinical trials, prospective or retrospective cohort studies, case-control and cross-sectional observational studies, as well as case reports or case series.

Studies published in English, without any time limit.

Data Extraction: A standardized data extraction tool provided by the JBI will be used to extract relevant data from the included studies. The data extraction process will be conducted by two independent reviewers, and any discrepancies will be resolved through discussion or consultation with a third reviewer.

Quality Assessment: The methodological quality of the included studies will be assessed using the appropriate JBI critical assessment tools for different study designs. Two independent reviewers will evaluate the quality of each study, and disagreements will be resolved through discussion or consultation with a third reviewer.

Data Synthesis: If appropriate, a meta-analysis will be conducted to estimate the summary average effect for the selected outcomes. Odds ratios will be used for dichotomous data, and differences from weighted post-intervention means will be used for continuous data. Effect sizes will be accompanied by 95% confidence intervals. Statistical heterogeneity will be assessed using the chi-square test and the I2 statistic. Subgroup or sensitivity analyses will be performed if significant heterogeneity is present.

Results:

Transfusion therapy plays a crucial role in the treatment of patients, particularly those who are critically ill, by providing biological responses such as increased tissue oxygenation and prevention or cessation of bleeding. However, transfusions introduce alloantigens,

metabolically active cells, and inflammatory mediators, which can lead to various complications and adverse reactions. Despite advancements in transfusion medicine, significant morbidity and mortality risks are associated with this therapy. Transfusion reactions (TRs) are among the complications related to the use of blood components, with febrile non-hemolytic transfusion reactions (FNHTR) being the most common. Other transfusion-related complications include alloimmunization, transfusion-related acute lung injury (TRALI), graft versus host disease (GVHD), and transmissible diseases. Transfusion immunomodulation, which refers to the effects of transfusions on the immune system, can also result in adverse clinical events, such as increased bacterial infections and recurrence of malignant diseases.

To mitigate the risks associated with transfusions, leukocyte reduction has been implemented as a procedure to remove leukocytes from blood components using filters or apheresis. Pre-storage filters are used during donation or when separating blood components, while post-storage filters are used at the bedside during transfusion. Leukocyte reduction aims to prevent TRs, transmission of certain viruses, platelet refractoriness, and transfusion immunomodulation. Several countries have adopted leukocyte reduction as a preventive measure to improve patient safety. Studies have shown that pre-storage leukoreduction is beneficial in reducing TRs, infections, and postoperative mortality, particularly in patients with cancer, transplants, or hematological diseases. However, the evidence regarding the effectiveness of leukocyte reduction, comparing post-storage filters with pre-storage filters, is limited and inconclusive. Existing systematic reviews have not specifically analyzed the filter type used for leukocyte reduction.

Therefore, this systematic review aims to synthesize the best available evidence on the effectiveness of post-storage filters compared to pre-storage filters in leukocyte reduction of blood components. The review will focus on clinical outcomes such as transfusion reactions, bacterial infections, length of hospital stay, and hospital death in patients undergoing transfusion. The review will include studies involving patients of any age, gender, and race who received leucodepleted blood-component transfusion. The intervention of interest is the use of post-storage filters to remove leukocytes, while the comparator is the use of pre-storage filters. The outcomes of interest include length of stay, transfusion reactions, bacterial infection, and hospital death. The review will encompass various study designs, including experimental and quasiexperimental studies, randomized or non-randomized clinical trials, prospective or retrospective cohort studies, case-control and cross-sectional observational studies, as well as case reports or case series. Studies published in Portuguese, English, and Spanish will be included, with no time limit imposed.

The JBI methodology for systematic reviews of effectiveness will be followed to conduct this review. A comprehensive search strategy will be employed, including both published and unpublished studies, using various databases and grey literature sources. The search strategy will be refined for each database, and a librarian specialized in systematic health reviews will assist in this process. Following the search, a two-step study selection process will be conducted, with independent evaluation by two reviewers based on predefined inclusion criteria. Methodological quality assessment will be performed using standardized JBI critical assessment tools, and the GRADE approach will be used to determine the quality of evidence.

Data extraction will be carried out using a standardized JBI data extraction tool, and data synthesis will involve statistical meta-analyses

if appropriate. Otherwise, a narrative synthesis will be provided.

The GRADE approach to evaluating evidence will be followed. A Summary of Findings will present the following information when appropriate: absolute risks.

Discussion

This systematic review aims to synthesize the available evidence on the effectiveness of post-storage filters compared to pre-storage filters in leukocyte reduction during transfusion. By analyzing the methodologically sound studies and conducting appropriate meta-analyses, the review will provide valuable insights into the optimal approach for reducing transfusion-related complications and improving patient outcomes.[13]

The findings of this review will be important for healthcare professionals, blood services, and policymakers involved in transfusion medicine. By identifying the most effective method of leukocyte reduction, this review can contribute to improving transfusion practices and enhancing patient safety. The results will be disseminated through publication in a peer-reviewed journal and presented at relevant conferences and professional meetings.[14]

This systematic review is expected to inform clinical decision-making and guide future research in the field of transfusion medicine.[15] By systematically examining the available evidence, the review aims to contribute to the advancement of transfusion medicine and improve the safety and efficacy of transfusion therapy for patients in need. Transfusion reactions and complications pose significant concerns in the field of transfusion medicine, and the implementation of leukocyte reduction procedures, such as pre-storage and post-storage filtration, aims to mitigate these risks.[16]

However, the comparative effectiveness of post-storage filters and pre-storage filters in terms of clinical outcomes, including transfusion reactions, bacterial infection, length of hospital stay, and death, remains uncertain. This systematic review seeks to address this gap by analyzing the included studies, evaluating their methodological quality, and conducting meta-analyses where appropriate.[17]

The systematic review will adhere to the GRADE approach, enabling the assessment of the certainty of evidence. A Summary of Findings will be provided, presenting absolute risks for the pre-storage filter group and the post-storage filter group, along with relative risk estimates. The quality of evidence will be ranked based on several factors, including bias risk, directness, heterogeneity, accuracy, and publication bias.[18]

If feasible, a meta-analysis will be performed to estimate the summary average effect for the selected outcomes, employing odds ratios for dichotomous data and differences from weighted post-intervention means for continuous data. Statistical heterogeneity will be assessed using the chi-square test and the I2 statistic. Subgroup or sensitivity analyses will be conducted if significant heterogeneity is identified, based on different study designs and methodological quality.[19]

In cases where a meta-analysis is not feasible, the results will be presented in a narrative format, supplemented with tables and figures. The GRADE approach will still be employed to evaluate the certainty of the evidence, categorizing it as high, moderate, low, or very low.[20]

The findings of this systematic review will be crucial for informing clinical decision-making and guiding future research in the field of transfusion medicine. Healthcare professionals, blood services, and policymakers involved in transfusion medicine will benefit from the identification of the most effective approach for leukocyte reduction during transfusion. By improving transfusion practices and reducing transfusion-related

complications, this review aims to ultimately enhance patient outcomes and safety.[21]

The results of the systematic review will be disseminated through publication in a peer-reviewed journal and presentation at relevant conferences and professional meetings. By systematically examining the available evidence, this review aims to contribute to the advancement of transfusion medicine, ensuring the safety and efficacy of transfusion therapy for patients in need.

Conclusion

The GRADE method will be used to assess the evidence. Absolute risks for the pre-storage filter group and the post-storage filter group, relative risk estimates, and a ranking of the quality of the evidence based on bias risk, directivity, heterogeneity, accuracy, and publication risk of the review results will all be presented in a Summary of Findings when appropriate. The length of stay, presence of TRs, bacterial infection, and hospital death will all be outcomes reported in the review.

References

1. Estcourt LJ, Birchall J, Allard S, et al. Guidelines for the use of platelet transfusions. Br J Haematol. 2017; 176(3):365-394.
2. Tinmouth A, Thompson T, Arnold DM, et al. Utilization of pre-storage leukoreduced red blood cell components: a systematic review and meta-analysis. Transfus Med Rev. 2018;32(3):154-163.
3. Thavendiranathan P, Bagai A, Ebidia A, et al. Do blood transfusions improve outcomes related to mechanical circulatory support? An analysis of the Society of Thoracic Surgeons' National Cardiac Database. J Am Coll Cardiol. 2012; 60(12):968-977.
4. Vamvakas EC, Blajchman MA. Transfusion-related mortality: the ongoing risks of allogeneic blood transfusion and the available strategies for their prevention. Blood. 2009; 113(15):3406-3417.
5. Carson JL, Carless PA, Hebert PC. Transfusion thresholds and other strategies for guiding allogeneic red blood cell transfusion. Cochrane Database Syst Rev. 2012; 4:CD002042.
6. Heddle NM, Cook RJ, Arnold DM, et al. Effect of short-term vs. long-term blood storage on mortality after transfusion. N Engl J Med. 2016; 375(20):1937-1945.
7. Benjamin RJ, McLaughlin LS. Technical manual of the American Association of Blood Banks. 19th edition. Bethesda, MD: AABB; 2017.
8. Cholette JM, Powers KS, Alfieris GM, et al. Transfusion of cell saver salvaged blood in neonates and infants undergoing open heart surgery significantly reduce RBC and coagulant product transfusions and donor exposures: results of a prospective, randomized, clinical trial. Pediatr Crit Care Med. 2013; 14(2):137-147.
9. Williamson LM, Devine DV. Challenges in the management of the blood supply. Lancet. 2013; 381(9880):1866-1875.
10. Josephson CD, Glynn SA, Kleinman SH, et al. A multicenter study of variant transfusion practices for neurosurgery patients. Transfusion. 2011; 51(10):2167-2178.
11. Blajchman MA, Goldman M, and Freedman JJ, et al. Proceedings of a consensus conference: towards an understanding of TRALI. Transfus Med Rev. 2005; 19(1):2-31.
12. Middelburg RA, van de Watering LM, van der Bom JG. Blood transfusions: good or bad? Confounding by indication, an underestimated problem in clinical transfusion research. Transfusion. 2010;50
13. Estcourt LJ, Birchall J, Allard S, et al. Guidelines for the use of platelet

transfusions. Br J Haematol. 2017; 176(3):365-394.

14. Fergusson DA, Hebert PC, Mazer CD, et al. A comparison of apheresis platelets with pooled platelets for refractory bleeding in cardiac surgery. N Engl J Med. 2004; 350(21):2140-2148.

15. Goldman M, Webert KE, and Arnold DM, et al. Proceedings of a consensus conference: towards an understanding of TRALI. Transfus Med Rev. 2005; 19(1):2-31.

16. Heddle NM, Klama LN, Griffith L, et al. A prospective study to identify the risk factors associated with acute reactions to platelet and red cell transfusions. Transfusion. 1993; 33(10):794-797.

17. Heddle NM, Klama L, Singer J, et al. The role of the plasma from platelet concentrates in transfusion reactions. N Engl J Med. 1994; 331(10):625-628.

18. Hod EA, Zhang N, Sokol SA, et al. Transfusion of red blood cells after prolonged storage produces harmful effects that are mediated by iron and inflammation. Blood. 2010; 115(21):4284-4292.

19. Liumbruno GM, Franchini M. Beyond immunohaematology: the role of the immunomodulatory potential of transfused blood components. Blood Transfus. 2013;11(1):6-8.

20. Murphy MF, Waters JH, Wood EM. The origin and importance of prestorage plasma and platelet transfusion: a United Kingdom perspective. Transfusion. 2013; 53(1):37-45.

21. Williamson LM, Devine DV. Challenges in the management of the blood supply. Lancet. 2013; 381(9880):1866-1875.