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Effect of Fibrinogen Concentrate vs Cryoprecipitate on Blood Component Transfusion After Cardiac Surgery

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ABSTRACT

Background: The literature surrounding the use of fibrinogen concentrate versus cryoprecipitate in the context of cardiac surgery reveals significant insights into the efficacy and safety of these two treatment modalities for managing bleeding complications. **Literature Review:** The literature reviewed provides a comprehensive analysis of the efficacy and safety of fibrinogen concentrate compared to cryoprecipitate in managing bleeding complications following cardiac surgery. The systematic review by (Augusto Azevedo Maranhão Cardoso et al., 2015) establishes fibrinogen concentrate as a promising first-line treatment, emphasizing its advantages such as complete viral inactivation which reduces the risk of transfusion-related infections. This review synthesizes data from four studies involving 161 patients, indicating that fibrinogen concentrate can lead to decreased blood product usage and reduced perioperative bleeding. **Conclusion:** In conclusion, the reviewed literature consistently supports the use of fibrinogen concentrate as an effective and potentially safer alternative to cryoprecipitate for managing bleeding in cardiac surgery. The findings highlight its role in reducing transfusion requirements, improving patient outcomes, and offering economic advantages. However, the need for further research, particularly larger multicenter trials, is essential to validate these findings and inform clinical guidelines.

Keyword: Effect, Fibrinogen Concentrate, Cryoprecipitate, Blood Component Transfusion, After Cardiac Surgery

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INTRODUCTION

The literature surrounding the use of fibrinogen concentrate versus cryoprecipitate in the context of cardiac surgery reveals significant insights into the efficacy and safety of these two treatment modalities for managing bleeding complications. The systematic review conducted by (Augusto Azevedo Maranhão Cardoso et al., 2015) highlights the advantages of fibrinogen concentrate, particularly its complete viral inactivation, which mitigates contamination risks associated with transfusions. This review meticulously analyzed randomized controlled trials (RCTs) and identified four studies involving 161 patients, demonstrating that fibrinogen concentrate could effectively reduce blood product usage and perioperative bleeding, thereby establishing its viability as a first-line therapy in cardiac surgery settings.

Expanding on this foundation, (Karkouti et al., 2018) presented the FIBRES trial, a phase III randomized study comparing fibrinogen concentrate and cryoprecipitate in patients experiencing acquired hypofibrinogenemia during cardiac surgery involving cardiopulmonary bypass (CPB). The authors noted that coagulopathy leading to excessive bleeding poses a serious risk, often necessitating massive transfusions of allogeneic blood products. Their study underscored the importance of having an active control, as cryoprecipitate remains a common treatment in North America despite safety concerns in Europe. This research is pivotal as it addresses the existing gap in literature regarding the comparative efficacy of these two therapies, laying the groundwork for further exploration into their respective roles in clinical practice.

In a post hoc analysis of the REPLACE trial, (Rahe-Meyer et al., 2019) evaluated the effects of fibrinogen concentrate during major aortic replacement surgery. Their findings indicated that fibrinogen concentrate administration significantly reduced blood loss and

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transfusion requirements, reinforcing the notion that rapid correction of hypofibrinogenemia is crucial in surgical settings. The study also contextualized the clinical effectiveness of fibrinogen concentrate against other treatments, thereby contributing to a broader understanding of its role in managing bleeding complications.

(Louise Crighton & J. Huisman, 2021) further investigated the use of fibrinogen concentrate in pediatric patients, noting that both fibrinogen concentrate and cryoprecipitate improved fibrinogen levels post-intervention. However, they identified a narrower interquartile range in the fibrinogen concentrate group, suggesting more consistent outcomes. Their study raised important considerations regarding dosing strategies, which may influence the efficacy of these treatments. While no significant differences were found in secondary outcomes or adverse events, the study highlighted the potential of fibrinogen concentrate as a safe alternative to cryoprecipitate in pediatric cardiac surgery, aligning with clinical guidelines that advocate for fibrinogen supplementation.

Most recently, (Abrahamyan et al., 2023) conducted a cost-effectiveness analysis comparing fibrinogen concentrate and cryoprecipitate for managing active bleeding in adult cardiac surgical patients. This study is crucial in evaluating not only the clinical outcomes but also the economic implications of using fibrinogen concentrate over cryoprecipitate, thereby contributing to the ongoing discourse about resource allocation in healthcare settings.

Overall, the reviewed literature underscores the evolving understanding of fibrinogen concentrate's role in cardiac surgery, particularly in managing bleeding and hypofibrinogenemia, while also highlighting the need for continued research to delineate the optimal treatment strategies in various clinical contexts.

LITERATURE REVIEW

The systematic review by (Augusto Azevedo Maranhão Cardoso et al., 2015) provides a

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comprehensive evaluation of the use of lyophilized fibrinogen concentrate in the context of cardiac surgery, particularly focusing on its efficacy in managing perioperative bleeding. The authors meticulously analyzed randomized controlled trials (RCTs) that explored the application of fibrinogen concentrate as a first-line therapeutic option for patients experiencing bleeding during cardiac procedures.

One of the significant advantages highlighted in the review is the complete viral inactivation of fibrinogen concentrate, which mitigates the risks of transfusion-related infections, a critical concern in blood component transfusion ((Augusto Azevedo Maranhão Cardoso et al., 2015)). This aspect is particularly relevant in cardiac surgery, where the need for multiple transfusions can elevate the risk of complications associated with blood product exposure.

The authors synthesized data from four relevant studies that collectively included 161 patients, providing a solid foundation for their conclusions. They found that the use of fibrinogen concentrate was associated with a notable reduction in the requirement for additional blood products and a decrease in overall bleeding during the perioperative period. This finding underscores the potential of fibrinogen concentrate not only to improve patient outcomes but also to optimize resource utilization in clinical settings.

However, while the review presents compelling evidence supporting the use of fibrinogen concentrate, it is essential to consider the limitations inherent in the included studies. The relatively small sample size across the studies may affect the generalizability of the findings. Additionally, variations in study design, patient populations, and definitions of bleeding could introduce bias and limit the comparability of results.

The article titled "Protocol for a phase III, non-inferiority, randomised comparison of a new fibrinogen concentrate versus cryoprecipitate for treating acquired hypofibrinogenaemia in bleeding cardiac surgical patients: the FIBRES trial" by (Karkouti et al., 2018)

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addresses a critical issue in cardiac surgery: the management of coagulopathy and excessive bleeding, particularly in patients undergoing cardiopulmonary bypass (CPB). This complication, which affects approximately 10% or more of these patients, often necessitates massive transfusions of allogeneic blood products (ABPs), thereby increasing the risk of further bleeding and associated complications.

The study's design is noteworthy for its pragmatic approach, aiming to enhance clinical relevance and generalizability. By utilizing an active control, cryoprecipitate, as the comparator for the new fibrinogen concentrate, the study ensures that all participants receive fibrinogen supplementation as clinically indicated. This is particularly important given the varying practices and regulatory environments surrounding the use of cryoprecipitate and fibrinogen concentrate in different regions. The authors highlight that while cryoprecipitate is commonly used in North America, its use has been curtailed in many European countries due to safety concerns regarding pathogen reduction ((Karkouti et al., 2018)).

The article emphasizes the need for rigorous comparative data between cryoprecipitate and fibrinogen concentrate, as there is currently a lack of substantial evidence to determine the most effective treatment for acquired hypofibrinogenaemia in this patient population. The study's large sample size of approximately 1200 patients provides a robust framework to achieve over 90% power in detecting the non-inferiority of fibrinogen concentrate compared to cryoprecipitate. This methodological rigor is essential for establishing clinical guidelines and improving patient outcomes in a high-risk population.

Furthermore, the authors discuss the mechanisms of fibrinogen loss, which can occur due to acute bleeding, dilution from fluid administration, and consumption during the coagulation cascade activation associated with CPB. Understanding these mechanisms is crucial for clinicians as it informs the

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timing and choice of therapy during the perioperative period.

The article titled "Randomized evaluation of fibrinogen versus placebo in complex cardiovascular surgery: post hoc analysis and interpretation of phase III results" by (Rahe-Meyer et al., 2019) presents a comprehensive examination of the efficacy of fibrinogen concentrate as a first-line treatment during major aortic replacement surgery. The study is particularly relevant in the context of managing severe bleeding following cardiopulmonary bypass, a critical concern in cardiac surgery.

One of the key insights from the article is the significant impact of fibrinogen concentrate on reducing blood loss and the necessity for transfusions in patients undergoing thoracic aneurysm repairs. The authors report that fibrinogen concentrate administration leads to a notable recovery of fibrinogen levels in patients experiencing hypofibrinogenemia, which is often exacerbated during extensive surgical procedures ((Rahe-Meyer et al., 2019)). This finding is critical as it underscores the potential of fibrinogen concentrate to serve as an effective therapeutic intervention to mitigate the risks associated with excessive bleeding and the subsequent need for blood component transfusions.

Moreover, the article discusses the implications of fibrinogen concentrate in reversing dilutional coagulopathy, a condition frequently encountered in the context of significant blood loss during surgery. The authors reference a porcine model that supports the clinical effectiveness of fibrinogen in this regard, suggesting that timely administration can enhance hemostatic function and improve patient outcomes ((Rahe-Meyer et al., 2019)). This insight is particularly valuable as it highlights the need for prompt intervention in managing coagulopathy, which can complicate recovery and increase morbidity.

In addition, the authors contrast the use of fibrinogen concentrate with other blood products, such as fresh frozen plasma, in the context of surgical bleeding. Their systematic review indicates that

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fibrinogen concentrate may provide a more targeted approach to coagulation management, potentially streamlining transfusion practices and reducing the reliance on multiple blood components ((Rahe-Meyer et al., 2019)). This aspect is essential for developing transfusion algorithms that prioritize patient safety and resource efficiency.

The article "Pediatric Fibrinogen PART II—Overview of Indications for Fibrinogen Use in Critically Ill Children" by (Louise Crighton & J. Huisman, 2021) provides a comprehensive examination of the use of fibrinogen concentrate and cryoprecipitate in pediatric cardiac surgery, particularly focusing on their effects on fibrinogen levels post-intervention. The authors highlight that both treatment options successfully improved fibrinogen levels, which is critical in managing postoperative bleeding and hypofibrinogenemia in this vulnerable population.

A notable aspect of the findings is the narrower interquartile range observed in the fibrinogen concentrate group, indicating less variability in fibrinogen levels achieved compared to the cryoprecipitate group. This suggests that the dosing strategy employed for fibrinogen concentrate, which was based on weight, may contribute to more consistent outcomes. In contrast, the standardized dosing of cryoprecipitate could lead to variability in fibrinogen levels achieved, which may have implications for its effectiveness in clinical practice.

However, the study does have limitations, including its non-blinded design and the fact that it was conducted across two centers with differing cardiopulmonary bypass protocols. These factors could introduce bias and variability in the results, making it difficult to draw definitive conclusions about the relative efficacy of the two treatments. Furthermore, the authors reference an important randomized controlled trial (RCT) in the adult population that did not demonstrate a difference in primary and secondary outcomes between the two treatment groups, reinforcing the notion that neither fibrinogen concentrate nor

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cryoprecipitate can be deemed superior based solely on the outcomes measured.

The article emphasizes that the fibrinogen concentrate used (Fibryga®) contains significantly higher levels of factor XIII compared to other fibrinogen concentrates, which may influence its effectiveness and safety profile. The authors advocate for the consideration of fibrinogen supplementation in pediatric patients with hypofibrinogenemia undergoing cardiac surgery, aligning with clinical guidelines that recommend treatment with either cryoprecipitate or fibrinogen concentrate based on diagnostic criteria.

The article "Cost-effectiveness of Fibrinogen Concentrate vs Cryoprecipitate for Treating Acquired Hypofibrinogenemia in Bleeding Adult Cardiac Surgical Patients" by (Abrahamyan et al., 2023) provides a comprehensive analysis of the economic implications associated with the use of fibrinogen concentrate compared to cryoprecipitate in managing bleeding complications in adult patients following cardiac surgery. The authors meticulously explore the clinical effectiveness and cost-effectiveness of these two blood products, which is critical given the increasing focus on healthcare resource management in surgical settings.

The study employs a robust methodology, utilizing a decision-analytic model to simulate patient outcomes and associated costs. This approach allows for a nuanced understanding of the financial impacts of each treatment option, factoring in variables such as the costs of products, administration, and potential complications arising from their use. The findings suggest that fibrinogen concentrate may offer a more favorable cost-effectiveness ratio, particularly in patients with significant hypofibrinogenemia, thereby highlighting its potential as a preferred treatment modality in this context.

Moreover, the article underscores the importance of timely intervention in managing bleeding, as delays can lead to worse clinical outcomes and increased healthcare

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costs. The authors provide a critical evaluation of the existing literature on bleeding management in cardiac surgery, reinforcing the need for evidence-based protocols that incorporate both clinical effectiveness and economic considerations.

A noteworthy aspect of the article is its discussion on the implications of using fibrinogen concentrate in terms of patient outcomes. The authors present data indicating that the use of fibrinogen concentrate is associated with a reduction in the need for additional blood component transfusions, which can be a significant cost driver in postoperative care. This finding is particularly relevant in the context of evolving transfusion practices aimed at minimizing exposure to allogeneic blood products.

However, while the authors advocate for the use of fibrinogen concentrate based on cost-effectiveness, they also acknowledge the need for further research to validate these findings in larger, multicenter trials. This call for additional studies is crucial, as it would help to establish a more comprehensive understanding of the long-term outcomes associated with each treatment option, thereby informing clinical guidelines and practice.

CONCLUSION

The literature reviewed provides a comprehensive analysis of the efficacy and safety of fibrinogen concentrate compared to cryoprecipitate in managing bleeding complications following cardiac surgery. The systematic review by (Augusto Azevedo Maranhão Cardoso et al., 2015) establishes fibrinogen concentrate as a promising first-line treatment, emphasizing its advantages such as complete viral inactivation which reduces the risk of transfusion-related infections. This review synthesizes data from four studies involving 161 patients, indicating that fibrinogen concentrate can lead to decreased blood product usage and reduced perioperative bleeding.

Further exploration in the FIBRES trial by (Karkouti et al., 2018) highlights the critical nature of managing coagulopathy during

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cardiac surgery, especially in patients undergoing cardiopulmonary bypass (CPB). This study, with a large sample size, aims to provide robust comparative data between fibrinogen concentrate and cryoprecipitate, addressing the current knowledge gap regarding their relative efficacy.

The post hoc analysis from the REPLACE trial by (Rahe-Meyer et al., 2019) reinforces the findings of reduced blood loss and transfusion requirements associated with fibrinogen concentrate during major aortic surgeries. This study emphasizes the importance of timely intervention in correcting hypofibrinogenemia, which is crucial for minimizing the risks of excessive bleeding during surgery.

In pediatric populations, the study by (Louise Crighton & J. Huisman, 2021) indicates that fibrinogen concentrate not only improves fibrinogen levels post-intervention but also does so with less variability compared to cryoprecipitate. This consistency in outcomes may enhance the treatment's effectiveness in managing hypofibrinogenemia during pediatric cardiac surgeries.

Lastly, the cost-effectiveness analysis conducted by (Abrahamyan et al., 2023) underscores the economic implications of using fibrinogen concentrate over cryoprecipitate. This study suggests that fibrinogen concentrate may provide a more favorable cost-effectiveness ratio, particularly in cases of significant hypofibrinogenemia, thus influencing resource allocation in healthcare settings.

In conclusion, the reviewed literature consistently supports the use of fibrinogen concentrate as an effective and potentially safer alternative to cryoprecipitate for managing bleeding in cardiac surgery. The findings highlight its role in reducing transfusion requirements, improving patient outcomes, and offering economic advantages. However, the need for further research, particularly larger multicenter trials, is essential to validate these findings and inform clinical guidelines.

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