Review Article

A Review on Therapeutic Plasma Exchange: Clinical Applications, Barriers to Equitable Use and Future Prospects

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Abstract

Therapeutic Plasma Exchange (TPE) is a vital extracorporeal procedure used in the management of various neurological, autoimmune and hematological disorders by eliminating pathological plasma components such as autoantibodies, immune complexes, toxins and inflammatory mediators. Its therapeutic efficacy has been particularly notable in conditions such as Guillain-Barré Syndrome (GBS), Thrombotic Thrombocytopenic Purpura (TTP) and myasthenia gravis. TPE works through apheresis technology, applying principles of mass transfer and diffusion to restore immune homeostasis and reduce disease burden. This review explores the current clinical applications of TPE, its underlying mechanisms and patient outcomes based on existing literature. Additionally, it highlights the procedural variations including intermittent and continuous TPE, centrifugation and filtration-based methods, and discusses both the clinical benefits and potential complications associated with the therapy. Furthermore, the review examines the critical socioeconomic challenges faced in implementing TPE in low-resource settings, such as limited healthcare infrastructure, economic barriers, policy gaps and lack of awareness. Emerging research also points to potential new indications for TPE, including its adjunctive role in managing severe COVID-19 cases and certain hepatic, dermatological and toxicological emergencies. As the therapeutic landscape evolves, efforts must be made to optimize treatment protocols, ensure standardized practices and make TPE more accessible across healthcare systems worldwide. Addressing these gaps is crucial for translating its proven benefits into broader clinical impact.

Key words: *Therapeutic Plasma Exchange, Apheresis, Plasmapheresis, TPE*

Date of received: *28.08.2024*

Date of acceptance: *29.11.2024*

DOI: https://doi.org/10.3329/kyamcj.v15i04.79622

KYAMC Journal. 2025; 15(04): 189-194.

Introduction

Therapeutic Plasma Exchange (TPE) is a clinical procedure that involves the extracorporeal removal of a patient's plasma, which is subsequently replaced with a substitution fluid such as albumin, normal saline or fresh frozen plasma. The rationale behind this therapy is to eliminate circulating pathogenic substances such as autoantibodies, immune complexes, cryoglobulins, myeloma light chains and inflammatory mediators that contribute to disease pathogenesis.[1]

Over the past few decades, TPE has gained acceptance as a standard treatment modality for several autoimmune, neurological, and hematological disorders. It has shown significant clinical efficacy in diseases like Guillain-Barré Syndrome (GBS), myasthenia gravis, and Thrombotic Thrombocytopenic Purpura (TTP), among others.[2-4] TPE operates based on the principles of mass transfer and selective removal, making it an effective intervention for conditions with known circulating pathogenic factors.[3]

Despite its wide-ranging applications and positive clinical outcomes, access to TPE remains constrained in resource limited settings. Factors such as the high cost of disposable kits, limited availability of apheresis machines, lack of trained personnel and insufficient healthcare funding contribute to the low utilization rates in many developing countries, including Bangladesh.[5,6] Additionally, sociocultural perceptions and inadequate public health policies often impede the integration of TPE into mainstream treatment protocols.[7]

Emerging evidence has expanded the scope of TPE to include novel applications, such as the management of cytokine storm

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syndromes in severe COVID-19 infections, autoimmune liver diseases, and certain dermatological and renal disorders.[8-11] These developments necessitate continuous evaluation and research to update existing guidelines and ensure optimal therapeutic use.

The primary objective of this review is to examine the clinical efficacy, complications and accessibility of Therapeutic Plasma Exchange. Special emphasis is placed on its use in low-resource settings and on identifying strategies to overcome existing barriers for broader implementation.

Definition

The term "therapeutic plasma exchange" specifically refers to a procedure that selectively separates plasma from blood cells using apheresis techniques. The core mechanism of action of TPE hinges on its ability to remove pathological substances from the plasma that contribute to the underlying disease process. By decreasing the levels of circulating autoantibodies, inflammatory cytokines and other harmful components, TPE can facilitate symptom relief and enhance functional outcomes.

Mechanism of Action

TPE operates on fundamental principles of mass transfer and diffusion, where the removal of pathological components from the bloodstream allows for the restoration of homeostasis within the patient's immune system. The removal of autoantibodies is particularly crucial in autoimmune conditions like GBS, where TPE effectively diminishes the circulating autoantibodies that target peripheral nerve tissues, thereby reducing demyelination and facilitating nerve repair.[2] The process generally involves the following steps:

1. Apheresis: Blood is drawn from the patient and processed through an apheresis machine, which separates the plasma from the cellular components (red blood cells, white blood cells and platelets).
2. Plasma Removal: The separated plasma, which contains the harmful components, is removed and discarded.
3. Replacement Therapy: The removed plasma volume is replaced with an appropriate solution, such as normal saline, albumin or fresh frozen plasma, ensuring the patient maintains hemodynamic stability and adequate oncotic pressure.
4. Reinfusion: The remaining blood cells are reinfused back into the patient, completing the procedure.

Types of TPE

TPE can be classified into several types based on the techniques and equipment utilized during the procedure. The primary types include:

1. Intermittent TPE: This method involves multiple sessions of plasma exchange conducted over a specified duration, often spanning days or weeks. Each session typically lasts several hours and encompasses the removal of a predetermined volume of plasma.[12]
2. Continuous TPE: Continuous techniques permit real-time plasma exchange throughout a single session. This approach is particularly advantageous for critically ill patients who require expedited removal of plasma components.[13]
3. Centrifugation-based TPE: In this common method, a centrifuge is employed to separate plasma from blood cells based on differences in density. The separated plasma is then discarded while the remaining blood components are reinfused back into the patient.[14]
4. Filtration-based TPE: This technique utilizes specialized filters to selectively remove plasma while retaining cellular components. It can be employed in specific clinical scenarios where rapid exchange is necessary.[15]

Indications for TPE

The clinical indications for TPE are extensive and encompass a variety of conditions, including but not limited to:

• **Neurological Disorders:** Conditions such as Guillain-Barré Syndrome and myasthenia gravis have demonstrated significant improvement with TPE. Early intervention during the acute phase of GBS, in particular, has been linked to enhanced functional recovery.[2]
• **Hematological Conditions:** TTP, characterized by microangiopathic hemolytic anemia and thrombocytopenia, is another condition where TPE has proven effective. The removal of von Willebrand factor multimers through TPE can rapidly reverse the clinical syndrome.[3]
• **Autoimmune Diseases:** Systemic lupus erythematosus, rheumatoid arthritis and other autoimmune diseases can benefit from TPE by reducing levels of autoantibodies and immune complexes, which contribute to disease progression.[16, 17]
• **Toxin-related Conditions:** In cases of acute kidney injury or drug toxicity, TPE can facilitate the removal of nephron toxins from circulation, offering a potential lifeline for affected patients.[11]

Benefits of TPE

The therapeutic benefits of TPE extend beyond simple plasma removal. Evidence from clinical studies underscores several advantages:

1. Rapid Symptom Relief: TPE has been shown to expedite symptom alleviation in acute autoimmune diseases. For instance, in cases of GBS, TPE has significantly improved motor function within a short timeframe, allowing for quicker patient recovery.[2]
2. Improved Quality of Life: Patients with chronic conditions such as myasthenia gravis frequently report enhanced quality of life following TPE, attributed to a reduction in exacerbations and better overall disease control.[4]
3. Reduction in Hospitalization: By effectively managing acute disease flares, TPE can lead to decreased hospital stays and overall healthcare costs. This is particularly relevant in resource-limited settings, where prolonged hospital admissions can strain healthcare resources.[7]
4. Flexibility in Management: TPE can be tailored to individual patient needs regarding frequency and volume, allowing for personalized treatment regimens that adapt to changes in disease status.[18]
5. Potential for Long-term Benefits: In certain chronic conditions, repeated courses of TPE may lead to sustained remission

or prolonged periods of disease control, improving long-term outcomes for patients.[19]

Complications Associated with TPE

While TPE is generally regarded as a safe procedure, it is not without risks. Potential complications include:

1. Allergic Reactions: Patients may experience allergic reactions to the replacement fluids or anticoagulants used during the procedure. Such reactions can vary in severity, necessitating immediate intervention and monitoring.[2]
2. Electrolyte Imbalances: The use of citrate as an anticoagulant during TPE can lead to hypocalcemia, resulting in symptoms such as muscle cramps or tetany. Continuous monitoring of calcium levels is critical throughout the TPE sessions to mitigate this risk.[20]
3. Infections: As with any procedure involving venous access, there exists a risk of infection. Rigorous aseptic techniques and careful monitoring of insertion sites are essential to minimize this risk.[13]
4. Mechanical Complications: The use of apheresis machines can result in mechanical issues, including malfunction or malfunction of venous access devices, leading to complications such as hematoma formation or thrombosis.[14]
5. Thrombocytopenia and Hypo-proteinemia: Patients may develop low platelet counts and decreased protein levels, necessitating close monitoring and potential supplementation. These complications can exacerbate the clinical situation for patients, especially those already at risk for bleeding or clotting disorders.[15]

Socioeconomic Barriers to Accessing TPE

Despite the potential benefits of TPE, access to this treatment remains limited in many low-resource settings, including Bangladesh. Various socioeconomic factors contribute to these challenges:

1. Awareness and Education: A lack of awareness regarding the benefits and indications for TPE among both healthcare providers and patients can limit its utilization. Educational initiatives aimed at improving understanding and acceptance of TPE as a treatment option are essential.[1]
2. Healthcare Infrastructure: The lack of adequately equipped healthcare facilities capable of performing TPE can significantly hinder access for patients. Limited availability of apheresis machines and trained personnel restricts the implementation of TPE in routine practice.[6]
3. Economic Constraints: The high cost associated with TPE procedures, combined with the economic challenges faced by patients in low-income settings, creates barriers to treatment. Many patients may forgo TPE due to financial limitations, leading to poorer health outcomes.[7]
4. Policy and Regulation: The absence of clear policies and guidelines governing the use of TPE in Bangladesh can result in inconsistencies in practice and further restrict access. The establishment of robust regulatory frameworks is necessary to ensure equitable access to TPE.[8]
5. Cultural Factors: Cultural beliefs and stigma surrounding blood products can also impact patient willingness to undergo TPE. Efforts to address these concerns through community engagement and education can improve acceptance.[11]

Current Applications and Future Directions

The clinical applications of TPE continue to expand as new indications are explored. Emerging research highlights the role of TPE in managing severe COVID-19 cases, where it may aid in reducing inflammatory responses and improving oxygenation.[8] As our understanding of the underlying mechanisms of autoimmune diseases evolves, TPE may find utility in previously unrecognized contexts.

Future directions in TPE research may include optimizing protocols for specific patient populations, investigating combination therapies and exploring the impact of TPE on long-term disease management outcomes. Moreover, efforts to enhance accessibility, particularly in low-resource settings, will be crucial in maximizing the potential benefits of this valuable therapeutic modality.[6]

Discussion

The findings from this narrative review reinforce the clinical relevance of Therapeutic Plasma Exchange in treating a wide spectrum of disorders, particularly those characterized by circulating pathogenic plasma components. The reviewed literature consistently demonstrates TPE's ability to offer rapid symptom relief, prevent long-term complications and improve the overall prognosis in conditions like GBS, TTP and myasthenia gravis.[1-3] These therapeutic effects are largely attributed to the procedure's fundamental mechanism – removal of autoantibodies, immune complexes and inflammatory mediators from the patient's plasma.

This review was designed as a narrative synthesis of the current literature on Therapeutic Plasma Exchange. An extensive literature search was conducted using electronic databases including PubMed, Google Scholar, Scopus, and Web of Science to identify relevant articles published between 2000 and 2024. The search strategy included terms such as "Therapeutic Plasma Exchange", "TPE", "apheresis", "plasmapheresis", "low-resource settings", "clinical efficacy" and "access barriers".

Studies included in the review were selected based on their relevance to the clinical utility, mechanism of action, practical applications, socioeconomic implications and accessibility of TPE. Priority was given to systematic reviews, clinical trials, cohort studies and significant case series. Reference lists of selected articles were also screened to identify additional studies.Reports and experience-based insights from Bangladesh and other low and middle-income countries were included to highlight regional perspectives and challenges. Articles not published in English or lacking access to full text were excluded. Due to the narrative nature of this review, formal quality appraisal tools were not applied.

The application of Therapeutic Plasma Exchange (TPE) across

Table I: Summary of Conditions Treated with TPE and Clinical Outcomes

Condition	Mechanism of Benefit	Clinical Outcome	Reference
Guillain - Barré Syndrome (GBS)	Removal of circulating autoantibodies	Rapid motor function recovery	2
Thrombotic Thrombocytopenic Purpura (TTP)	Clearance of vWF multimers and ADAMTS13 inhibitors	Platelet count normalization, symptom relief	3
Myasthenia Gravis	Reduction of acetylcholine receptor antibodies	Fewer exacerbations, improved muscle strength	1
Systemic Lupus Erythematosus (SLE)	Immune complex and cytokine clearance	Decreased flare frequency, stabilization	13
Severe COVID - 19	Modulation of cytokine storm	Reduced inflammation, improved oxygenation	8

a variety of clinical settings has demonstrated notable efficacy in patient outcomes, particularly in managing autoimmune and hematological disorders. The findings from the reviewed studies are summarized below:

• **Symptom Alleviation and Functional Improvement:** TPE effectively reduces the levels of circulating pathogenic substances such as autoantibodies, cytokines and immune complexes, leading to rapid symptom relief and functional recovery in conditions like GBS, TTP and myasthenia gravis.

• **Reduced Hospitalization Duration:** Studies have shown that early TPE intervention can shorten hospital stays and expedite recovery, especially in acute phases of neurological diseases.

• **Quality of Life Enhancement:** Repeated TPE sessions in chronic cases such as myasthenia gravis and autoimmune diseases contribute to better long-term disease management and improved quality of life.

• **Access Barriers in Low-Resource Settings:** The high cost of disposables, inadequate trained personnel and lack of infrastructure hinder widespread adoption of TPE in countries like Bangladesh.

• **Expanding Indications:** Beyond traditional indications, emerging evidence supports the use of TPE in managing cytokine storm in COVID-19, autoimmune hepatitis and selected dermatological conditions.

One of the most significant aspects underscored by this review is the disparity in TPE access between high-income and low-resource countries. Although international guidelines and numerous studies support the inclusion of TPE in treatment algorithms for various diseases, its practical implementation remains a challenge in countries like Bangladesh. High procedural costs, limited availability of trained personnel and inadequate infrastructure are consistent barriers across low-income settings.[4-7]

Moreover, there is a noticeable lack of policy integration and government-supported apheresis programs in many developing countries. The inclusion of TPE in national health schemes or insurance policies could potentially improve patient access and affordability. Cultural hesitations regarding blood manipulation and lack of awareness among physicians about the indications and benefits of TPE further contribute to its underutilization.[6-8] Community-level education, structured training programs for medical personnel and institutional investment in apheresis infrastructure are essential to overcoming these gaps.

The expansion of TPE into emerging areas such as cytokine modulation in severe COVID-19 cases reflects its evolving clinical potential. Studies conducted during the pandemic illustrated the ability of TPE to rapidly lower inflammatory markers and improve respiratory parameters.[8,19] This application highlights TPE's adaptability as an adjunctive treatment option in critical care, which may pave the way for its use in other inflammatory or immunological crises.

Although complications such as hypocalcemia, allergic reactions and catheter-related infections remain a concern, these are generally manageable with proper protocols and monitoring.[5] Risk-benefit evaluation suggests that with skilled operation and appropriate patient selection, the benefits of TPE substantially outweigh its risks.

This review reaffirms that TPE is a clinically effective and versatile treatment modality. Its adoption and sustainability in low-resource settings, however, require focused policy reforms, economic support and increased medical education.

Conclusion

Therapeutic Plasma Exchange has established itself as an indispensable therapeutic tool for the management of a range of autoimmune, hematologic and neurological conditions. Its mechanism of action – by removing pathological components from the plasma addresses the root cause in many immune-mediated diseases, resulting in rapid and meaningful clinical improvements.

This review consolidates existing evidence demonstrating that TPE is not only effective in symptom control but also improves patient outcome such as functional recovery, reduction in hospital stay and enhancement of quality of life. Its versatility has also allowed it to be applied in novel scenarios, such as in patients with severe COVID-19 and autoimmune liver conditions, thereby reinforcing its therapeutic promise.

However, this potential is far from fully realized in low and middle-income countries, where infrastructure deficits, economic constraints, and policy shortfalls significantly hamper TPE implementation. Bangladesh, as a representative example, illustrates the challenges associated with limited apheresis resources, lack of institutional capacity and poor health financing models. Addressing these issues requires a multipronged strategy involving: inclusion of TPE in public health programs, development of local guidelines and registries, cost-sharing or subsidy models and strategic partnerships between government, academic and private institutions.

Furthermore, research and data collection must continue to evolve for better defining of the indications, long-term outcomes and safety profiles of TPE. Regional case studies and multicenter trials in underrepresented populations can provide critical insights that inform evidence-based practices suited for low-resource environments.

In closing, TPE represents a cornerstone of modern extracorporeal therapy with expanding clinical frontiers. Its integration into global health frameworks should be prioritized not only to improve disease outcomes but also to ensure health equity through accessible and affordable care.

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