REVIEW

Indonesian Journal of Blood and Transfusion (*IDJBT*) 2025, Volume 3, Number 1 : 1-8
P-ISSN 3032-7520

Therapeutic apheresis: a literature review

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Published by
The Indonesian Society Blood Transfusion Physician

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Received: 2024-12-20
Accepted: 2025-02-23
Published: 2025-03-27

ABSTRACT

Introduction: Therapeutic apheresis is an extracorporeal procedure designed to remove pathogenic components from the blood and reinfuse the remaining elements to the patient. Despite established guidelines such as those from the American Society for Apheresis (ASFA), comprehensive reviews integrating clinical efficacy, safety, and evolving technologies remain limited. This literature review aims to synthesize current evidence of therapeutic apheresis across diverse medical conditions to support optimized patient management and guide future research.

Methods: A narrative literature review was conducted for relevant studies published within the last ten years. Keywords included "therapeutic apheresis," "plasma exchange," and disease-specific terms. Inclusion criteria covered original research, clinical trials, meta-analyses, systematic reviews, and professional guidelines related to therapeutic apheresis. Data were extracted and thematically analyzed to assess indications, techniques, outcomes, and complications.

Results: The history and advancement of apheresis technologies were summarized, emphasizing centrifugation and membrane filtration methods. Indications for therapeutic apheresis span hematologic, autoimmune, and neurological disorders, with ASFA categories guiding clinical decision-making. The procedure is generally safe, though risks such as citrate toxicity, hypovolemia, and allergic reactions exist, particularly in vulnerable populations. Monitoring through laboratory testing is critical for safety and efficacy. Despite some complications, mortality is rare and primarily associated with plasma use in specific conditions.

Conclusions: Therapeutic apheresis is a valuable treatment modality with broad clinical applications. Careful patient selection, guided by evidence-based indication categories and vigilant monitoring, optimizes outcomes and minimizes risks.

Keywords: ASFA guidelines, plasma exchange, therapeutic apheresis.
Cite This Article: Muhiddin, R.A., Muchtar, F., Arif, M. 2025. Therapeutic apheresis: a literature review. *Indonesian Journal of Blood and Transfusion* 3(1): 1-8

INTRODUCTION

Therapeutic apheresis is an extracorporeal medical procedure designed to remove pathogenic substances from the bloodstream by separating and selectively extracting specific components, followed by the reinfusion of the remaining blood constituents into the patient's circulation. This technique has been increasingly utilized as both a primary and adjunctive therapy in a wide range of clinical conditions, including autoimmune diseases, renal and hepatic disorders, gastrointestinal pathologies, and hematological abnormalities.[1]

The rationale for therapeutic apheresis lies in its ability to target and eliminate disease-mediating factors, such as autoantibodies, immune complexes, toxins, or abnormal plasma proteins, thereby modulating the course of the disease and improving clinical outcomes. The effectiveness of apheresis therapy is closely linked to the concentration and kinetics of the pathogenic agents, as well as the ability to monitor these parameters throughout the therapeutic course.[2]

Technological advancements in apheresis equipment have significantly contributed to the precision and efficacy of this modality. Two critical determinants of apheresis success are the technical specifications of the apheresis device and the physicochemical properties of the target molecule, such as size, charge, and affinity to the separation medium.[3] Furthermore, the therapeutic utility of apheresis varies depending on the specific disease entity and its pathophysiological basis.

In clinical practice, the indication for therapeutic apheresis is guided by consensus-based categorization systems. For instance, the American Society for Apheresis (ASFA) employs a four-tiered classification system (Categories I–IV) that correlates the strength of indication with clinical efficacy and evidence-based outcomes. Diagnoses are considered within their pathological context (e.g., myasthenia gravis, liver transplantation), while indications delineate the intended therapeutic aim (e.g., acute symptom relief). This classification assists clinicians in making informed decisions regarding patient selection and procedural appropriateness.[2,4]

Despite the widespread use of therapeutic apheresis and the existence of guidelines such as those provided by the ASFA, there remains a paucity of comprehensive reviews that critically compare its clinical efficacy across different disease categories and procedural indications. Most existing literature focuses narrowly on specific

conditions or technical aspects without integrating broader perspectives on outcome determinants, patient selection criteria, and the evolving role of apheresis technologies. Furthermore, inconsistencies in the interpretation and application of ASFA categories in clinical decision-making highlight the need for a consolidated framework that aligns guideline recommendations with real-world practice. Given the expanding clinical applications and technological advancements in therapeutic apheresis, this literature review aims to synthesize current evidence regarding its efficacy, safety, and indication across diverse medical conditions.

METHODS

This narrative literature review was conducted to synthesize current knowledge on therapeutic apheresis across a broad spectrum of clinical indications. Relevant studies were identified through systematic searches of major electronic databases, including PubMed, Science Direct, Proquest, Scopus, and Web of Science. The search strategy included combinations of keywords such as "therapeutic apheresis," "plasma exchange," "immunoadsorption," "ASFA guidelines," and disease-specific terms (e.g., "autoimmune," "renal," "hepatic," "hematologic," and "neurologic disorders"). Articles published in Bahasa and English in the last ten years were considered eligible to ensure a decade-wide scope reflecting the most recent evidence and guideline updates.

Eligible studies included original research articles, clinical trials, systematic reviews, meta-analyses, and professional guideline statements addressing the clinical indications, mechanisms, efficacy, safety, and procedural techniques of therapeutic apheresis. Exclusion criteria were non-English publications, case reports, conference abstracts without full texts, and studies lacking direct relevance to therapeutic apheresis.

Each selected article was assessed for methodological quality and relevance based on clarity of objectives, rigor of study design, and consistency with established apheresis practices. Extracted data were thematically analyzed to identify key findings regarding clinical indications, treatment outcomes, device technology, target molecule characteristics, and guideline applicability. The synthesis focused on highlighting current clinical trends, procedural challenges, and areas warranting further research.

RESULTS AND DISCUSSION

History of apheresis

The Greek term *"aphairesis,"* which means "to separate," "to take away by force," or "to remove," is the root of the English word "apheresis." Abel, Rowntree, and Turner used this phrase to refer to manual plasma exchange, which involves removing units of whole blood that have been anticoagulated with heparin and then centrifuging the blood to separate the plasma and cellular components. After that, the cellular components were combined with a substitute for the wasted plasma and reinfused. Since then, the phrase has been used more widely to refer to a number of processes, all of which entail separating whole blood into its constituent parts and removing or altering one or more of them.[5]

Early advancements in apheresis started in the early 1950s when Harvard scientist Dr. Edwin J. Cohn in Boston developed a large-scale technique to extract albumin from pooled human plasma. This technique was based on a basic milk centrifuge and was called the Cohn centrifuge. The use of pooled dead plasma, which entailed the risk of spreading induced hepatitis, was replaced by this process and pasteurized as a safer medicinal treatment for resuscitating injured troops.[6] The first documented therapeutic plasmapheresis technique was carried out in the 1960s by A. Solomon and J.L. Fahey, who separated whole blood into plasma and red blood cells using centrifuge technology.[5–7]

George Judson, a research engineer at IBM Corporation, and Emil J. Freireich, a physician at the National Cancer Institute, worked together to create the first continuous-flow apheresis system in 1965. Plasmapheresis, a technique for collecting donor plasma for fractionation, was established in the same decade. By the 1970s, one cellular component was being extracted via apheresis while the remaining blood was being returned to the donor. The membrane plasma separator, a therapeutic plasma exchange technique, was introduced in 1978. Numerous businesses have created apheresis technologies based on the same ideas since the creation of these early pioneering techniques.[7]

Today's apheresis method still involves separating a tiny volume of whole blood from a patient or donor into its constituent parts, despite the fact that the technology is far more sophisticated than it was in its early years of development. After being gathered and stored, one or more of the components are reassembled and given back to the person. Apheresis can be done on a patient to extract specific blood components for medical use (therapeutic apheresis) or on a donor to extract particular blood components (donor apheresis). Plasmapheresis is the term for the removal of plasma. Apheresis technology can also be used to extract (or collect) platelets (platelet apheresis), red blood cells (erythrocyte apheresis), or white blood cells (leukocyte apheresis).[7]

Method of apheresis

The type of pathogen to be eliminated or disposed of determines the apheresis technique that is employed. Filtration and centrifugation techniques can be used in pathogen disposal operations. Separating pathogenic materials by centrifugation according to their molecular weight and type, whether they are dissolved materials or pathogenic materials in the form of pathogen cells, is a frequently employed centrifugation approach. The pathogenic material's characteristics and its capacity to pass through the device's filter determine whether the filtering method is used.[8–10]

Centrifugation methods can be divided into two basic categories, including continuous flow centrifugation and intermittent flow centrifugation. Because continuous flow centrifugation (CFC) involves collecting, centrifuging, and returning blood all at once, it used to need two venipunctures. However, as constant flow centrifugation technology advanced, it is now possible to utilize just one venipuncture. Patients prefer continuous flow centrifugation with a single venipuncture because it offers greater flexibility. The centrifugation

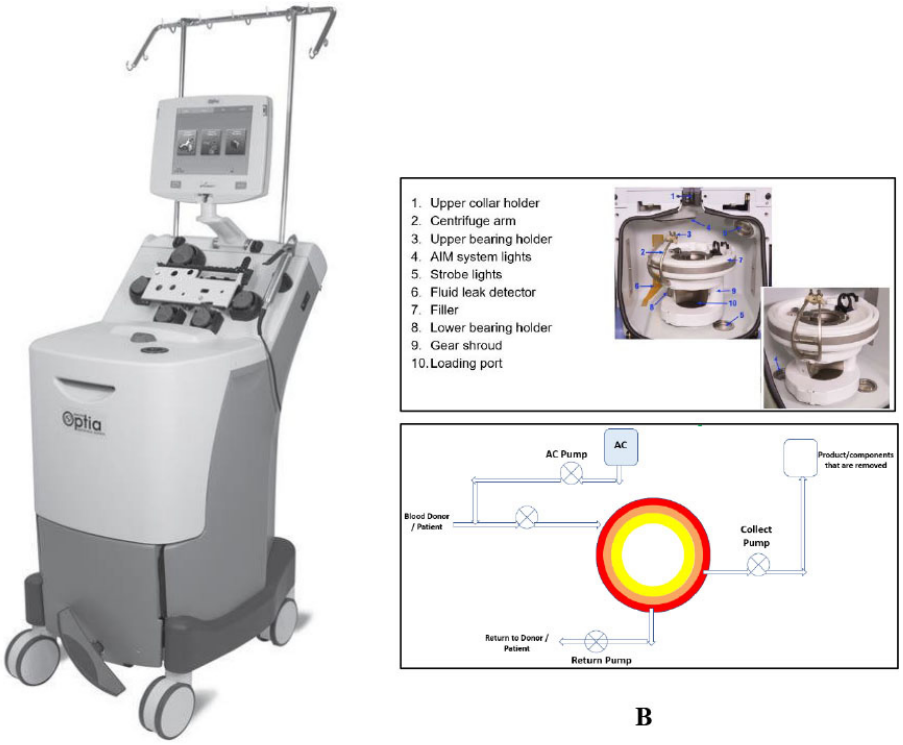

Figure 1. CFC methods. (A) CFC Method from The Spectra Optia, (B) Details of the elements in the Spectra Opticia centrifuge, the working principle of the CFC Spectra Opticia tool.[7,15]

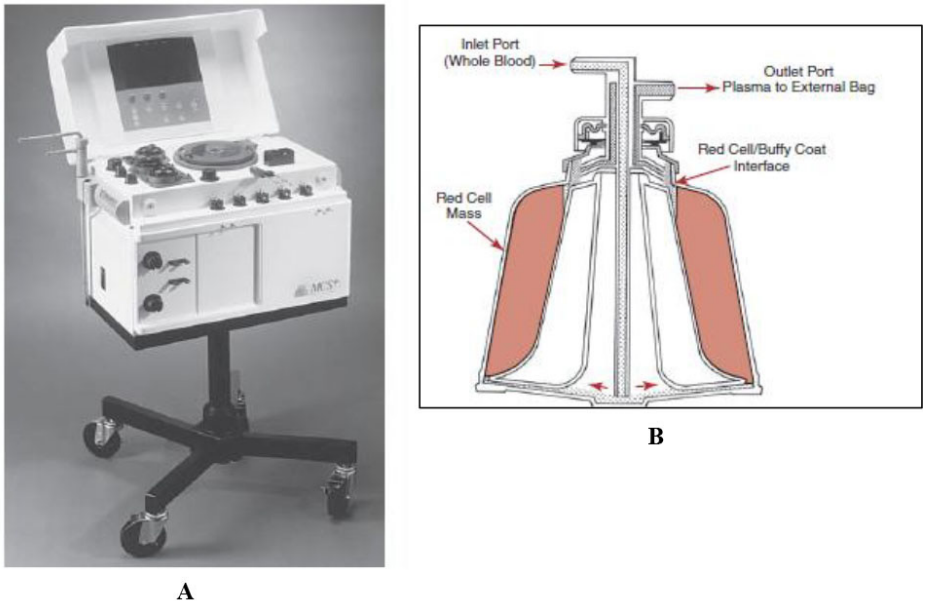

Figure 2. IFC methods. (A) The Haemonetics MCS Plus LN9000, (B) Cross-section of Haemonetics Centrifuge Bowl (IFC procedure).[7]

technique involves an instruction for the action on the monitor, which is either the cytoreduction or the plasmapheresis operation. The apparatus will function in accordance with the process that is chosen; it will automatically draw blood by vena puncture and transfer it into a centrifuge-equipped apparatus, after which the components will be separated immediately. After that, the parts that need to be taken out or thrown away are poured into a collecting container, and the remaining parts are venipuncture back into the patient's body. Until the therapeutic volume entered on the device monitor is achieved, this process keeps going. This system's primary benefit is its low extracorporeal volume, which may be beneficial for both youth and older people. This volume is determined by the apheresis chamber volume, donor hematocrit, and total donor blood volume (Figure 1).[7,11–14]

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Similar to the CFC technique, intermittent flow centrifugation (IFC) uses a monitor screen to choose apheresis treatment operations, such as cito reduction or plasmapheresis. A gadget with a bowl and centrifuge is filled with blood. To separate the components of the blood, the centrifuge will revolve the bowl at a specific speed. The components or cells that need to be decreased are then transferred into a collecting bag, and the patient's blood is then returned. One venipuncture site is the primary benefit. Apheresis therapy is only used on stable patients because it requires a larger extracorporeal volume and takes a lot longer to complete through IFC. When blood is pumped into the apheresis machine from the body, anticoagulants are immediately combined with it (Figure 2).[13,14]

Four factors in the centrifugation process can be adjusted to extract the components that need to be removed. The first is the bowl diameter and rotation speed; the second is the centrifuge duration; the third is the solute supplied; and the fourth is challenging to control: the donor cell content and plasma volume. Usually, the end product is a sedimented blood sample with plasma at the top, white blood cells (lymphocytes, granulocytes, and monocytes), and a brownish layer of platelets and red blood cells at the

bottom.[14]

The IFC devices are appropriate for use in mobile donor collections since they are usually more compact and portable. While two venipunctures are often needed for a CFC operation, one venipuncture can be utilized for an IFC procedure. Nonetheless, new protocols (Amicus and Spectra) have been created that enable specific CFC machines to function with a single needle. The extracorporeal blood volume, or the volume of blood extracted from the donor in the centrifuge cup/chamber and tube, should never be more than 10.5 milliliters per kilogram of body weight throughout the process, following AABB guidelines. Generally speaking, IFC machines have a larger extracorporeal volume than CFC devices. For those with tiny blood volumes, such as youngsters and the elderly, this might be a crucial factor to take into account because the extra volume taken during the treatment could make the patient hypovolemic.[8]

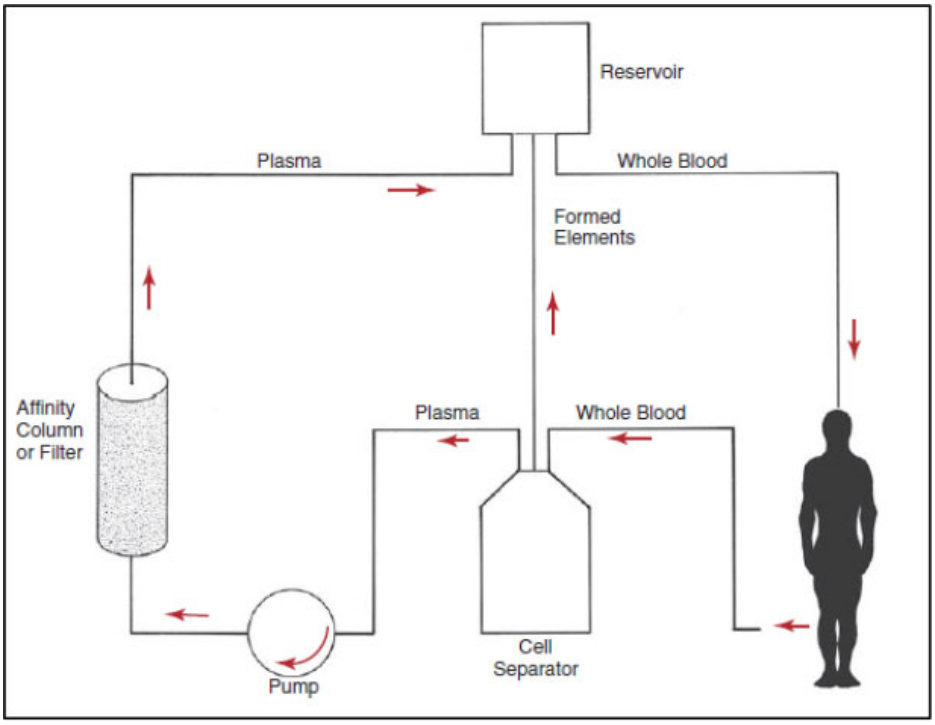

Figure 3. Perfusion of plasma over columns or filters.[7]

Membrane filtration method

Using a filter or membrane—a group of hollow fibers or flat plate membranes with specific pore sizes—the filtering procedure separates the components of blood. Certain qualities allow components to get past the filter. The process to be followed is entered on the tool monitor, the same as in tools that use the CFC and IFC approaches. While the remaining cellular components are returned to the donor, plasma travels through the pores in the fiber or membrane when whole blood runs over it. Because the holes may be sized to block the passage of even tiny cellular components, this technique is very adaptable for plasma collection. The collection of cell-free products and the capacity to extract specific plasma proteins by altering the pore size are two benefits of filtration over centrifugation. The Fenwal Autopheresis-C device uses tiny spinning cylindrical filters to combine membrane filtration and centrifugation technologies. This method is exclusively utilized for plasma collection, much like other filtering technologies (Figure 3).[8]

Procedural therapeutic apheresis

The decrease of abnormal cells using the apheresis process is known as cytoreduction. In cases of essential thrombocytosis, hyperleukocytosis, or leukostasis, cytoreduction is carried out. Leukostasis brought on by hyperleukocytosis is linked to a worse

Table 1. ASFA guidelines for hyperleukocytosis[16]

Indication	Condition	Recommendation	Category
Hyperleukocytosis secondary to leukemia	Leukostasis	Grade 1B	I
AML, WBC >100 x 10^9/L; ALL, WBC >400 x 10^9/L	Prophylaxis	Grade 2C	III

Table 2. IPSET score-ET thrombosis[16]

Variables	Risk Categories	Therapy
Age ≤ 60 years, Prior Thrombosis JAK2V617F Mutation	Very Low (age ≤ 60 years, Thrombosis JAK2 wild type, no Prior Thrombosis)	Management of CV Risk Factors, observation, or low-dose aspirin, unless contraindicated
	Low (age ≤ 60 old years, Thrombosis JAK2 V617F positive, no Prior Thrombosis)	Management of CV Risk Factors, low dose aspirin, unless contraindicated, Higher dose aspirin may be used if CV Risk Factors present.
	Intermediate (age > 60 years, Thrombosis JAK2 wild type, no Prior Thrombosis)	Management of CV Risk Factors and cytoreduction therapy and low dose aspirin unless contraindicated, Higher dose aspirin without cytoreduction therapy if no CV risk factors
	High (age > 60 old years, Thrombosis JAK2 V617F positive, or Prior Thrombosis)	Management of CV Risk Factors and cytoreduction therapy plus low-dose aspirin

Table 3. Indication categories for therapeutic apheresis[7]

Disease	Procedure	Indication Category
Hematologic Diseases		
Liver	Plasma exchange	III
Erythrocytosis/polycythemia vera	Erythrocytapheresis	III
Leukocytosis and thrombocytosis, symptomatic	Cytapheresis	I, II
Thrombotic thrombocytopenic purpura	Plasma exchange	I
Post-transfusion purpura	Plasma exchange	III
Sickle cell disease	RBC exchange	I – II
Hyperviscosity associated with monoclonal gammopathy	Plasma exchange	I
Coagulation factor inhibitors	Plasma exchange	IV
	Immunoadsorption	III
Aplastic anemia	Plasma exchange	III
Cutaneous T-cell lymphoma	Photopheresis	I
Red blood cell alloimmunization in pregnancy (if intrauterine transfusion is not available)	Plasma exchange	II
	not available)	not available)
Malaria or babesiosis	RBC exchange	I, II
Erythropoietic porphyria	Plasma exchange	III
HELLP syndrome	Plasma exchange	III
HLA desensitization for HSC transplantation	Plasma exchange	III
Sickle cell disease	RBC exchange	I–II
Neurological Disorders		
Acute inflammatory demyelinating polyneuropathy (Guillain-Barré syndrome)	Plasma exchange	I
Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)	Plasma exchange	I
Lambert-Eaton myasthenic syndrome	Plasma exchange	II
Multiple sclerosis		
Acute CNS inflammatory disease	Plasma exchange	II
Chronic progressive	Plasma exchange	III
Myasthenia gravis	Plasma exchange	I
Paraneoplastic neurological syndromes	Plasma exchange	III
Immunoadsorption III	Immunoadsorption	III
Paraproteinemic polyneuropathy		
Due to IgG, IgA, or IgM	Plasma exchange	I
Due to multiple myeloma	Plasma exchange	III
Rasmussen's encephalitis	Plasma exchange	II
N-methyl-D-aspartate receptor antibody encephalitis	Plasma exchange	I
Progressive multifocal leukoencephalopathy associated with natalizumab	Plasma exchange	I
Hashimoto's encephalopathy	Plasma exchange	II
PANDAS*	Plasma exchange	I

PANDAS = Pedatric Autoimmune Neuropsychiatric Disorders with *Streptococcus*

chance of survival in some acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL) subtypes. As a prophylactic measure to avoid leukostasis or alleviate its clinical manifestations, leukocyte apheresis is frequently employed.[7,15]

Five to twenty percent of individuals with acute leukemia will experience hyperleukocytosis, which is characterized by a WBC count of more than 100×10^9/L. Leukostasis, tumor lysis syndrome, and disseminated intravascular coagulation (DIC) can all result from hyperleukocytosis. Compared to erythrocytes, leukocytes are less malleable, and viscosity rises logarithmically as fractional white blood cell volume increases. Leukemic blasts have a greater rate of oxygen consumption, which can result in cellular hypoxia. Vascular blockage from blast accumulation can induce ischemic tissue damage, which can cause cerebral hemorrhage and respiratory failure. In the neurological system, leukostasis manifests as altered mental status, delirium, confusion, headache, dizziness, and tinnitus; in the lungs, it manifests as tachypnea, dyspnea, and hypoxia. Leukostasis has also been linked to vascular problems, including retinal hemorrhage/thrombosis, cardiac ischemia/infarction, and priapism.[15]

Acute leukemia patients with hyperleukocytosis and leukostasis symptoms have a dismal prognosis; respiratory failure and cerebral bleeding are the leading causes of death. It seems to be especially true in AML, where individuals with WBC counts as low as 50 × 109/L may have leukostasis symptoms.

Perhaps as a result of the cells' malignant character, chronic myelogenous leukemia (CML) and chronic lymphocytic leukemia (CLL) have lower incidences of leukostasis. In CML, ALL, and CLL, symptoms often do not appear until the WBC count is more than 300 × 109/L. The increased occurrence in AML may be explained by leukostasis, which is observed at lower WBC numbers in AML compared to CML and ALL.[15]

Leukocyte apheresis is a cytoreduction technique that eliminates pathogenic leukocytes. The leukocytes are gathered in a container and subsequently destroyed, while the patient receives other blood components such as plasma, platelets, and erythrocytes. Although leukocyte apheresis is primarily used to treat AML, it has also been used to treat leukostasis and hyperleukocytosis linked to ALL, CML, and CLL. Acute promyelocytic leukemia with chromosomal translocation between 15 and 17 is contraindicated because it is associated with a higher risk of fatal or near-fatal outcomes, particularly hemorrhage. Because acute promyelocytic leukemia is linked to thrombocytopenia and DIC, bleeding problems are common in these individuals. Therefore, it is imperative that laboratory and clinical testing be done prior to apheresis (Table 1).[6,15]

CFC or IFC separation can be used for leukocyte apheresis, and the majority of treatments are carried out with a continuous flow device like the Cobe Spectra. The patient's symptoms and the first white blood cell count determine the target leukocyte apheresis. 1.5–2 liters of blood are typically processed.[15]

The bone marrow exhibits proliferation primarily of the megakaryocyte lineage with an increase in the number of enlarged and mature cells that meet the WHO criteria for BCR-ABL1+ CML, PV, PMF, myelodysplastic syndrome, or other myeloid neoplasms. Essential thrombocythemia (ET), one of the myeloproliferative neoplasms (MPN), is characterized by a persistent platelet count ≥450 × 10^9/L.[16]

Relieving symptoms and reducing illness consequences (such as bleeding and thrombotic events) are the objectives of ET therapy. Cytoreductive treatment, either chemically or by thrombocyte apheresis, should be used to reduce the platelet count in patients with severe thrombocytosis and bleeding. Although survival is impacted by the illness parameters used for risk categorization, the majority of ET patients have a normal life expectancy. The risk score determined for each patient using the IPSET-thrombosis model—which takes into account the patient's age, history of thrombosis, the existence of the JAK2 V617F mutation, and cardiovascular risk factors—determines whether or not treatment should be started, as well as the kind of medication. High-risk TE are advised to undergo cytoreduction based on their IPSET-thrombosis score (Table 2).[16]

Therapeutic plasma exchange

The process known as Therapeutic Plasma Exchange (TPE) involves taking a significant amount of a patient's plasma and replacing it with plasma that contains pathogenic materials such as cytokines, immune complexes, and pathological antibodies. A replacement fluid with the same volume and material content as the one that was withdrawn is used to replace the lost volume. TPE can be used to treat a wide range of illnesses that different medical practitioners handle. Table 3 lists the conditions that the ASFA has suggested be treated with TPE.[6,7]

Mechanism of plasma removal

Filtration and centrifugation are two techniques that can be used to exchange therapeutic plasma. Centrifugation is the primary technique for TPE. The replacement fluid is crucial in TPE. Because it replaces crucial chemicals lost during the TPE technique, replacement fluid is administered during the operation and is necessary to accomplish TPE.[2,5–7]

The following exponential equation can be used to describe the elimination of chemicals in plasma that are limited to the intravascular space: Y/Y0 _ e_x, where X is the number of times the patient's plasma volume is exchanged, Y is the substance's ultimate concentration, and Y0 is its beginning concentration. About 60% to 70% of the material that was initially present in the plasma will be eliminated for every 1-1.5 plasma volume that is exchanged. Although 60%–70% removal still takes place, the absolute amount eliminated decreases with the exchange of greater plasma volumes. Because of this, it is standard procedure to exchange just 1-1.5 plasma volumes during TPE.[5]

In addition to lengthening the operation and exposing the patient to additional replacement fluids and anticoagulants, treatment with quantities more than 1.5 plasma volumes eliminates the smaller, less clinically significant pathogenic chemicals present in the plasma. The outcome is a higher chance of problems without a greater advantage for the patient. Above 1.5 plasma volumes, therapy has declining results.[5,7]

Normal saline containing 4%–5% human albumin is the most often utilized replacement fluid. The benefit of this solution is that it prevents transfusion responses (such as transfusion-related acute lung damage) and disease transfer, which may happen with plasma. The primary drawback of albumin is that it is more expensive than plasma. This replacement fluid can increase the intravascular volume since it is a little more oncotic than plasma. The prevention of hypovolemia may benefit from this impact. Some practitioners will utilize lesser amounts of albumin, such as 70% albumin and 30% saline, because albumin replacement fluid is the most costly part of the TPE treatment, and using 100% albumin as a replacement does increase the intravascular volume.[5]

In order to prevent hypovolemia brought on by crystalloid redistribution, albumin, and saline are administered alternately during this operation, with the bulk of albumin being administered toward the conclusion. It should be mentioned that using albumin and saline together has been linked to a greater incidence of hypovolemic responses than using albumin alone. In a limited number of conditions, plasma is used as a replacement fluid. For instance, it can be used to treat coagulation factor deficits, avoid dilutional coagulopathy in patients who are bleeding, and replace ADAMTS13 in the treatment of thrombotic thrombocytopenic purpura.[5]

All apheresis methods require venous access. Although peripheral access may

be used, it is advised to place a dialysis-compatible central venous catheter (CVC) for a number of reasons, including the possibility that patients with acute leukemia may be unstable, that multiple procedures may be necessary, and that insufficient access may compromise the effectiveness of the apheresis procedure. CVCs are inserted by interventional radiology or at the patient's bedside (after surgery or in the critical care unit).[15]

Laboratory examination in therapeutic apheresis

Laboratory testing is strongly advised before, during, and after apheresis therapy to ensure patient safety and treatment efficacy. Key recommended assessments include complete blood count, serum calcium and albumin levels, total immunoglobulin G, electrolytes, hemostasis parameters such as prothrombin time (PT) and activated partial thromboplastin time (APTT), fibrinogen levels, excreted cytokines, and inflammatory markers.[5,7]

Before beginning the procedure, at the halfway point, to evaluate the reduction of the white blood cell count and to track hemoglobin, and after leukocyte apheresis is finished, a complete blood count (CBC) should be carried out. If clinically appropriate, further leukocyte apheresis treatments might be carried out to alleviate leukostasis symptoms.[15] As a control measure for the use of TA, several laboratory tests are advised prior to the action. The foundation for carrying out such measures is the monitoring of laboratory tests conducted during each TPE session. Before doing further TPE in situations where the examination findings fall outside of the usual range, rectification is advised.[5]

Anything circulating in the plasma is eliminated during TPE, which involves the removal of plasma in bulk. The nonselective process eliminates both diseased and normal plasma components. For instance, the activity of coagulation factors is reduced, and coagulation tests may become abnormal when plasma volume exchange is performed using albumin as a replacement fluid. The activity of factors V (FV), FVII, FVIII, FIX, FX, and VWF has significantly decreased. Within 4 hours following TPE, the activity of FVIII, FIX, and VWF returns to normal, and within 24 hours, the activity of the remaining coagulation factors reaches pre-TPE levels. Fibrinogen is an exception, reaching 66% of pre-apheresis levels in under 72 hours. Coagulation inhibitors including antithrombin and pseudocholinesterase, which are essential for the metabolism of several medications, are among the other chemicals eliminated. Every "round" or session lasts a few hours. For a total of five to ten sessions, plasma exchange is carried out every two to three days. Before, during, or after the surgery, blood tests could be conducted.[5]

Adverse effects

Although apheresis therapy is generally safe, problems may arise based on the procedure type, the patient's characteristics (e.g., young age, feminine gender, small total blood volume), and underlying medical disorders.[5,7,15] Citrate toxicity is generally found during the collection of apheresis cyto components when anticoagulant plasma is returned at a high rate. The liver typically metabolizes citrate, an anticoagulant used in apheresis, quickly. Ionized calcium levels will drop and the donor may get paresthesia, or numbness or tingling around the mouth, if the amount of citrate infused is more than what the body can metabolize. Oral calcium supplements can also be used to avoid this issue. During therapeutic apheresis operations, citrate toxicity is also somewhat prevalent. Untreated symptoms may result in heart arrhythmias and tetany. During therapeutic plasmapheresis, the patient may receive an intravenous infusion of parenteral calcium (calcium gluconate or calcium chloride) to avoid hypocalcemia symptoms. Citrate toxicity is more likely to happen when FFP is used as a replacement fluid during therapeutic plasma exchange because of the combined effects of the citrate used in the apheresis operation and the anticoagulant in FFP.[5,7,15]

Like any treatment, plasmapheresis has its uses, but some dangers and side effects should be discussed with the patient before the process. Depending on where they are placed, larger IV catheters might result in lung punctures, hemorrhage, and infection if they are kept in place for an extended period. A vagus nerve-mediated malaise is known as a vasovagal episode. When this leads to syncope or "fainting," the most frequent kind of fainting is known as vasovagal syncope. A vasovagal response is another mechanism that results in hypotension during apheresis. Hypovolemia causes the blood pressure to drop in this response. As previously mentioned, the sympathetic nervous system's output is increased in response to this volume depletion through physiological compensation. A vasovagal response, on the other hand, slows the heart rate and lowers vascular tone because the parasympathetic output, which typically opposes the sympathetic output, is enhanced. Hypotension is the effect of this. Younger age, low body weight, first-time donation, and careless collection personnel are all factors linked to vasovagal responses in whole blood donors.[5,7,15]

Adverse reactions during therapeutic apheresis include hypovolemia—more frequent with IFC devices—necessitating careful fluid balance monitoring to avoid volume imbalances. Allergic reactions commonly occur with replacement fluids like fresh frozen plasma (FFP) and, less frequently, albumin infusions. Hemolysis typically results from mechanical issues, such as tubing kinks, requiring vigilant return line observation. Rare complications include air embolism and clotting factor deficiencies. Plasma protein levels decrease by 50–60% after standard plasmapheresis, with most analytes recovering within eight days, except for ceruloplasmin, which takes longer. Mortality is rare but mainly linked to circulatory or respiratory complications, often associated with plasma use, which is reserved for specific indications like thrombotic thrombocytopenic purpura (TTP) or hemolytic uremic syndrome (HUS), acknowledging plasma's risk of disease transmission.[7]

This literature review on therapeutic apheresis presents several inherent limitations that must be acknowledged for accurate interpretation of the findings. Firstly, the review is constrained by the availability and heterogeneity of published studies, which vary widely in study design, patient populations, indications,

and apheresis modalities. This variability limits the ability to generalize conclusions across diverse clinical contexts. Secondly, many included studies are observational or retrospective in nature, lacking randomized controlled trials that would strengthen evidence quality and causal inference. Thirdly, there is potential publication bias, as studies reporting positive outcomes may be overrepresented, while negative or inconclusive results remain underreported. Furthermore, rapid technological advances in apheresis devices and protocols may render some older data less relevant to current practice. Lastly, the review relies on secondary data extraction without access to individual patient data, restricting the capacity for in-depth subgroup analyses or adjustment for confounders. These limitations underscore the need for well-designed prospective trials to establish standardized therapeutic apheresis guidelines and optimize patient outcomes.

CONCLUSION

Therapeutic apheresis effectively treats various conditions by removing pathogenic substances from the blood, with treatment guided by clinical efficacy and pathogen monitoring. Indication categories assist clinicians in appropriate patient selection. While generally safe, risks of complications increase in younger patients, females, those with low blood volume, and underlying diseases. Therefore, careful patient evaluation and monitoring are essential to optimize outcomes and minimize adverse effects, highlighting the need for ongoing research to enhance safety and efficacy.

DISCLOSURES

Funding

The authors declare there was no external funding in this study.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Author Contribution

RAM conceived the study concept and designed the literature search strategy. FM conducted the data collection, screening, and extraction of relevant articles. MA performed the critical appraisal and synthesis of findings. All authors contributed to drafting, revising, and approving the final version for publication.

Ethical Consideration

Not applicable.

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