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Plasmaphersis

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Abstract:
Plasmaphersis is a method of treating a variety of diseases of frequently uncertain etiology and poorly understood pathogenesis for which there is no adequate therapy. It is a procedure in which plasma is separated from the blood cells and is replaced with fresh frozen plasma, or a plasma substitute. The rationale for plasmaphersis is based on the fact that circulating substance such as toxins or auto antibodies accumulate in the plasma, removal of these factors can be therapeutic in certain situations .The replacement solutions use depends on the severity and type old disease, the patient's tolerability and various other factors. Saline is relatively safe for small volume exchange, or in even larger quantities.

Key words: Plasmaphersis, Plassma protein factor, Therapeutic plasma exchange, Centrifugation, Membrane filtration

INTRODUCTION:

It is a method of removing blood plasma from the body by withdrawing blood, separating it into plasma and cells, and transfusing the cells back into the blood stream. It is performed especially to remove antibodies in treating autoimmune conditions.

The underlying mechanism of this procedure is accomplished by either centrifugation or filteration using semipermeable membrane. While centrifugation based on the principles using different specific gravities of various blood components, membrane plasma separation filters blood components based on their partical size (1,2). The preferred method of plasmaphersis in most centers worlds wide is by automated centrifuge-based technology (3). The exact mechanism through which plasmaphersis exerts its therapeutic effect is unknown, although it seems likely that plasmaphersis could work by eliminating pathological substance from the plasma or decreasing their concentrations. These harmful substance can include antibodies ,immunocomplexes , monoclonal proteins , cryglobulins ,complement components ,lipoproteins ,toxins bonded to proteins. The concepts of plasma exchange was first tried therapeutically in man in the year 1959.Michael Rubinstein was the 1st person to use plasmaphersis to treat an immune related disorders when he saved the life of an adolescent boy with Thrombin Thrombocytopenic Purpura [TTP] at the old cedars of Lebanon hospital in Los Angeles(4).

Aphersis is derived from the Greek word "aphaeresis" to take away. Since antiquity mankind has hypothesized there are bad substance called "humors" which accumulate in blood of sick patients and that the removal of these humors would make patients feel better .Bloodletting the practice of draining blood from sick patients, has been around since the Egyptians ,dating back one thousand years B.C .The practices of bloodletting peaked in the 18th century and evolves with modern technology to this day .Blood has four major components : red blood cells, white blood cells, platelets, and plasma .With

modern machinery ,blood can be separated into each of these four components. Thus, if a particular blood component is causing harm, it can be selectively removed and placed with the same blood component from healthy donor (5)

The Plasma Protein Fraction [PPF] has been found to be superior to Fresh Frozen Plasma [FFP]. As added with albumin, the PPF is free of the risk of transmitting hepatitis, but because of its low content of calcium and potassium, supplementation with these ions is necessary (6) But the plasma protein fraction contains a vasoactive substance i.e., bradykinin which may cause severe adverse reaction (7). The cellular elements were then mixed with a replacement for the discarded plasma and renifused. Since this intial use, the term has been used more broadly to described several procedures ,all of which involve the separation of whole blood into its components with removal or modification of one or more of these components .(8)

Cancer is becoming the second most common cause of death in the world. Traditional treatment methods include surgery ,chemotherapy, radiotherapy and hormone therapy as well as various combination therapies.(9) Modern treatment approaches are multi model, including emerging molecular and targeted therapies(10) therapeautic Plasma Exchange [TPE] is one such way plasma replacement therapy has been in development for more than 50 years and has become a common and relatively safe treatment(11,12). TPE is a blood component aphersis technology used mainly for symptomatic treatment ; it is used to remove pathological plasma while supplementing a certain amount of normal plasma or solution to treat patients with cancer and related complications(13). TPE can eliminate macromolecules proteins and antibodies, and its precisely because of this immunological property that it is useful in the treatment of patients with malignant tumors (14). TPE therapy plays an important role in treatment of a variety of tumors, such as multiple myeloma and Waldenstrom macroglobulineia, and can also be used to eliminate paraneoplastic syndrome and excessive levels of chemotherapeutic drugs (15, 16, 17).

There are two types of process.

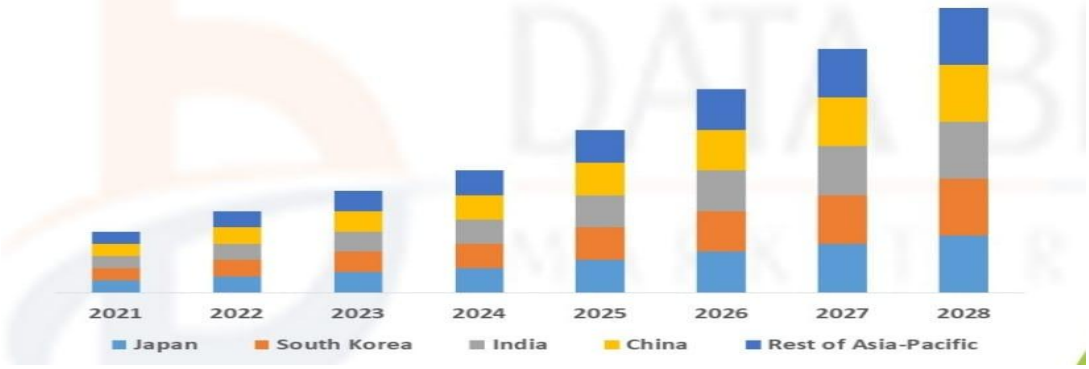
CENTRIFUGATION: This process spins the blood, which divides it according to the density of the parts.

FILTRATION: This involves passing the blood through a filter to separate plasma.

Therapeutic Plasma Exchange

It is a procedure where patients blood is passed through a aphersis machine, filtered plasma is removed by reinfusion of RBC along with plasma or albumin into the patient.

INCIDENCE



Asian –pacific Plasma Fractionation Market is expected to gain market growth in the forecast period of 2021to 2028. Data Bridge Market analyses that the market is growing with a CAGR of 7.5% in the forecast period of 2021 to2028 and is expected to reach USD 7,111.80 million by 2028.

Why undergo a plasma exchange?

Brain and nervous system conditions: such as acute Guillain Barre syndrome
Blood disorders: Such as thrombotic thrombocytopenic purpura ,a rare disorder that cause blood clots.
Some kidney conditions: Such as Good pasture syndrome, a disease that causes antibodies to attack the kidneys and lungs.
Hyper viscosity syndromes: Including myeloma. These conditions cause the blood to thicken, which can lead to organ damage or a stroke.

INDICATIONS OF PLASMAPHERSIS:

- Plasmaphersis has been used with good effect in the following disease:
- Myasthenia Gravis
- Thrombocytopenic purpura
- Guillian-Barre syndrome
- Rheumatoid Arthritis
- Insulin dependent diabetes mellitus
- Pemphigus Vulgaris
- Bullous Pemphigoid
- Systemic lupus erythematousus
- Erythema myeloma
- Psoriasis
- Multiple myeloma
- Hyper cholesterolemia
- Sever sepsis and shock
- Neuromyelitis of the eye

CONTRAINDICATIONS:

- Sever Hypersensitivity reactions
- Hypotension

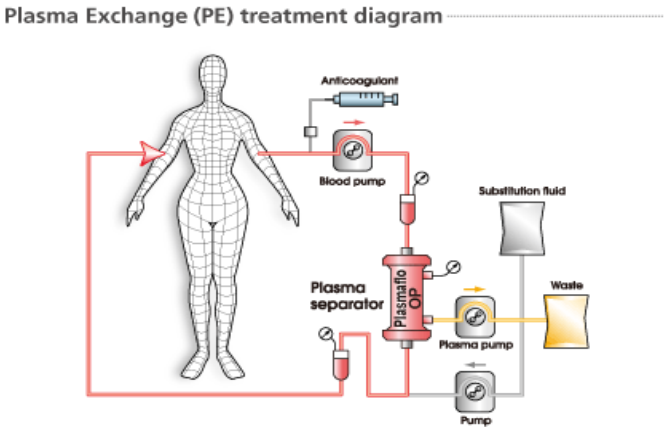
TECHNICAL CONSIDERATIONS:

1) Centrifugation technique
   a) Continuous flow technique
   b) Intermittent flow technique
2) Membrane filtration technique

CENTRIFUGATION TECHNIQUE:

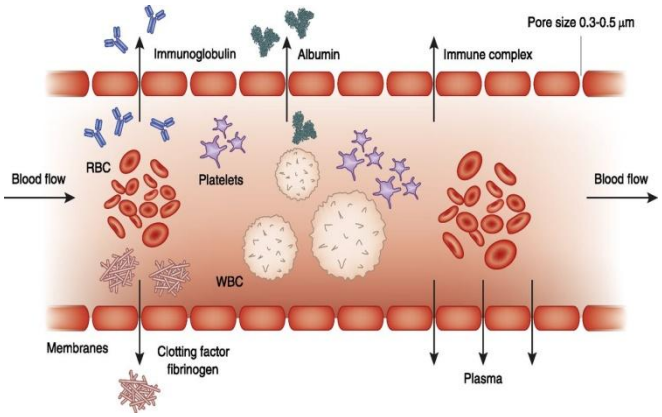
Continuous Flow Technique: In this technique , the blood withdrawal of blood is fed continuously into a rapidly rotating bowl in which red cells, leukocytes, plasma ,platelets are separated in to different layers. Any of these layers are removed and the remainder is returned to the patient with the replacement fluid. The advantage of this procedure is that it is faster and completely automated .But it requires the use of a dual lumen catheter and the equipment is immobile. It is an expensive technique .The anticoagulant used in this technique is citrate.

Intermittent technique: In this technique blood is drawn in successive batches and separated. This cycle is repeated as often as necessary to remove the desired volume of plasma (i.e.1-1.5 plasma volume).The equipment is portable unlike that in the continuous flow technique and a single needle peripheral venous puncture is sufficient .The limitation of this technique include the time taken i.e. it takes more than 4 hours for one cycle and a large extra corporeal blood volume is required (>225ml).



MEMBRANE FILTRATION TECHNIQUE:

This technique is used as an alternative to centrifugation technique.The patients blood is pumped through a parallel plate or hollow fiber filter at a continuous flow rate(50-200ml/min). the membranes have pores of 0.2-0.6um diameter which is sufficient to allow passage of plasma while retaining cells.Plasma is thus collected and separated from theblood.The average time required for membrane filtration is less than three hours.In general ,the plasma can be removed at a rate of23-50ml/min.Unlike the intermittent technique ,a large vein catheter is required .The anticoagulant used in this technique is heparin.



Membrane filtration technique

GUDIELINES:

- The Director-General has the honour to place this memorandum before the executive Board for its consideration , in accordance with the privileges accorded to non governmental organizations in official relation with WHO.
- In view of the wide range of views and intresets concerning this issue and the time constraints imposed by the programme budget review, it is doudtful that full justice could be given to this matter during the present session of the Board. Should members wish to study the issue in depth and possibly establish and ad hoc comitee to this end, the board could examine it fully at its seventy-third session in January 1984 and should it so decide , present a report to the thirty-seventh World Health Assembly.
- Donor must be advised of any known risks and hazards involved in plasma donation by an appropriately qualified professional,and must be given an opportunity to understand clearly the procedures involved. Once so advised, donor shall be free at any time to consent or decline to participate in the plasma collection programe.
- The quantities of plasma collected from individual donor must have full regard for the donors health and be in conformity with appropriate limitations or standards set by local or national(or where none exists, international) Health Authority, based on sound medical data.
- Be aware of the higher risk of transmitting disesase when blood procedure have been obtained from paid rather than from voluntary donors, and of the harmful consequences to the health of donor of too frequent blood donations(one of the causes being remuneration).
- To assist in establishing co-operation between countries to secure adequate supply of blood procedure based on voluntary donations.

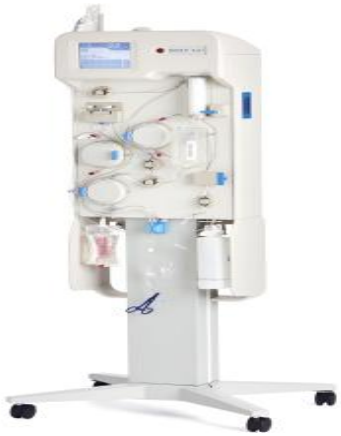
Atrribute	cTPE(spectral optia system)	mTPE system
Time to setup and *prime,minutes	11[11]	23-40[11,12]
Procedure time*,minutes	91-120[11-13]	133-160[11-13]
Time to exchange 1lit of plasma *minutes	25-3311-13	36-37[11-13]
PRE%	80-93[11,13-17]	27-53[10,11,13]
Lnlet/blood flow rate,ml/min	5-140[2,11,12,14-17] (<5 can be used for small patients)	50-100[7,11,12,15] (depending on filter type used)

TABLE: Summary of distinctions between centrifugal therapeutic plasma exchange with the spectra Optia and membrane filtration therapeutic plasma exchange system.

PLASMAPHERSIS MACHINE:

Donating, removing blood plasma, separating its components and returning some persons, while holding out others to become blood products that this persons donates for those in need. In such a plasma donation procedure, blood is removed from the body, blood cells and plasma are separated, and

the blood cells are returned, while the plasma is collected and frozen to preserve it for eventual use as fresh frozen plasma or as an ingredient in manufacture of blood products(18).



PLASMAPHERSIS MACHINE

PROCEDURE:

A needle is inserted into a vein in each arm; patients has to stabilize his arm during insertion of the needle. Blood is taken from one arm and circulated through cell separators following one of the previously mentioned technique .To replace the plasma that is removed, a plasma substitutes is given with returned blood cells. The treatment takes several hours and it can be done on outpatients basis .The number of times the treatment is needed varies greatly depending on the disease and person general conditions. An average course of plasmaphersis is six to ten treatment over two to ten weeks. Most patients begin to improve with in the first few days of the treatment. Patients who have received three to four exchanges over a week would remain healthy for one to two months.

COMPLICATIONS OF PLASMAPHERESIS:

Plasmaphersis is an extracorporeal purification technique that has many indications with different grades of evidence .It is generally well tolerated and safe. The rate of complications ranges from 5% to 12%.The most common symptoms are paresthesias , muscle cramps, hypotension and urticaria and other anaphylactoid reactions. Most complications mild (i.e., they do not require intervention) or moderate , but the plasmaphersis treatment can be completed. Severe complication (i.e., those that require plasmaphersis treatment to be dicountinued represent only 0.08% of cases (19) . Although eight deaths have been reported in the more than 15,000 plasmaphersis treatments done

(20),many of these occurred in paitents with severe disease and the plasmaphersis procedures were not in themselves the precipitating cause. In the most recent literature , no deaths related to the technique have been detected(19,21,22).

Symptoms	Percentage (%)
Urticaria	0.7-12
Paresthesia	1.5-9
Muscle Cramps	0.4-2.5
Nausea	0.1-1.1
Hypotension	0.4-4.2
Chest pain	0.03-1.3
Arrhythmias	0.1-0.7

CONCLUSION:

Plasmaphersis is a major undertaking that should be rescued for severe illness. Plasmapherasis is a valuable treatment in patients with auto-immune disorder. It can be employed to treat certain autoimmune disease. Plasmaphersis technique is mostly successful worked in nephrological related patients. Nephroloogical disorders (65%), Neurological Disorders (19%), Hematological Disorders (12%), Miscellanous (1%). The drawback of this plasmaphersis is mostly expensive procedure.

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