GUJTRANSCON 2022

Therapeutic Plasma Exchange (TPE) In various clinical scenarios

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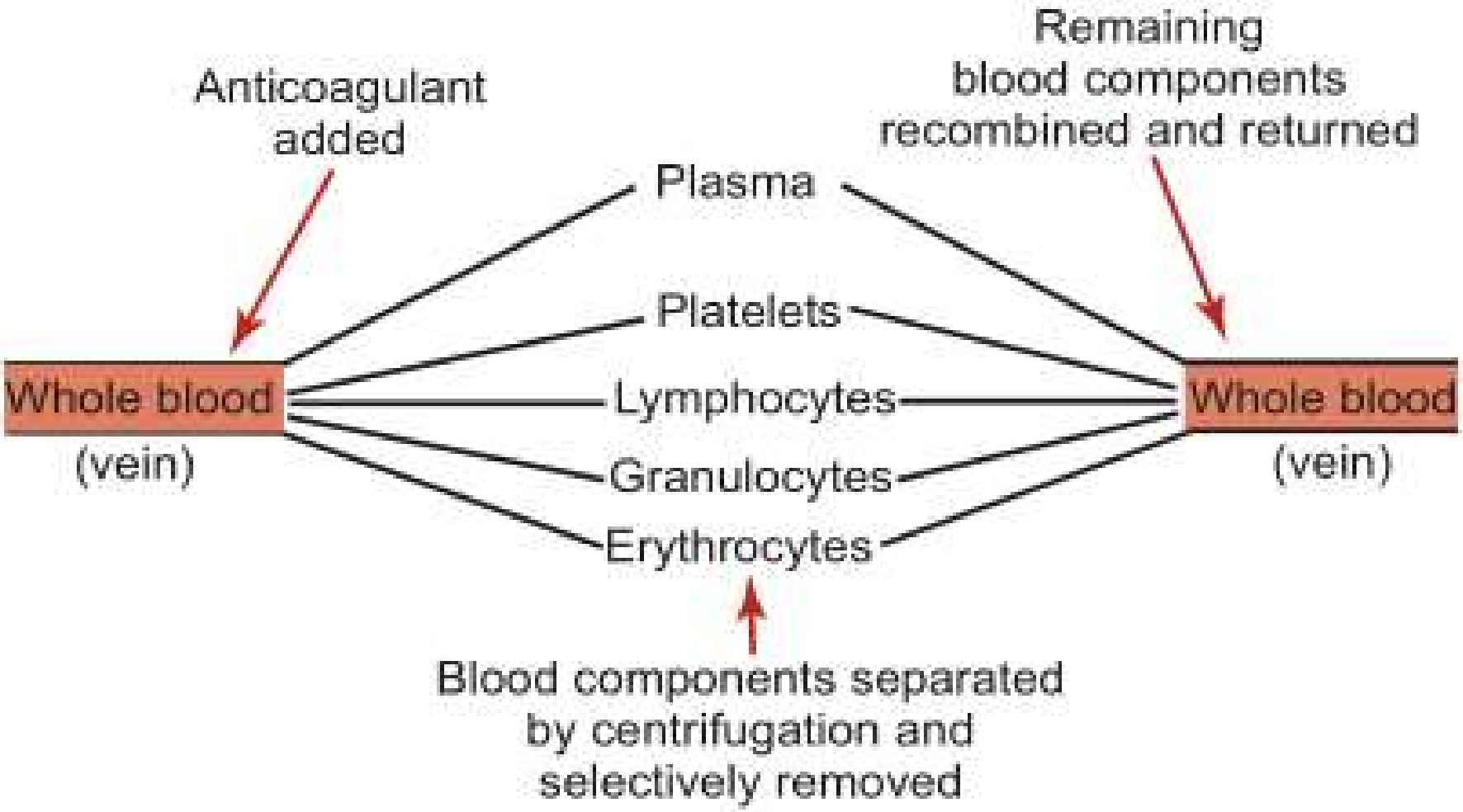
LAYOUT

- BACKGROUND AND BASICS
- MEDICAL EVALUATION
- SPECIAL POPULATION
- ASFA CATEGORIES
- INDIVIDUAL SYSTEMS AND TPE: OUR EXPERIENCE

Background

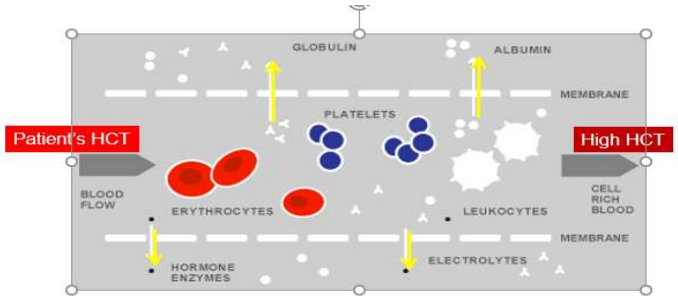
- Therapeutic plasma exchange (TPE) is the removal and retention of the plasma, with return of all cellular components to the patient along with physiological fluid.
- The effectiveness of TPE is related to the volume of plasma removed and the concentration of the pathological substance in the blood.
- It is recommended that approximately 1 to 1.5 plasma volumes be exchanged per procedure.

TPE aka PLEX aka Patient Plasmapheresis


Anticoagulant
added
Remaining
blood components
recombined and returned
Plasma
Platelets
Lymphocytes
Granulocytes
Erythrocytes
Whole blood
(vein)
Whole blood
(vein)
Blood components separated
by centrifugation and
selectively removed

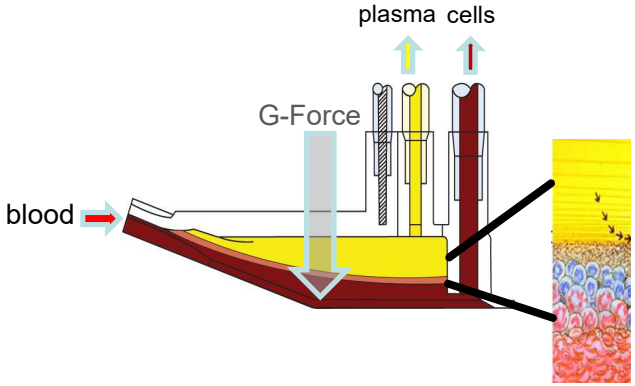
Pre-procedural considerations

Filtration-Membrane



Based on difference in particle size to separate plasma from cellular components

Centrifugation



Based on specific gravity of blood components

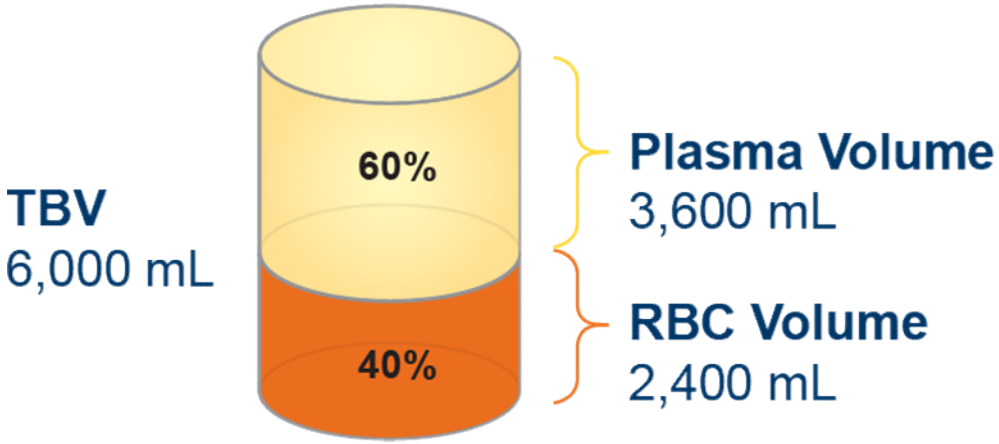
Plasma Volume Calculation Example

Patient with a 40% HCT

Example:

TBV x (1 – Hct) = Plasma Volume

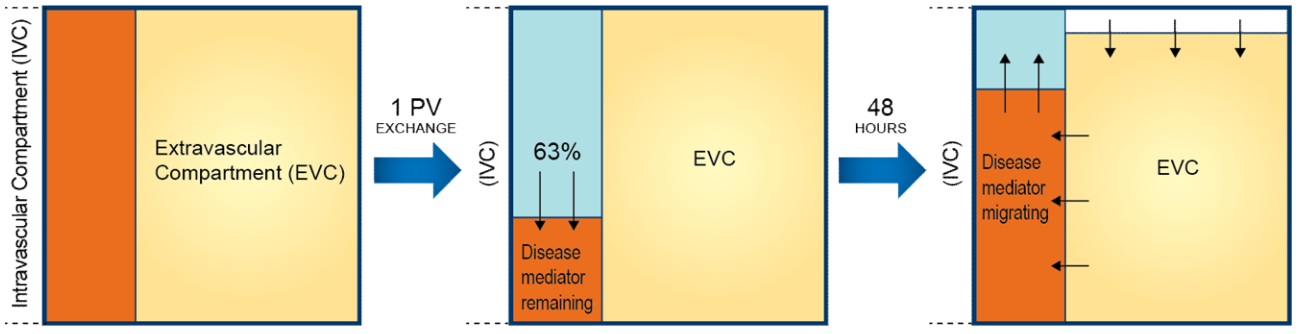
6,000 x 0.60 = 3,600 mL



Treatment frequency and number of procedures needed

Intravascular and Extravascular Distribution

Low- to mid-molecular-weight disease mediators



IVC is less than 10% Total Body Volume. Therefore, our EVC is more than 10 times bigger than IVC.

1

When 1 Plasma Volume (PV) is exchanged, 63% of disease mediator in plasma is removed, but none from EVC.

2

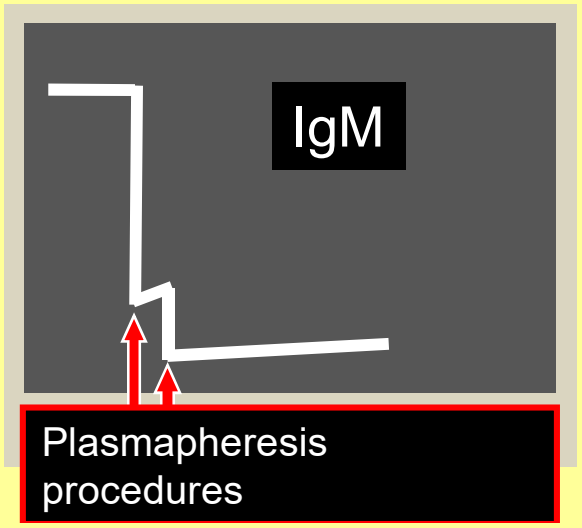
After 48 hours, 45% of IgG, IgA are recovered in the IVC from the EVC.

3

Rationale for Number of Procedures Needed

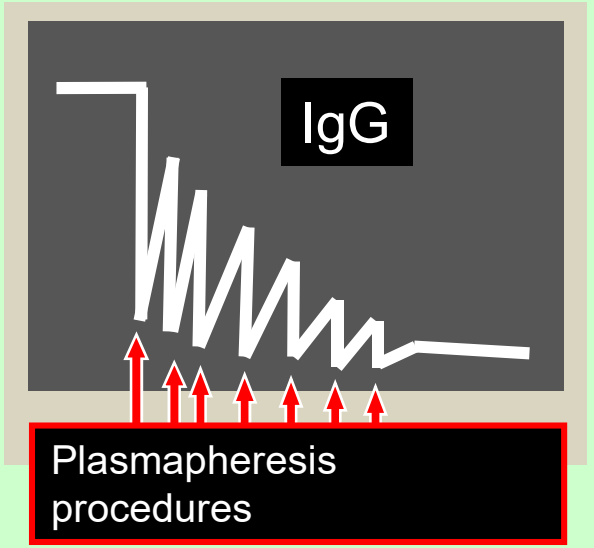
According to D. M. Ward, MD; UCSD, San Diego, CA

Generally:
Single TPE − 1 volume = 63%



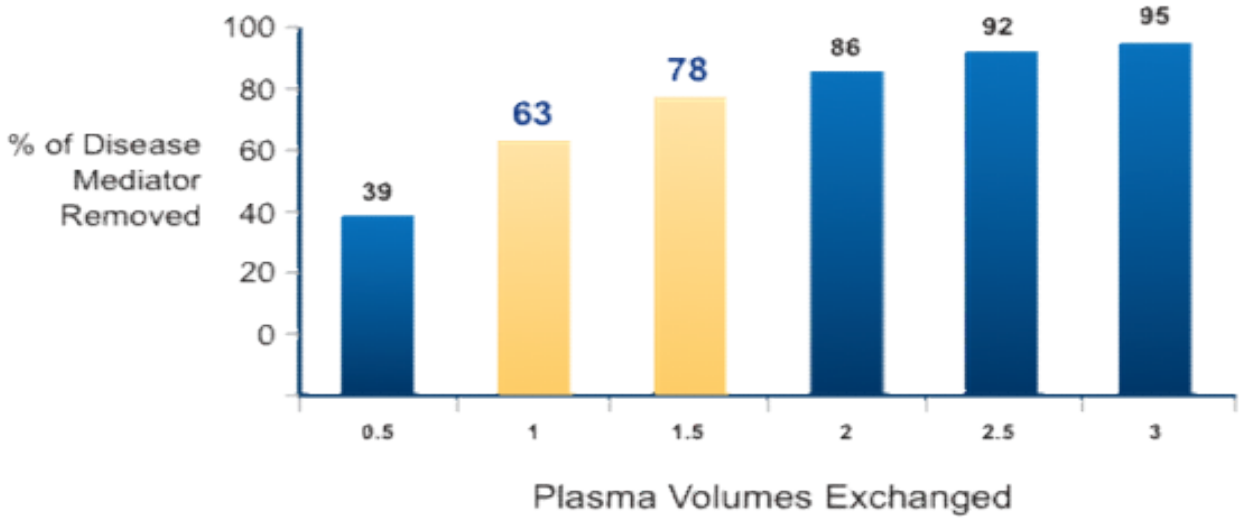
- IgM is large (~970 kDa)
- 90% of IgM stays intravascular

Generally :
Single TPE − 1 volume = 60%
4 to 6 TPE sessions = 70% to 90%



- IgG is smaller (~146 kDa)
- Only 25% to 30% is intravascular

Plasma Volumes Exchanged vs. Percentage of Disease Mediator Removed Equals Therapeutic Effectiveness of TPE[9]



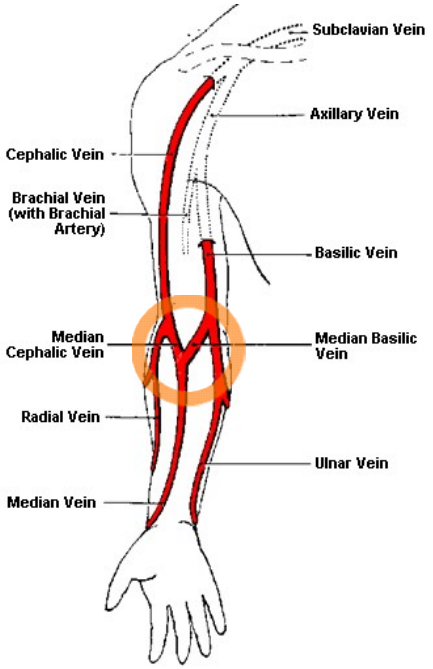
Kaplan AA, "Therapeutic Plasma Exchange: Core Curriculum 2008." *American Journal of Kidney Diseases* 2008; 52 (6): 1180–1196.

Small vs. Large Volume Exchange

- **1.0 to 1.5 PV Exchange:** Considered standard of care[2]
- **Less than 1.0 PV Exchange:** Not enough disease mediator removed; considered not therapeutically effective
- **Greater than 1.5 PV Exchange:** Requires considerably more time and replacement fluid with only marginal benefit for removal of disease mediator; considered not cost-effective

Vascular Access: Peripheral Venous Access

- **Peripheral venous access is preferred**
  - 17 -gauge-or-larger for draw
  - 18 --gauge-or-larger for return
- **Draw- Antecubital veins**
  - Median cubital/cephalic/basilica
- **Return- Forearm/hand/foot**
- **Draw and return should NOT be placed in the same extremity**
- **If veins are not good, arm exercise and warm compress may be helpful**
  - Ultrasound-Guided Peripheral Deep Vein Cannulation
- **Patients who may not be candidates for peripheral access include:**
  - poor vascular or muscle tone
  - unable to contract muscles to increase blood flow in the upper extremity
  - uncooperative or have altered mental status, weakness, or fatigue
- **Studies have reported successful peripheral access in 30% to 50% of neurology patients**



Superficial veins of the right upper limb

Vascular Access: Central Venous Access (CVC)

- **Use CVC in case peripheral access cannot be obtained and for very long procedures**
- **CVC should:**
  - be rigid and not collapse during withdrawal of blood
  - not be temperature sensitive
- **Placed in an internal jugular (IJ), subclavian, or femoral vein**
  - IJ is preferred-allows straight access to vena cava superior and right atrium
  - Positioning is controversial
- **Catheter care is important!**
  - Regular dressing
  - Inspection of insertion site
  - Flush catheter with saline and heparin after use

Fluid Balance (FB)

- **Isovolemic = 100%**
  - Fluid Returned = Fluid Removed
- **Hypovolemic < 100%**
  - Fluid Returned < Fluid Removed
- **Hypervolemic > 100%**
  - Fluid Returned > Fluid Removed

Replacement Fluids According to Content

- **Protein content**
  - Contain protein (colloids) that help stabilize blood pressure
    - 5% albumin
    - FFP and cryo-poor plasma
  - Do not contain protein (crystalloids)
    - Normal saline
- **Citrate content**
  - FFP and cryo contain significant amounts of citrate (approx 17 mmol/L)
  - 5% albumin contains small amounts (approx 4 mmol/L)
  - Normal saline does not contain citrate
- **Dilutional Coagulopathy**

Medical Evaluation

- **General physical**
  - Vital signs, Height, Weight
- **Hematologic**
  - Hemoglobin and hematocrit, Platelet count, Coagulation status and anticoagulation therapy, History of thrombosis
- **Cardiopulmonary**
  - Adequate oxygenation, Adequate cardiac function, History of current cardiac disease, arrthymias etc, Hemodynamic stability, Sepsis/systemic inflamatory response
- **Renal/Metabolic**
  - Volume status and fluid balance, Electrolyte abnormalities (Ca,K,Mg), History of renal or hepatic dysfunction
- **Neurologic**
  - Mental status,History of seizures or cerebrovascular accidents, Autonomic dysfunction or neuropathy that may impact peripheral access, Medication
- **Drugs**

Medical Evaluation: Disease Specific Testing

Autoimmune disease	Autoantibodies
Thrombotic thrombocytopenic purpura(TTP), sporadic type	ADAMTS13 (von Willebrand factor protease)
Myasthenia gravis, classic type	Acetylcholine receptor
Myasthenia gravis, MuSK type	Muscle-specific kinase
Guillain-Barre syndrome	Neuronal gangliosides:
(1) Miller–Fisher variant	(1) GQ1b
(2) other variants	(2) GM1, GM1b, GD1a, GalNAcGd1a, GD1b,Gd3, etc.
Neuromyelitis optica (Devic's disease)	Aquaporin 4
Stiff-person syndrome and relatedneuropathies	Glutamic acid decarboxylase (GAD65antigen)
Anti-GBM glomerulonephritis (GN),including Goodpasture's syndrome	Alpha-3 chain of collagen type IV 13
ANCA-associated GN(focal necrotizing GN,microscopic polyangiitis,Wegener's granulomatosis)	Myeloperoxidase (MPO), proteinase 3 (PR3),other lysosomal antigens,possibly lysosomal membrane protein 2(LAMP2)
Idiopathic dilated cardiomyopathy	Cardiac beta-1 receptors and cardiac myosin

Special Patient Population: May require extra attention!

- Patients with :
  - Anemia
  - Heart Disease or Hemodynamic Instability
  - Fluid Volume Abnormalities
  - Abnormal Citrate Metabolism
  - Drug Interactions
  - Pregnant Patients
  - Increased Risk of Bleeding

ASFA CATEGORIES

WILEY

Guidelines on the Use of Therapeutic Apheresis in Clinical Practice – Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Eighth Special Issue

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ABSTRACT

The American Society for Apheresis (ASFA) Journal of Clinical Apheresis (JCA) Special Issue Writing Committee is charged with reviewing, updating and categorizing indications for the evidence-based use of therapeutic apheresis (TA) in human disease. Since the 2007 JCA Special Issue (Fourth Edition), the committee has incorporated systematic review and evidence-based approaches in the grading and categorization of apheresis indications. This Eighth Edition of the JCA Special Issue con-

- **ASFA JCA special issue writing committee is charged with reviewing updating and categorizing indications for the evidence based use of therapeutic apheresis**
- **The eight edition of JCA Special issue continue to maintain the same**

Category Definitions for Therapeutic Aphaeresis

Category	Description
I	Disorders for which aphaeresis is accepted as first-line therapy, either as a primary standalone treatment or in conjunction with other modes of treatment.
II	Disorders for which aphaeresis is accepted as second-line therapy, either as a standalone treatment or in conjunction with other modes of treatment.
III	Optimum role of aphaeresis therapy is not established. Decision making should be individualized.
IV	Disorders in which published evidence demonstrates or suggests aphaeresis to be ineffective or harmful.

Journal of Clinical Apheresis 31:149–162 (2016)

SPECIAL CONSIDERATIONS IN TPE FOR PEDIATRIC PATIENTS: TECHNICAL CONSIDERATIONS

- PRINCIPLES ARE THE SAME
- THE INSTRUMENT IS DESIGNED FOR ADULTS
- ECV, fixed volume deficit persists for the procedure
- ECV vary with
  - Equipment
  - Procedure
- TBV of children should be calculated
- Spectra cannot calculate for < 25 kg children
- Manual weight based formula especially for children under age of 30 Kg

Cell Separator	Disposable Tubing Set	ECV (mL)	ERCV (mL)
Caridian* Spectra	Plasma/red cell exchange	170	68
Version 4.7	MNC procedure	285	114
Version 6.0	AutoPBSC	165	66
Baxter/Fenwal† CS3000+	Plasma/red cell exchange	393	68
Fresenius‡ AS 104	Plasma/red cell exchange	150	90

*CaridianBCT, Lakewood, CO.
†Fenwal, Lake Zurich, IL.
‡Fresenius Kabi, Redmond, WA.
ECV = extracorporeal volume; ERCV = extracorporeal red cell volume; MNC = mononuclear cell; PBSC = peripheral blood stem cell.

SPECIAL CONSIDERATIONS IN TPE FOR PEDIATRIC PATIENTS: VASCULAR ACCESS

- Peripheral access: antecubital vein
  - 16 G/18 G for draw and 18G or larger for return
- CVC may be placed:
  - Short term use inserted percutaneously (non tunneled)
    - IJ better than SC than femoral for children
    - Curved extensions are better
  - Long term (tunnelled and cuffed)
- Large bore dual lumen catheters for dialysis are suitable
- 3 factors:
  - Urgency for the need fro therapeutic apheresis
  - Expected frequency and duration
  - Ease of catheter care

Recommendations for CVC size by patient weight

Weight (kg)	Size of CVC
<3	Consider two single-lumen CVCs, 5 French (Fr.)
3-10	7 Fr., double-lumen
10-20	8 Fr. or 9 Fr., double-lumen
20-50	9 Fr. or 10 Fr., double-lumen
>50	11.5 Fr., 12 Fr., or 13.5 Fr., double-lumen

SPECIAL CONSIDERATIONS IN TPE FOR PEDIATRIC PATIENTS: ANTICOAGULATION

- Citrate toxicity
- Screen for underlying coagulopathy
- Symptoms are mild and vague
- Monitoring of citrate induced ionised hypocalcemia is difficult in children
- Citrate toxicity higher with FFP vs Albumin (4 times)
- Combination of citrate and heparin may be preferred

SPECIAL CONSIDERATIONS IN TPE FOR PEDIATRIC PATIENTS: Psychological considerations

- Tailored made
- Anxiety and lack of cooperation
- Communication with the child and parents
- Divert child's attention to age appropriate activities
- Sedation may be required

Assessing safety and efficacy of TPE in pediatric patients: A single centre experience

Original Article

Access this article online
Quick Response Code:
Website: www.ajts.org
DOI: 10.4103/ajts.AJTS_25_20

Assessing safety and efficacy of therapeutic plasma exchange in pediatric patients: A single-center experience

Mohit Chowdhry, P. J. Mutjhukamaravel, Soma Agrawal, Shiva Prasad Gajulapali, Uday Kumar Thakur

Abstract:

INTRODUCTION: Therapeutic plasma exchange has been widely employed by clinicians for removal of the toxic constituents from plasma by filtration of whole blood and subsequent removal of plasma and reinfusion of cellular components along with a replacement fluid. It has become an accepted therapeutic modality in paediatric patients for numerous indications including but not limited to renal transplant, haemolytic uremic syndrome and Guillain Barre Syndrome. But, data on safety and efficacy are mainly derived from studies in the adult population with very limited data available in the paediatric age group. However, it is technically challenging in children due to their small circulating volume. This study discusses the clinical indications, efficacy, and safety of therapeutic plasma exchange in paediatric population.

METHOD: We retrospectively reviewed the data of children (up to 18 years of age) who underwent TPE between January 2017 and March 2019 at our Hospital. Main features of the TPE procedures i.e. frequency of TPE, site of vascular access, type of replacement fluid used, instrument used, plasma volume processed, priming of the circuit, adverse events if any and outcome of the patients were analysed.

RESULTS AND CONCLUSION: A total of 114 procedures were performed on these 24 patients. Fifteen patients with Category I indication showed good clinical outcome in terms of attainment of target ABO titre and/or decrease in the donor specific antibody. TPE is an effective therapeutic option in selected paediatric disorders. Our series of data on TPE procedures from paediatric perspective has shown safety and efficacy of the therapy.

Keywords:

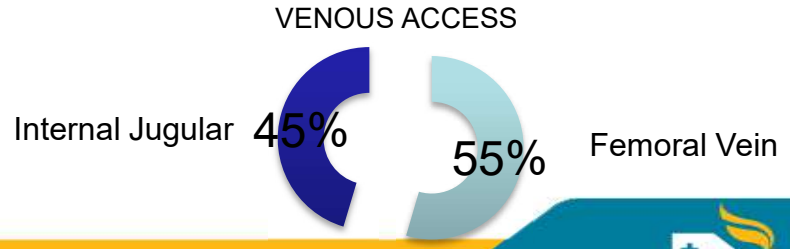
American Society for Apheresis, pediatric, therapeutic plasma exchange

Period: 2017- Mar 2019
Study population: Patients under 18 years of age
No of patients: 24 cases
No of exchanges: 114
Effectiveness of therapy: effective therapy

Table 2: Indication for therapeutic plasma exchange in patients as per the American Society for Apheresis and clinical outcome

Indication	Number of cases	ASFA category	Clinical outcome
Desensitization for renal transplant	15	I	Target ABO titer and decrease in the donor-specific antibody was achieved in all
Antibody-mediated rejection postliver transplant	6	III	1 - graft failure 4 - mortality 1 - decrease in the donor-specific antibody was achieved
HUS, infection-associated	1	III	LAMA
GBS (post-IVIG)	2	III	1 - LAMA 1 - neurological improvement
Total	24		

ASFA=American Society for Apheresis, IVIG=Intravenous immunoglobulin, LAMA=Left against medical advice, GBS=Guillain-Barre Syndrome, HUS=Hemolytic uremic syndrome, ABO blood group



SUMMARY OF TPE IN PEDIATRIC PATIENTS

- Our series of data on TPE procedures from paediatric perspective has shown safety and efficacy of the therapy.
- Following evidence-based guidelines for TPE, the procedure was the most effective in patients for desensitisation and titer reduction before renal transplant (Category I).
- Overall the paediatric group tolerated the procedure well with no major adverse event.
- TPE is a safe procedure when performed in experienced units.
- No patient mortality was related to the TPE therapy.

TPE IN SOLID ORGAN TRANSPLANTS

- Despite an increase in the rate of successful live donor renal transplantation done annually, the number of potential recipients with acceptable donors are relegated to the ever-expanding cadaver-donor waiting list due to sensitization to HLA antibodies.
- If not sufficiently suppressed, these preformed HLA antibodies can trigger AMR and early graft loss.
- ABOi is the second immunological barrier and requires lowering of corresponding ABO titers before preceding with the transplant
- To ameliorate this situation, various TPE associated desensitization treatments are administered to provide a survival benefit to highly sensitized patients

Breaching the Immunohematological barriers

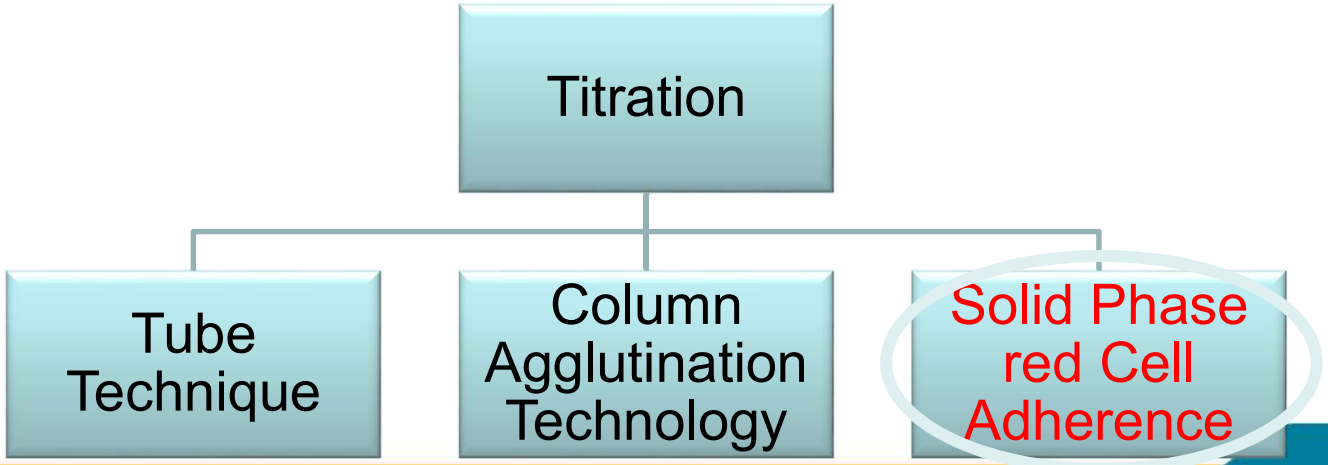
- Fully ABO-incompatible kidney transplants have been performed using protocols with extra immune suppression, removal of pre existing ABO antibodies by plasmapheresis.
- Pre & Post Transplant ABO titer studies provide the liberty to remove the unwanted antibodies from the body.
- Pre & Post Transplant HLA antibody titer studies provide the liberty to remove the unwanted antibodies from the body.

Applications of ABO Antibody titration

- ABO incompatible solid organ transplantation: ABO antibodies can cause hyper acute rejection of incompatible kidney, liver, and heart transplants.
- ABO incompatible Hematopoietic stem cell transplant (HSCT): HSC donot express ABO antigens ,so ABO is often disregarded when selecting stem cell donor. However, major ABO incompatibility may lead to hemolysis of infused red cells with a bone marrow transplant.
- Transfusion of platelets containing ABO incompatible plasma: screening for donor anti-A and anti-B hemolysins, and high titers of IgM and IgG is suggested when using ABO non-identical platelets.

Titration: methods

- Titration is semi-quantitative technique of measuring the concentration of an antibody in a serum.
- Performed using Double dilution technique (Serial dilution).
- Dilution is expressed as: 1 in 16 which means that the dilution factor is 16.
- Titer is simply the inverse of dilution at which the end point agglutination (1+) is achieved.



Isohemagglutination titering performed on an automated solid-phase and hemagglutinin-based analyzer

- **Insight into ABO-incompatible transplants***
  - High and low titer **ABO titration assays** on the Automated platform
    - Provide standardization so that you feel confident in the results you report
    - Flexibility to run either IgG or IgM titer

- **Identify donor units with high and low titer reverse group antibodies:**
  - IgG and IgM **ABO titration assays** available
    - High and low titer range assays provide flexibility

** "Isohemagglutination titering performed on an automated solid-phase and hemagglutinin-based analyzer is comparable to results obtained by manual gel testing", Transfusion, Volume 60 March 2020*

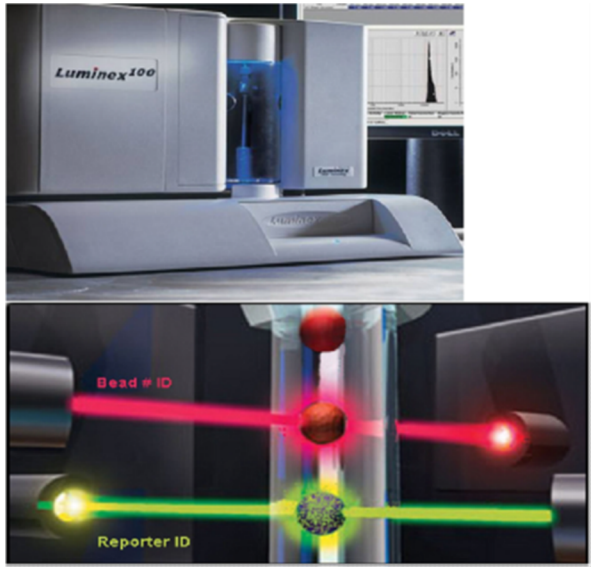
Comparative Evaluation of Five Different Methods of Anti-ABO Antibody Titration: An Aid for ABO-Incompatible Organ Transplants

Sweta Nayak [1], Raj Nath Makroo [1], Bindu Prakash [1], Trilok Chandra [1], Soma Agrawal [1], Mohit Chowdhry [1], Archisman Mohapatra [1]

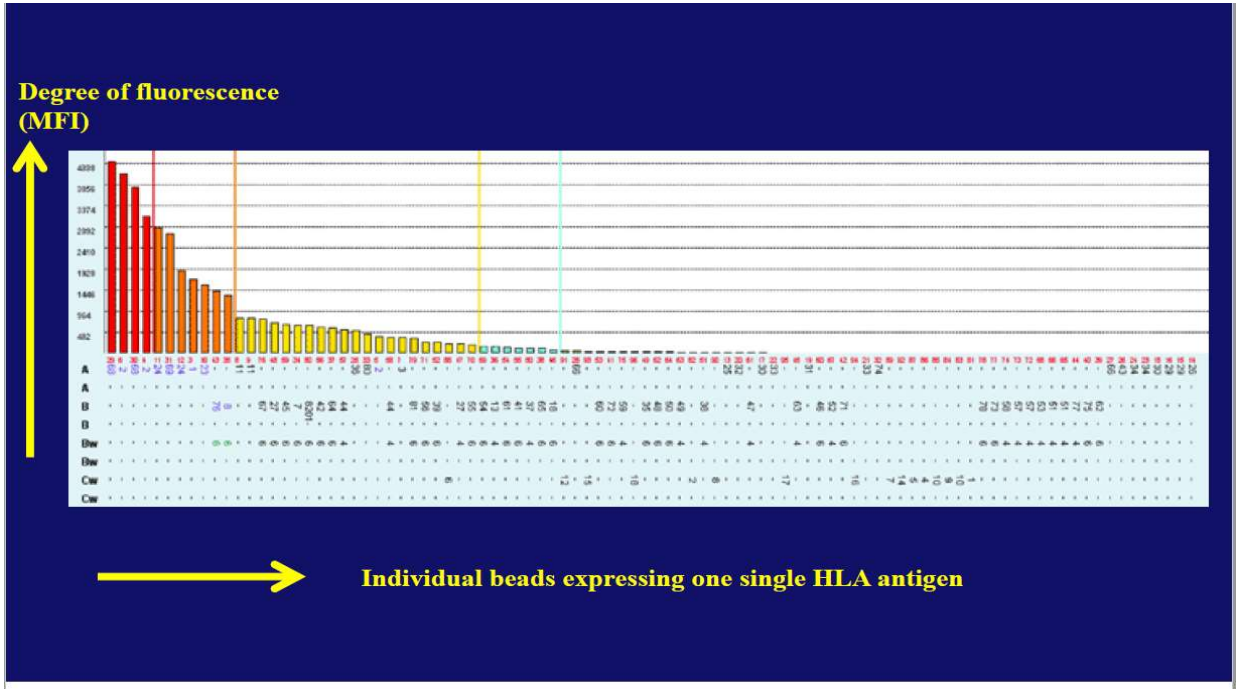
- We aim to compare five different methods of titration and analyze the data. Samples of 48 O group blood donors who donated during the month of December 2015 to January 2016 in our institution were subjected to ABO antibody titration by five different methods: immediate spin (IS) tube titer, antihuman globulin phase tube titer, Coomb's gel card titer, gel card titer after dithiotreitol (DTT) treatment of plasma, and the solid phase red cell adherence method.
- The AHG phase tube and gel cards titers showed poor agreements. There are differences in the interpretability of the ABO antibody titer among different techniques. Consistent and uniform application of the method for titration throughout the treatment of a patient is highly essential.

Applications of HLA Antibody titration

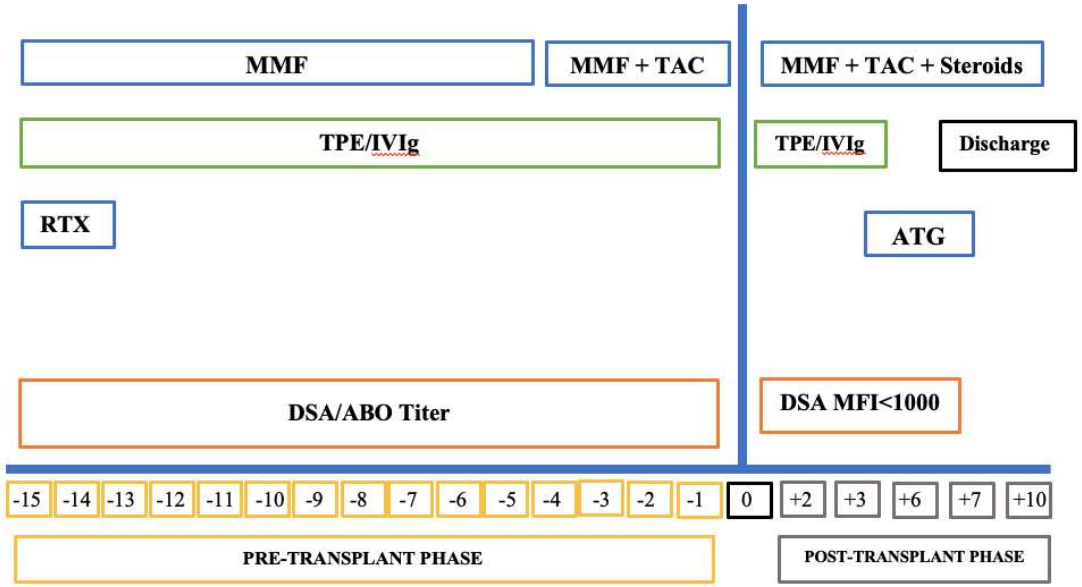
- **Prevents AMR**
- Erstwhile Cell based assays
- Luminex based assays available
- More sensitive and specific
- Can give MFI values
- Can be monitored post desensitisation



Luminex single antigens beads are excellent tools to define HLA antibody specificity.



DESENSITISATION PROTOCOL IN RENAL TRANSPLANTS



Double Barriers can be overcome!

Saudi J Kidney Dis Transpl 2018;29(3):698-704

Saudi Journal
of Kidney Diseases
and Transplantation

Case Report

A Case Report of Successful Renal Transplantation in an ABO Incompatible Patient with a Preformed Donor-Specific Antibody and Negative CDC Human Leukocyte Antigens Crossmatch

Mohit Chowdhry[1], Raj Nath Makroo[1], Brinda Kakkar[1], Sanjiv Jasuja[2], Gaurav Sagar[2], Yogita Thakur[1]

Departments of [1]Transfusion Medicine and [2]Nephrology, Indraprastha Apollo Hospital, New Delhi, India

ABSTRACT. ABO incompatibility and preformed antibodies against the human leukocyte antigen (HLA) are two impermissible barriers to a successful renal transplantation, especially in highly sensitized patient population. With the availability of effective desensitization regimens, good patient and graft outcomes have been reported. As transfusion medicine specialists we report our experience, where patient presented with dual histocompatibility barriers i.e. ABO incompatibility along with preformed donor-specific antibodies (DSA) and negative complement dependent lymphocytotoxicity (CDC) HLA crossmatch. The desensitization strategy followed for our patient included rituximab (375 mg/m^2), bortezomib (1.3 mg/m^2) and eleven pre-transplant therapeutic plasma exchange (TPE) followed by intravenous immunoglobulin (100 mg/kg per TPE session). Anti-B titer of 1:1 and negative Luminex crossmatch (LumXm) class II DSA (less than 1000 mean fluorescence intensity; MFI), was achieved prior to renal transplantation. Fifteen months post-transplant, patient is doing well with serum creatinine level of 0.8 mg/dL with repeat LumXm class II DSA negative (891 MFI). The desensitization regimen followed proved to be effective in our case.

Introduction

The complement dependent lymphocytetoxicity (CDC) assay is a classical method for detection of antibodies against human leukocyte antigens (HLA) in patients awaiting solid organ transplantation. With the emergence of Luminex-based assay, the detection and characterization of HLA antibodies are easier due to greater sensitivity, in comparison to CDC and enzyme-linked immunoassay.[1] Both HLA alloimmunization and ABO incompatibility are considered two major histocompatibility barriers to successful organ transplantation and graft survival.[2-4] Whether the coexistence of anti-A/B antibody and preformed donor-specific antibody (DSA) have an impact on the

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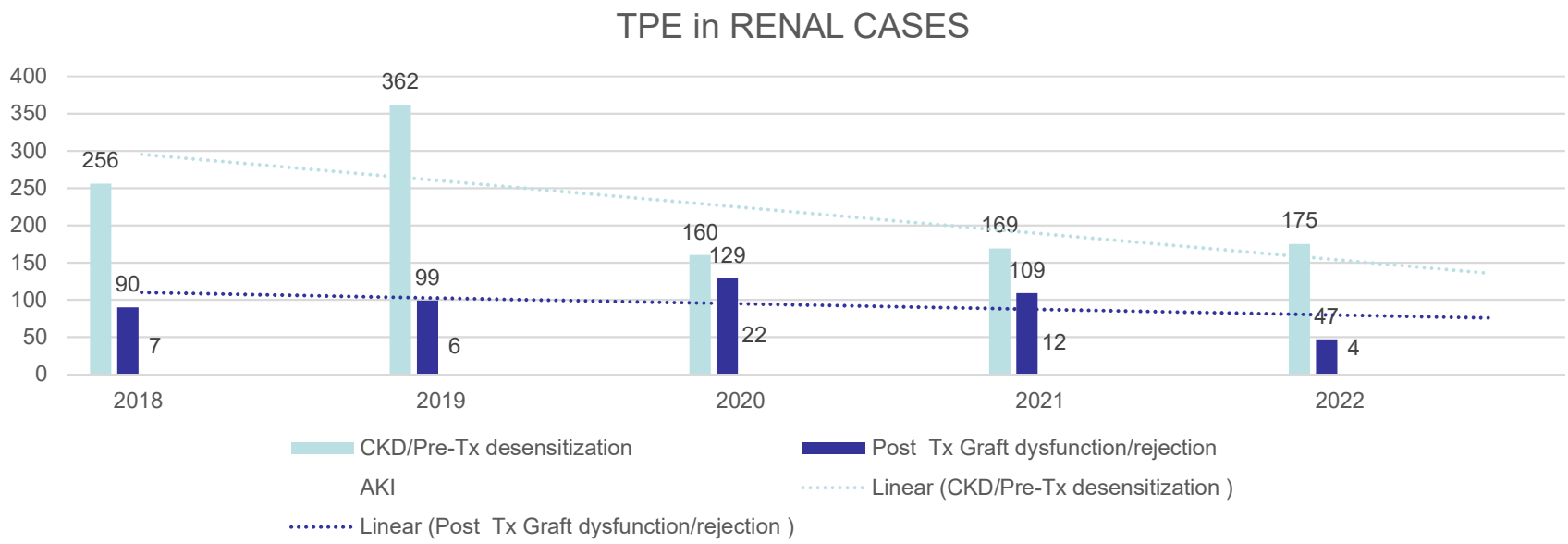
TPE IN RENAL CASES: OUR EXPERIENCE



Role of TPE in Acute Humoral rejection patients LR renal Transplant

Original Article

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Website: www.ajts.org
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Role of therapeutic plasma exchange in acute humoral rejection patients undergoing live-related renal transplantation: A single-center experience

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Abstract:

BACKGROUND AND AIM: Renal transplantation (RT) is the most successful and ideal renal replacement therapy for end-stage renal disease patients. Renal allograft rejection has always been one of the major barriers in successful RT. Our aim was to report the role of therapeutic plasma exchange (TPE) in acute humoral rejection (AHR) patients who underwent live-related RT (LRRT) and their renal allograft outcome at our center.

MATERIALS AND METHODS: A prospective observational study was conducted from July 1, 2014, to December 31, 2016. Patients with biopsy-proven AHR and treated with TPE along with other lines of treatment after undergoing LRRT were included in the study. ABO-incompatible individuals, pediatric patients, and patients undergoing second transplants were excluded from the study. Clinical history, donor and graft details, management, and patient and graft survival were noted.

RESULTS: Of the 1608 patients who underwent LRRT, 49 (37 males, 76%; 12 females, 24%; mean age 39.5 ± 13.3 years) had biopsy-proven AHR (3.04%) and were treated with TPE. A total of 281 TPEs were performed with an average of 5.7 TPE/patient (range 2–12). Of the 49 patients, 38 patients (78%) with favorable response underwent 213 (75.8%) TPEs (average of 5.6 TPE/patient; range: 2–12), whereas 11 patients (22%) with unfavorable response underwent 68 (24.2%) TPEs (average of 6.2 TPE/patient; range: 3–8). Blood urea ($P = 0.012$) and serum creatinine ($P = 0.038$) levels at the time of rejection were significant predictors of response to TPE therapy. The average length of stay in our study population was 33 ± 22 days. Six months posttransplant, the patient and graft survival were 93.3% and 89.5%, whereas at 12 months, they were 89.3% and 81.5%, respectively.

CONCLUSION: TPE is a safe and effective adjunct therapy for treating AHR patients.

Keywords:

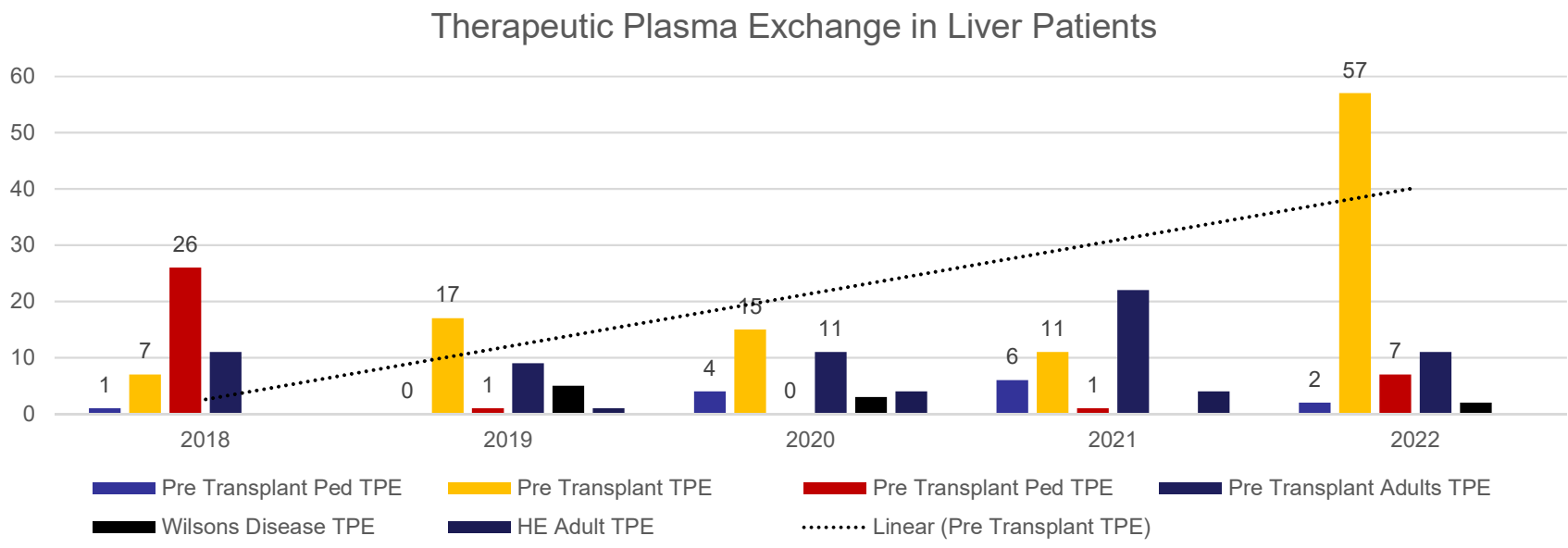
Acute humoral rejection, graft survival, renal transplantation, therapeutic plasma exchange

No of patients: 49/1608
No of exchanges: 281
Average TPE no: 5.7 TPE/patient

TPE IN LIVER DISORDERS

- Therapeutic plasma exchange (TPE) has been used as a treatment modality in various liver disorders.
- Acute liver failure causes progressive hepatic, synthetic and metabolic dysfunction, which leads to severe coagulopathy, jaundice, renal failure, metabolic dysfunctions, and worsening encephalopathy.
- Several studies on TPE showed *improved cerebral blood flow, mean arterial pressure, cerebral perfusion pressure, cerebral metabolic rate, increased hepatic blood flow, and improvements in other laboratory parameters such as cholinesterase activity or galactose elimination capacity.*
- TPE may also improve hemostasis by providing coagulation factors and removing activated clotting factors, tissue plasminogen activator, fibrin and fibrin degradation products.
- According to the ASFA guidelines, high volume TPE comes under category I indication and conventional TPE as the category III indication in acute liver failure.
- TPE is also category I indication for ABO-incompatible prospective live donor liver transplant and acts as a bridging therapy till a transplant is done.

Therapeutic Plasma Exchange in Liver Patients: OUR EXPERIENCE



TPE IN HEMATOLOGICAL DISEASE/NEUROLOGICAL: THROMBOTIC MICROANGIOPATHIES

- Thrombotoc thrombocytopenic purpura (TTP)
- Hemolytic uremic syndrome (HUS)
- aHUS
- Disseminated intravascular coagulation (DIC)
- Hemolysis, Elevated liver enzymes and Low platelet count (HELLP syndrome)

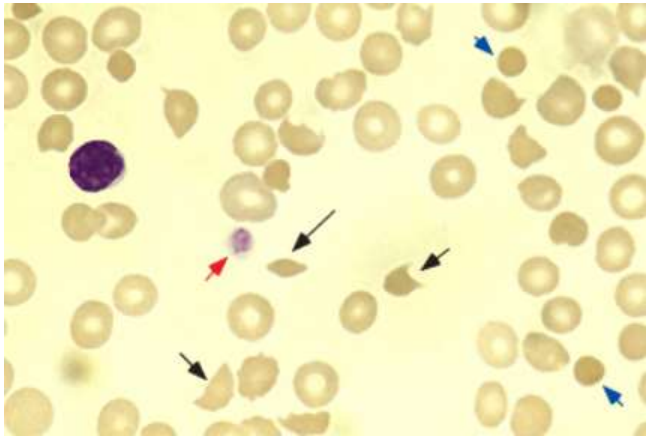
TTP

TTP belongs to a category of disorders known as thrombotic microangiopathies, a term coined by Symmers in 1952

TTP defined the “classic” clinical pentad of TTP:

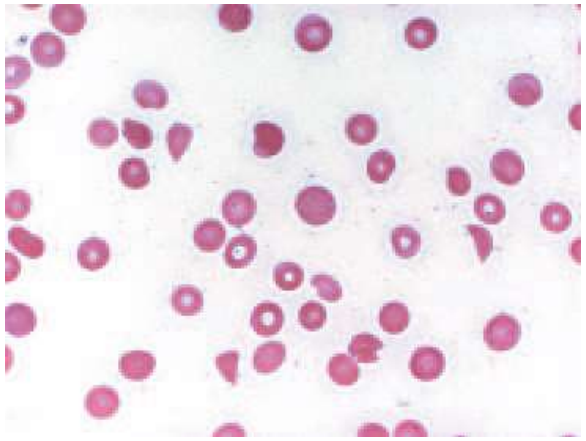
1) Thrombocytopenia,
2) Hemolytic anemia with schistocytosis
3) Neurologic symptoms ranging from transitory mental status alterations to seizures and coma
4) Renal impairment
5) Fever

Dyad should be there to be considered as

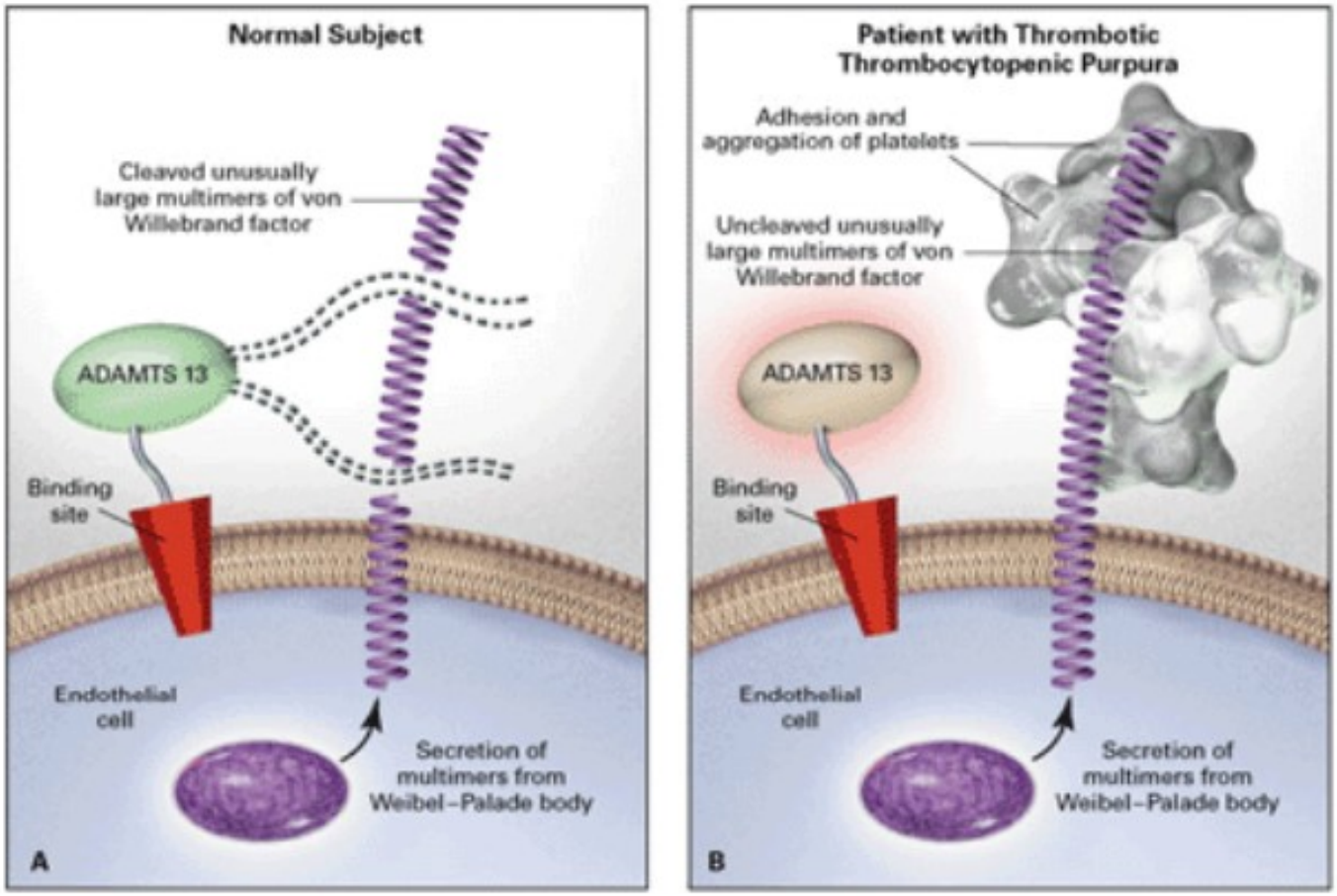


PS: marked red cell fragmentation, multiple helmet cells (small black arrows), other fragmented red cells (large black arrow); microspherocytes are also seen (blue arrows).

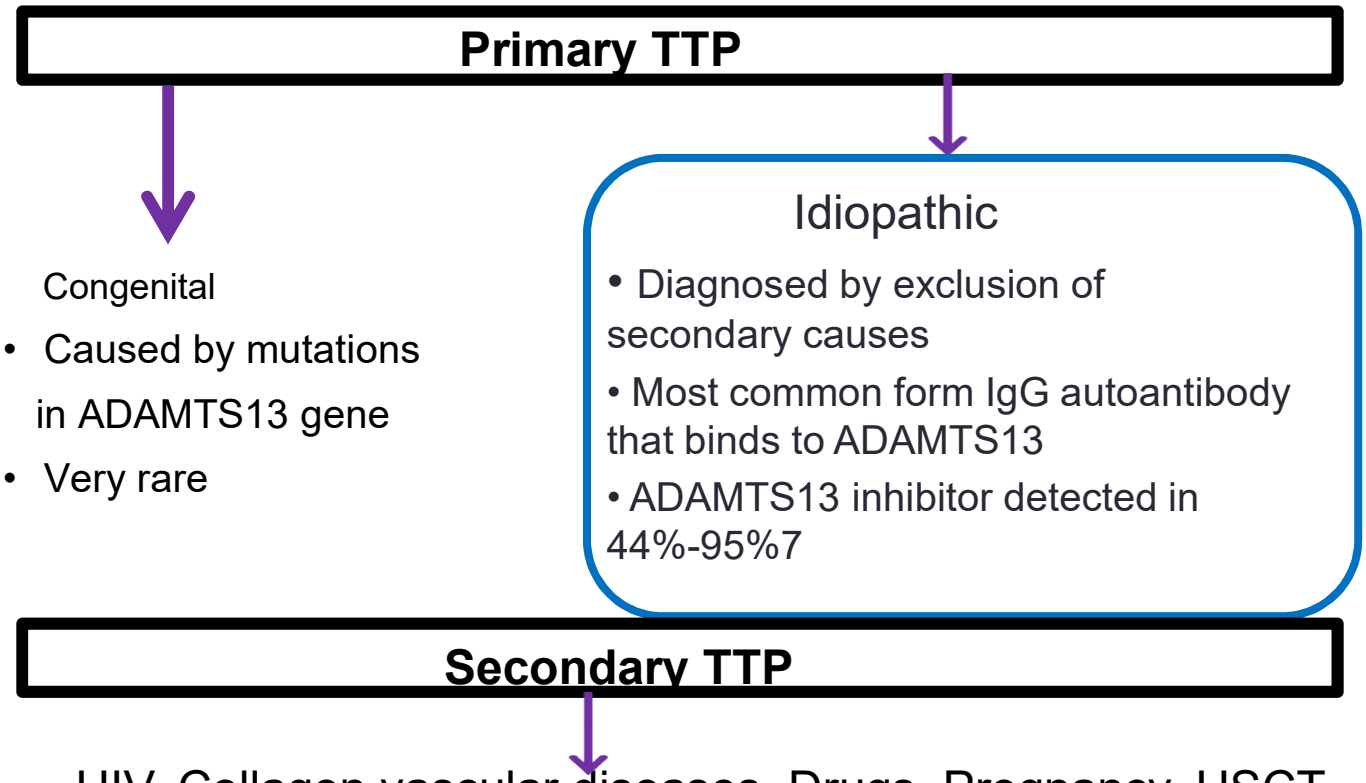
The platelet number is reduced; the large platelet in the center (red arrow) suggests that the thrombocytopenia is due to enhanced destruction.



Fragmented red cells (schistocytes), polychromatophilic red cells (reticulocytes), and a lack of platelets


Normal Subject
Cleaved unusually large multimers of von Willebrand factor
ADAMTS 13
Binding site
Endothelial cell
Secretion of multimers from Weibel–Palade body
A
Patient with Thrombotic Thrombocytopenic Purpura
Adhesion and aggregation of platelets
Uncleaved unusually large multimers of von Willebrand factor
ADAMTS 13
Binding site
Endothelial cell
Secretion of multimers from Weibel–Palade body
B

Classification

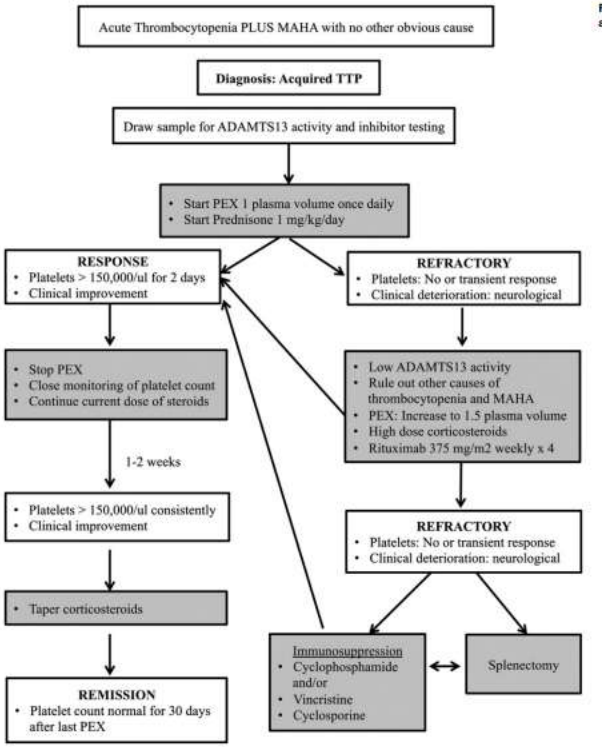


	MAHA	Thrombo cytopenia	Coagulo pathy	HBP	Abdominal symptoms	Renal Impairment	Neurological symptoms
PET	+	+	±	+++	±	±	++
HELLP	+	++	±	+	+++	+	±
TTP	++	+++	-	±	+	++	+++
HUS	+	++	±	++	+	+++	±
AFLP	±	+	+++	+	+++	++	+
SLE	+	+	±	+	±	++	+
APLS	+	++	±	±	±	±	±

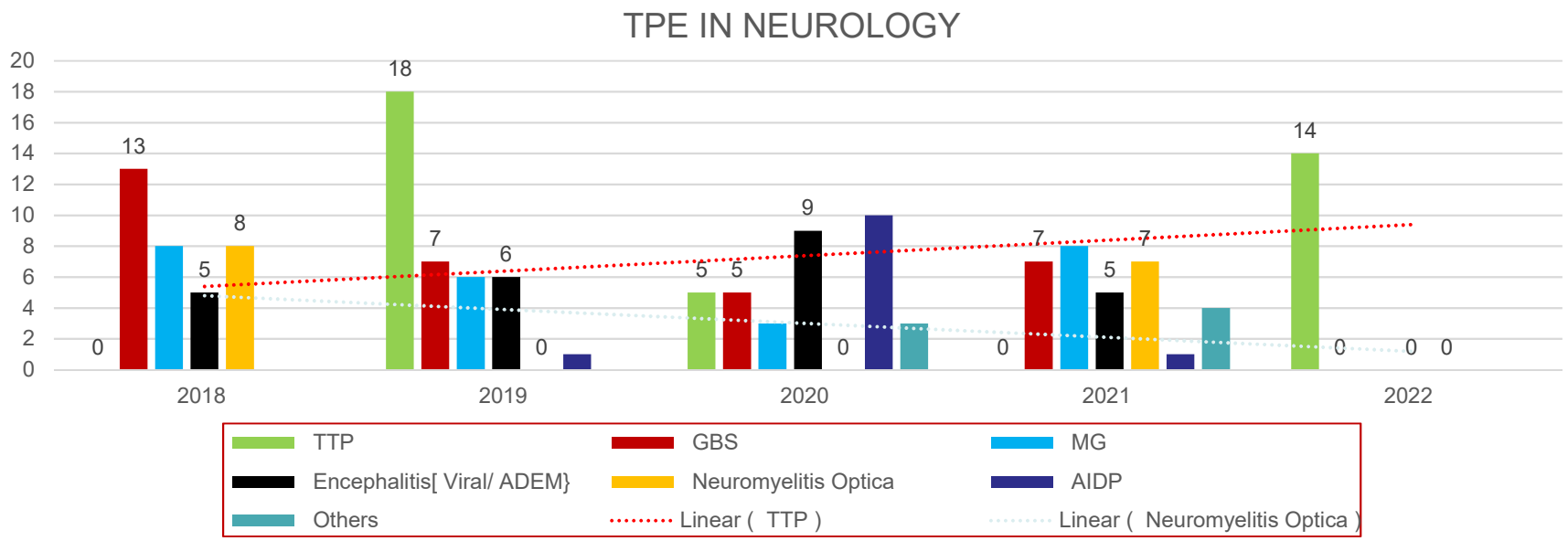
TPE in TTP

- TTP is rated as a Category I (as per ASFA)
- The Canadian Apheresis Study Group compared plasma infusion (30 mL/kg initially, then 15 mL/kg daily) with TPE (1.5 plasma volumes/day for 3 days, then 1 plasma volume per day)
- TPE not only delivers a greater dose of ADAMTS13 without circulatory overload but also depletes antibodies to ADAMTS13
- The treatment approach consists of 1 to 1.5 plasma volume exchanges daily with plasma replacement until clinical symptoms have resolved and the platelet count exceeds 150,000/µL
- The LDH level reflects ongoing tissue ischemia as well as hemolysis.
- Clinical experience suggests that a normal LDH is not necessary to safely discontinue TPE; a level below 1.5 times the upper limit of normal may be an acceptable endpoint. Persistent schistocytosis alone is not a reason to continue TPE
- **The Society for Hemostasis and Thrombosis (SHT) recommends continuing daily TPE for 2 days after attainment of remission**

Approach to treatment of TTP



TPE IN HEMATOLOGICAL/NEUROLOGY



TPE in HELLP syndrome

No of patients: 9 cases, 7 post partum, 2 second trimester
Effectiveness of therapy: Significant decrease in LDH and increase in Platelet counts.
Adequate, if initiated within 24 hrs post partum

Original Article

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Therapeutic plasma exchange in HELLP syndrome: A life savior

Mohit Chowdhry, Soma Agrawal, Shiva Prasad Gajulapalli, Uday Kumar Thakur

Abstract:

BACKGROUND: HELLP (hemolysis, elevated liver enzymes, low platelet count) syndrome occurs in about 0.5%–0.9% of all pregnancies, but its prevalence is higher in patients with severe preeclampsia, accounting for a substantial maternal and perinatal morbidity and mortality. According to the latest American Society for Apheresis guidelines, Therapeutic plasma exchange (TPE) performed for postpartum cases and antepartum HELLP syndrome cases fall in Categories III and IV, respectively.

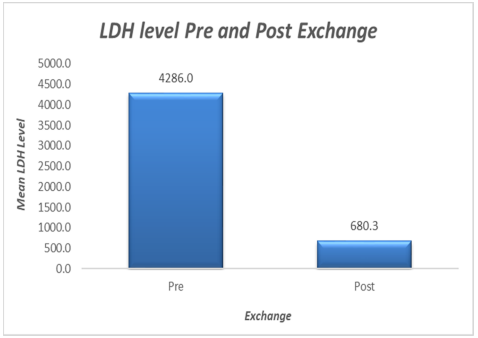
Materials and Methods: Retrospective analysis was done at our tertiary care center from January 2014 to June 2019 for patients diagnosed with HELLP syndrome. Clinical data for age, gestational age at the time of diagnosis, type of delivery, outcome of pregnancy, history of preeclampsia /eclampsia, hemoglobin levels, AST, ALT, LDH, platelet counts, prothrombin time, activated partial thromboplastin time, international normalised ratio, complete blood count, was obtained from patients' electronic medical records. The TPE was initiated within 24 hrs of diagnosis. All TPE was done on Spectra Optia apheresis system (Terumo BCT, Inc, USA). Statistical testing was conducted with the statistical package for the social science system version SPSS 20.0 and R-3.2.0. Continuous variables were expressed as mean±SD and were compared between Pre and Post TPE records of patients by using the paired *T* test.

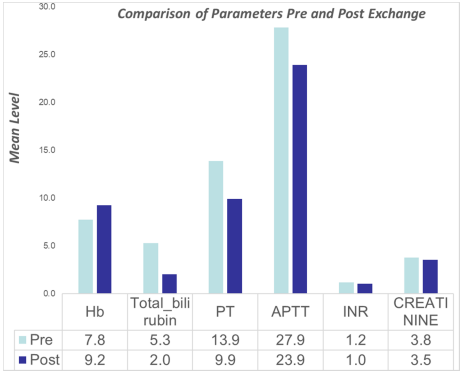
RESULTS: Nine patients fulfilled the criteria of HELLP syndrome. Seven (77.8%) were diagnosed in the postpartum period and 2 (22.2%) during the second trimester. Out of the total nine patients, two patients (22.2%) recovered completely and were discharged on day 15 ± 7 days, whereas 4 (44.4%) patients were discharged on day 21 ± 7 days with the advice of hemodialysis. Two (22.2%) patients had an intrauterine death and were discharged 3–4 days after the demise. In all these patients (except one), the TPE was initiated within 24 h of the diagnosis. A significant increase in platelet count and decrease in the lactate dehydrogenase levels ($P < 0.05$) was observed post TPE.

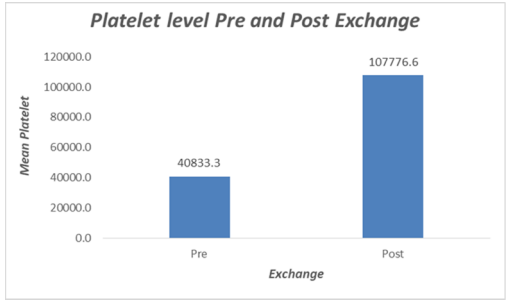
CONCLUSION: Our data showed that TPE improved the treatment outcome in patients with HELLP syndrome despite being a Category III and IV indication among postpartum and antenatal females, respectively. However, a timely diagnosis and management are of paramount importance for a favorable outcome. TPE needs to be performed within 24 h of the diagnosis postdelivery when the patient is not responsive to the usual therapies, especially in class I HELLP syndrome.

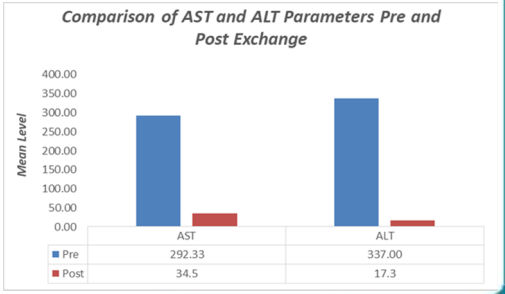
Keywords:

American Society for Apheresis, elevated liver enzymes, hemolysis, low platelet count, therapeutic plasma exchange

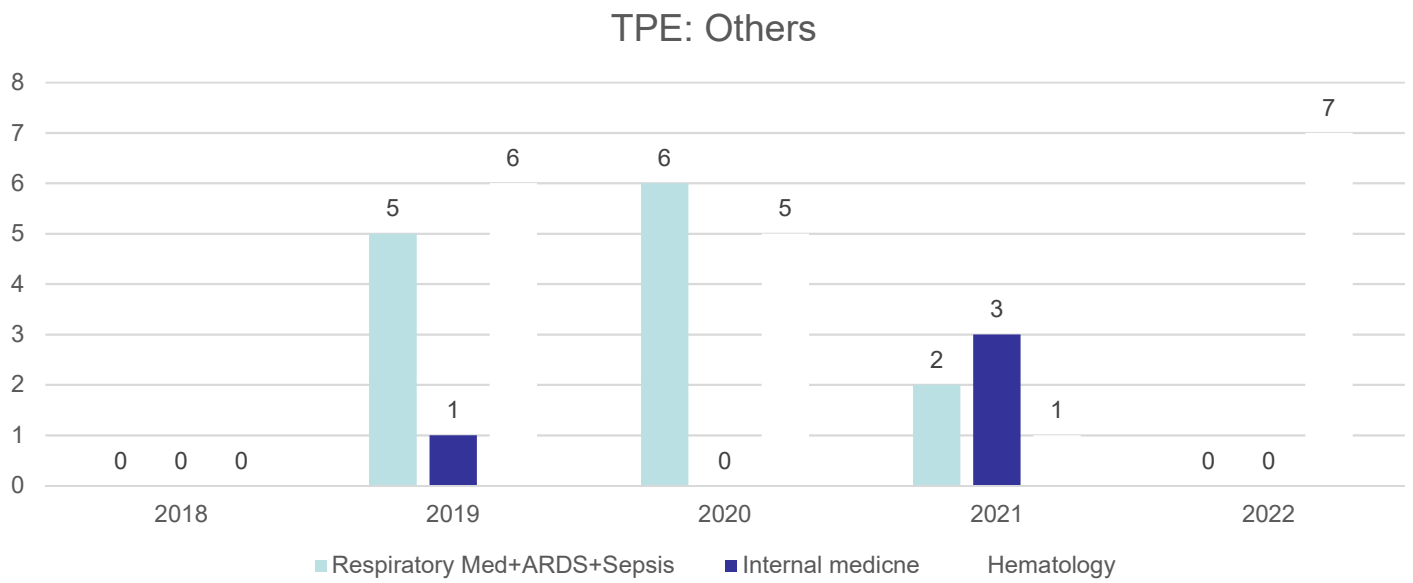








TPE: Others: Our Experience

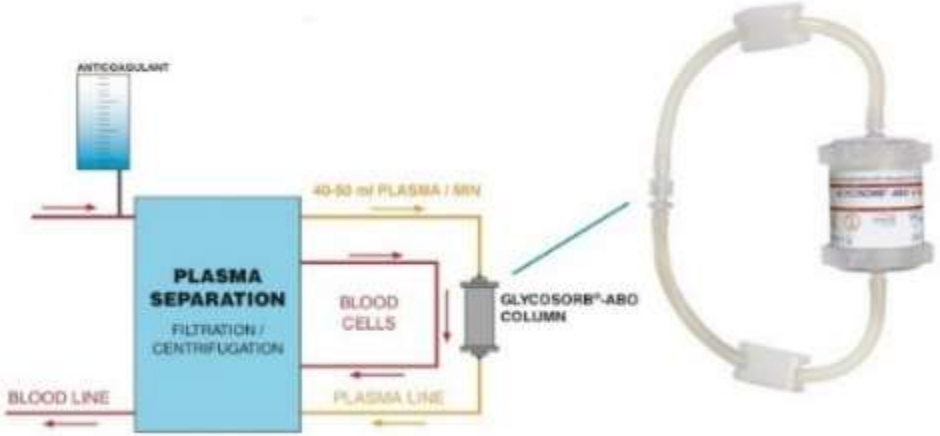


Non Selective Vs Selctive Extraction of Plasma Constituents

- TPE is used to remove plasma that may contain disease mediators
- During a 1-volume TPE, 150 g of plasma protein is removed, consisting of 110 g of albumin and 40 g of globulins and other proteins.
- In TPE, the majority of removed plasma components are substances that have important physiologic functions; thus TPE has the potential to alter normal physiology.
- Replacement fluid lacks all or most normal plasma constituents.
- Most physiologically important substances are soon replenished through normal homeostatic mechanisms (4 hours for Factors VIII and IX; 24 hours for almost all other coagulation factors except fibrinogen, which reaches 66% of pre-apheresis values at 72 hours**),**
- **They may not be replenished rapidly** enough to avoid patient complications, especially when TPE is performed intensively.
- The potential for bleeding and infection also exists
- In addition, the replacement fluids used in TPE may have undesirable effects.

Selective Extraction of Plasma Constituents

- Such techniques vary in their degree of selectivity.
- Extremely selective—removing only antibodies directed toward a specific antigen
  - ABO Glycosorb immunoadsorption Column
- Relatively selective—removing only immunoglobulins or lipoproteins;
- Minimally selective—removing substances above a certain size
  - Double filtration/Cascade filtration



Therapeutic Immunoadsorption and Conventional Plasma Exchange in ABO incompatible Renal Transplant: An Exculpatory evidence

Cureus

Open Access Original Article

DOI: 10.7759/cureus.4787

Therapeutic Immunoadsorption and Conventional Plasma Exchange in ABO-incompatible Renal Transplant: An Exculpatory Evidence

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Disclosures can be found in Additional Information at the end of the article

Abstract

Aim

The objective of this study was to compare the efficacy of immunoadsorption (IA) with conventional therapeutic plasma-exchange (cTPE) in ABO-incompatible (ABOi) renal transplant.

Methods

Data of patients from July 2015 to June 2017 (category-I, number of patients (N) = 11; IA±cTPE) on the average length of stay (ALOS), number of cTPE/IA, antibody-titers (AT), creatinine, patient and graft survival at one year were compared retrospectively with patients in period from February 2012 to June 2015 (category-II, N = 29; cTPE only). AT of patients not decreasing to less than one fold after two cTPE were shifted for IA. For patients undergoing IA, real-time AT was done and IA stopped after target titer (TT <1:8) was achieved. Post-transplant cTPE was done if, titers rebounded to ≥1:8. Intravenous immunoglobulin (IVIG) was given after every cTPE/IA. Cost comparisons were made.

Results

In category-I, seven patients (63.63%) were shifted to IA from cTPE. The mean cTPE procedures in category I and II are 3.5 ± 2.4 and 4.8 ± 2.5, respectively ($p = 0.206$). The mean IA procedures in category-I are 1.6 ± 0.5. The number of patients requiring post-operative TPE was less in category-I than category-II, i.e., $N = 5$, 45.5% vs $N = 20$, 69%, respectively ($p = 0.171$). The expense of IA in category-I vs cTPE in category-II was statistically not significant ($p = 0.422$) but had significant lesser ALOS ($p = 0.044$). Expenses, when a patient undergoes both cTPE and IA (category-I), are significantly higher to category-II ($p = 0.003$). The two groups were comparable in AT, creatinine value, graft and patient survival rates at one year.

Conclusion

Contrary to the general judgment of IA being expensive than cTPE, this study shows equivalent expenditures with comparable therapeutic outcomes.

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Published 05/30/2019

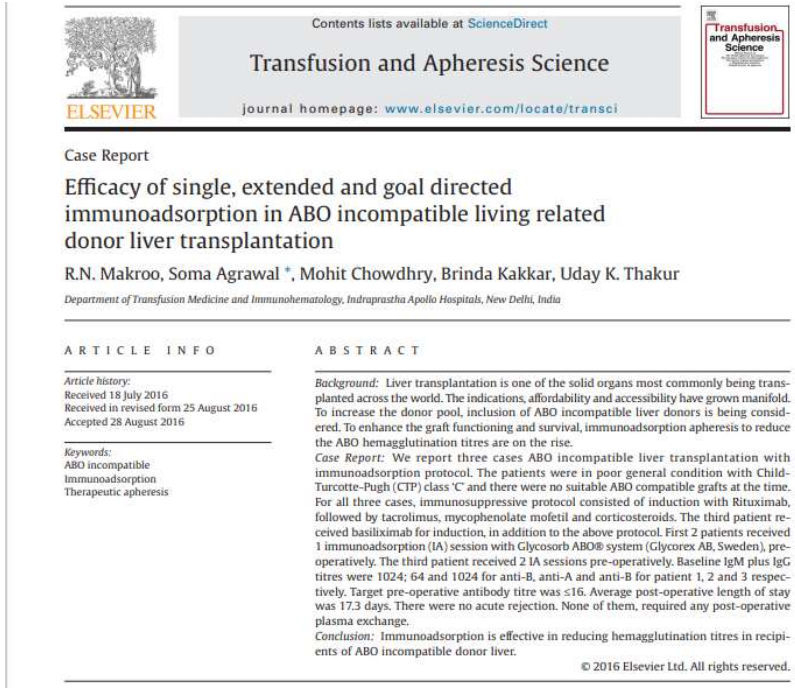
No of patients: 49/1608
No of exchanges: 281
Average TPE no: 5.7 TPE/patient

To compare efficacy and overall expenditures of immunoadsorption (IA) with conventional therapeutic plasma-exchange (cTPE) in ABO-incompatible (ABOi) renal transplant.

Category 1: patients undergoing IA±cTPE for ABOi renal transplant between July-2015 to June

Category 2: ABOi renal transplant in period from February-2012 to June-2015 using cTPE only

Immunoadsorption in ABOi LRLT



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Case Report

Efficacy of single, extended and goal directed immunoadsorption in ABO incompatible living related donor liver transplantation

R.N. Makroo, Soma Agrawal *, Mohit Chowdhry, Brinda Kakkar, Uday K. Thakur

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Keywords:
ABO incompatible
Immunoadsorption
Therapeutic apheresis

ABSTRACT

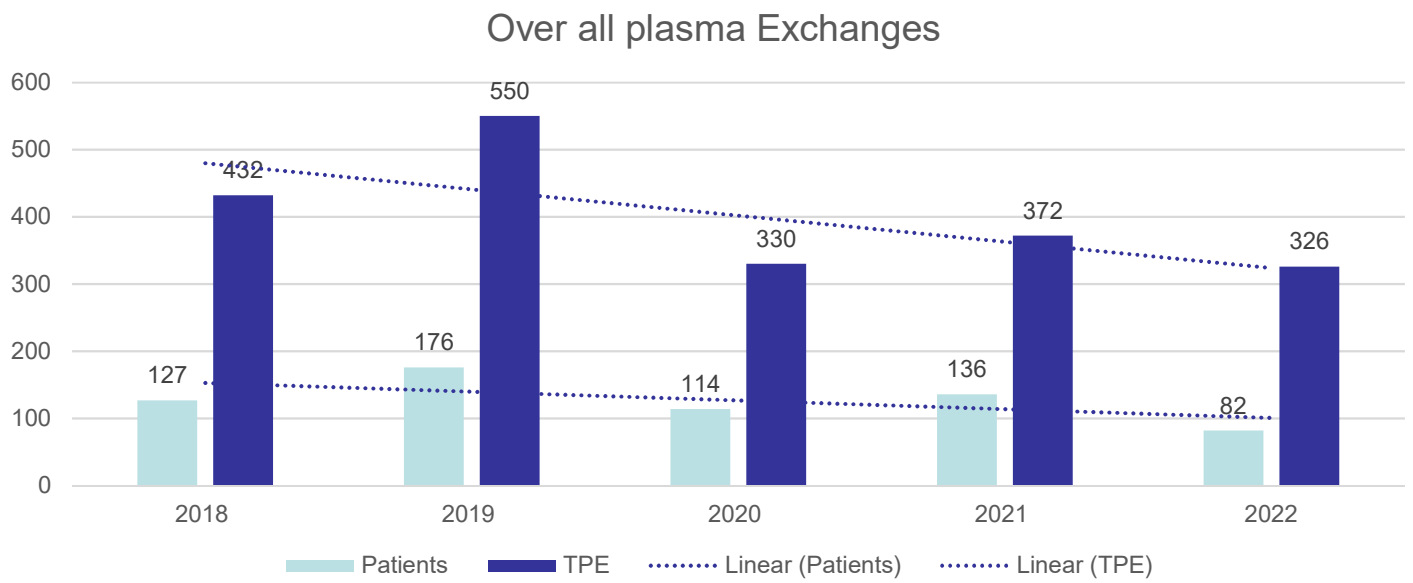
Background: Liver transplantation is one of the solid organs most commonly being transplanted across the world. The indications, affordability and accessibility have grown manifold. To increase the donor pool, inclusion of ABO incompatible liver donors is being considered. To enhance the graft functioning and survival, immunoadsorption apheresis to reduce the ABO hemagglutination titres are on the rise.

Case Report: We report three cases ABO incompatible liver transplantation with immunoadsorption protocol. The patients were in poor general condition with Child-Turcotte-Pugh (CTP) class 'C' and there were no suitable ABO compatible grafts at the time. For all three cases, immunosuppressive protocol consisted of induction with Rituximab, followed by tacrolimus, mycophenolate mofetil and corticosteroids. The third patient received basiliximab for induction, in addition to the above protocol. First 2 patients received 1 immunoadsorption (IA) session with Glycosorb ABO® system (Glycorex AB, Sweden), pre-operatively. The third patient received 2 IA sessions pre-operatively. Baseline IgM plus IgG titres were 1024; 64 and 1024 for anti-B, anti-A and anti-B for patient 1, 2 and 3 respectively. Target pre-operative antibody titre was ≤16. Average post-operative length of stay was 17.3 days. There were no acute rejection. None of them, required any post-operative plasma exchange.

Conclusion: Immunoadsorption is effective in reducing hemagglutination titres in recipients of ABO incompatible donor liver.

No of patients: 3 cases
No of exchanges: 1 IA for 2 patients, 2 IA for 1 patient
Baseline titer: 1024/64/1024
Target titer: ≤16

OVERALL PLASMA EXCHANGES: Our Centre



A Case of Bickerstaff encephalitis and overlapping Gullian Barre syndrome in a pediatric patient treated with TPE

Transfusion and Apheresis Science xxx (xxxx) xxx

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Case Report

A case of Bickerstaff encephalitis with overlapping Gullian Barre syndrome in a pediatric patient treated with therapeutic plasma exchange

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ARTICLE INFO

Keywords:
BBE
GBS
TPE
ASFA

ABSTRACT

Bickerstaff brain stem encephalitis (BBE) is a rare brainstem disorder characterized by acute onset of ophthalmoplegia, ataxia, and altered consciousness. Guillain Barre syndrome (GBS), Miller Fischer syndrome and BBE share certain similarities such as the presence of anti-ganglioside antibodies. The use of Therapeutic Plasma Exchange (TPE) has been reserved for severe to fulminant cases of BBE mostly as an 'off label' use. The role of TPE in the overlapping syndrome of BBE and GBS has not been explored much, especially in the paediatric population. Herein, we describe a case of 2-year-old male who presented with features of BBE and later evolved to an overlapping syndrome with BBE and GBS. A multi-disciplinary team managed the patient and TPE was initiated as a part of the treatment plan. Five cycles of TPE were done from day 24 after which the patient improved. In our case, TPE was used as rescue therapy in patients with BBE overlapping with GBS. The effectiveness of TPE can be further explored as a modality in such disorders.

No of patients: 1 cases
No of exchanges: 5
Effectiveness of therapy: Adequate

TPE in Voltage gated potassium channel Al encephalitis

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Transfusion and Apheresis Science

journal homepage: www.elsevier.com/locate/transci

A case study: Therapeutic plasma exchange in voltage-gated potassium channel autoimmune encephalitis

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ARTICLE INFO

Keywords:
Limbic encephalitis
Voltage-gated potassium channel
Therapeutic plasma exchange

ABSTRACT

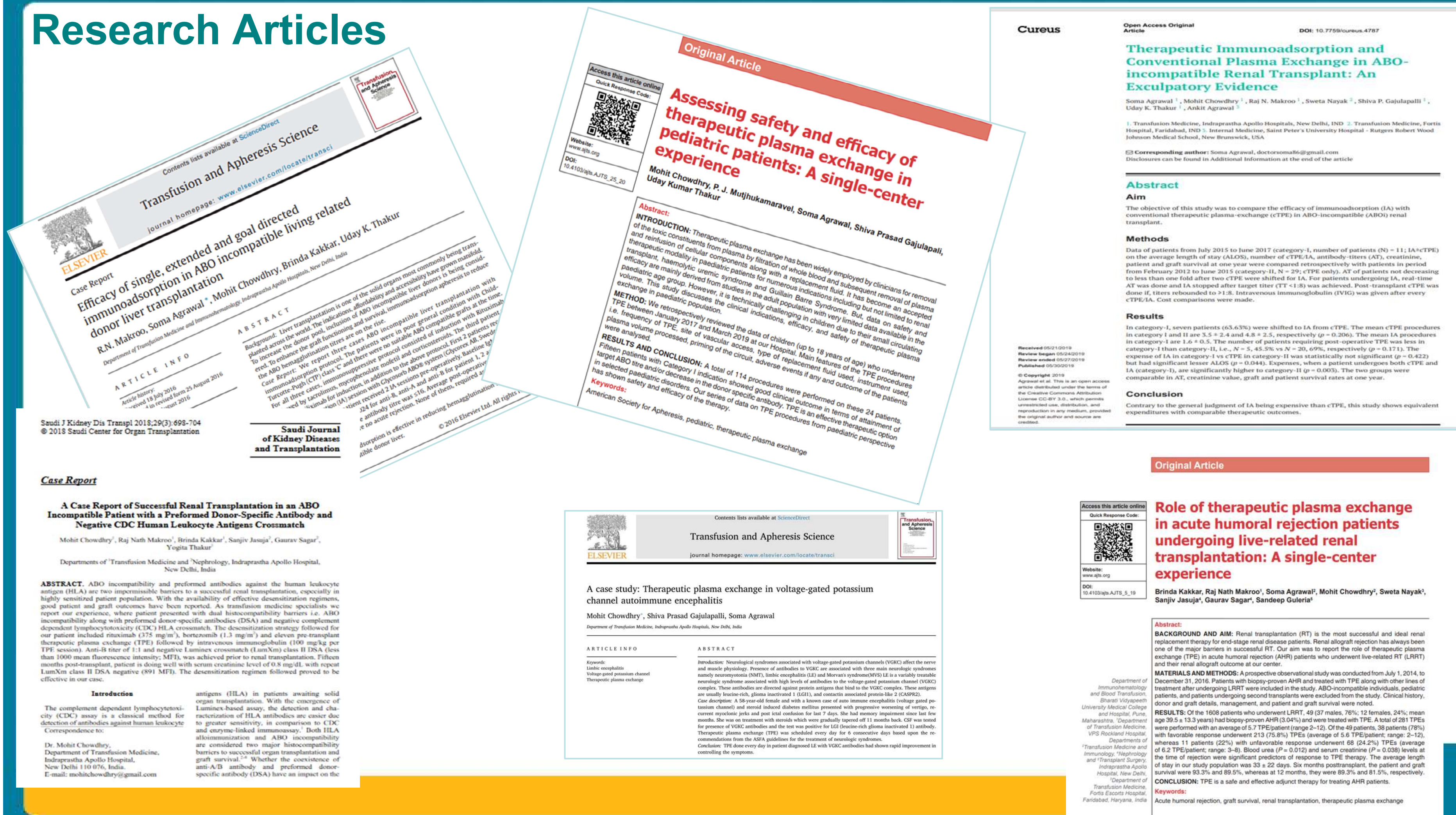
Introduction: Neurological syndromes associated with voltage-gated potassium channels (VGKC) affect the nerve and muscle physiology. Presence of antibodies to VGKC are associated with three main neurologic syndromes namely neuromyotonia (NMT), limbic encephalitis (LE) and Morvan's syndrome(MVS) LE is a variably treatable neurologic syndrome associated with high levels of antibodies to the voltage-gated potassium channel (VGKC) complex. These antibodies are directed against protein antigens that bind to the VGKC complex. These antigens are usually leucine-rich, glioma inactivated 1 (LGI1), and contactin associated protein-like 2 (CASPR2).

Case description: A 58-year-old female and with a known case of auto immune encephalitis (voltage gated potassium channel) and steroid induced diabetes mellitus presented with progressive worsening of vertigo, recurrent myoclonic jerks and post ictal confusion for last 7 days. She had memory impairment since last few months. She was on treatment with steroids which were gradually tapered off 11 months back. CSF was tested for presence of VGKC antibodies and the test was positive for LGI (leucine-rich glioma inactivated 1) antibody. Therapeutic plasma exchange (TPE) was scheduled every day for 6 consecutive days based upon the recommendations from the ASFA guidelines for the treatment of neurologic syndromes.

Conclusion: TPE done every day in patient diagnosed LE with VGKC antibodies had shown rapid improvement in controlling the symptoms.

No of patients: 1 cases
No of exchanges: 6, everyday
Effectiveness of therapy: Adequate

Research Articles



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Original Article
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Keywords: American Society for Apheresis, pediatric, therapeutic plasma exchange

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Saudi J Kidney Dis Transpl 2018;29(3):698-704
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Keywords: Acute humoral rejection, graft survival, renal transplantation, therapeutic plasma exchange

Take Home Message!

- TPE is an effective modality
- ASFA categories are ready reckoner
- Has various indications across various systems
- In Categories I and II, therapeutic apheresis has known benefits
- For Categories III and IV, benefit may or may not happen. However, often the last modality
- Special considerations for special populations
- Selective TPE in some indications
- TPE is still evolving and it’s a long way ahead…..

Thank You