BASIS OF PLASMAPHERESIS & HOW TO PRESCRIBE IT

SEETHAL PADMANATHAN
ICU REGISTRAR
NEPEAN HOSPITAL
What is Plasmapheresis?
Separation of blood into cellular and fluid components offers the opportunity to discard or modify those components. Accomplished by either a centrifuge or by porous membrane filtration. No size barrier.
For therapeutic plasmapheresis to be justified, the disease process must have

- a circulating factor involved in pathogenesis,

- expected to persist in the circulation without sufficiently rapid endogenous clearance,

- acutely toxic and/or resistant to conventional therapy
Modalities of plasmapheresis

- **Plasma exchange** - whole plasma is removed in bulk and replaced with replacement fluid, usually 4% albumin.

- **LDL apheresis** - triglycerides and cholesterol are removed from the plasma, and the plasma is reinfused into the patient.

- **RBC apheresis** - red cells are separated from donor blood for storage and later re-transfusion.
- **RBC exchange** - defective red cells are removed from a patient and "good" red cells are retransfused

- **Platelet apheresis** - donated blood undergoes separation so that platelets can be stored for separate use; or for removing platelets and discarding them in patient’s with severe thrombocytosis.

- **Leukopheresis** - leukocytes are separated from the blood
  - to remove defective cells or to harvest the white cells for transfusion
Extracorporeal photopheresis is a variety of leukopheresis where the white cells are exposed to UV light after being treated with psoralen (a weird mutagen which intercalates into DNA upon exposure to ultraviolet radiation). The mutant leukocytes are then reinfused into their original host so they might undergo apoptosis and trigger a variety of immunomodulatory effects.
Methods of blood separation by plasmapheresis apparatus

- **Size-based separation** using porous filters (less common)
- **Density-based separation** using centrifuges (more common)
For every 1-1.5 plasma volumes exchanged, about 60-70% of the plasma substances are removed.

For every subsequent volume exchanged, the absolute amount of the substances decreases but the proportion remains the same.
Disease-causing blood components one might want to extract:

- Antibodies
- Immune complexes
- Abnormal plasma proteins, eg. myeloma light chains
- Immunoglobulins
- Protein-bound drugs
- Monoclonal antibody drugs, eg. rituximab
- Cryoglobulins
- Bacterial endotoxin
- High molecular weight toxins, eg. animal venom
- Cholesterol-containing lipoproteins /triglycerides
- Abnormal cells (eg. leukaemia blasts, excess RBCs or platelets)
Desirable molecules removed by plasma exchange and not replaced with standard replacement fluids:

- Antithrombin
- Pseudocholinesterases and plasma esterases
- Useful antibodies, including monoclonal biological agents
- Useful medications
- Nutrients, eg. glucose, amino acids, water-soluble vitamins
- Diagnostically interesting antibodies (i.e. for serology)
Indications for urgent plasma exchange

- Thrombotic thrombocytopenic purpura
- Catastrophic antiphospholipid syndrome
- Hyperviscosity syndrome (e.g. myeloma)
- Guillain-Barre syndrome
- Myasthenia gravis
- Acute fulminant hepatitis with encephalopathy
- *Amanita phalloides* poisoning
Less urgent plasma exchange:

- Erythrodermic cutaneous T-cell lymphoma
- Wegeners granulomatosis
- Goodpasture's syndrome
- Eaton-Lambert syndrome
- Babesiosis
- Autoimmune haemolytic anaemia
- Cryoglobulinaemia
- Dermatomyositis/polymyositis
- Hemolytic uremic syndrome
- Familial hypercholesterolaemia
- Focal segmental glomerulosclerosis
- Paraproteinaemic polyneuropathy
- Antibody-mediated renal transplant rejection
- Fulminant Wilson's disease.
DISEASE AND DISORDERS TREATED WITH PLASMA EXCHANGE
Disease

ABO-incompatible hematopoietic stem cell transplantation
  BM
  Peripheral blood

ABO-incompatible solid organ transplantation
  Kidney
  Heart (age < 40 mo)
  Liver

Acute disseminated encephalomyelitis

Acute inflammatory demyelinating polyradiculopathy (Guillain-Barré Syndrome)

ANCA-associated rapidly progressive glomerulonephritis/vasculitis
  (Wegener granulomatosis)
  Dialysis independent
  Alveolar hemorrhage
  Dialysis dependent

Antiglomerular basement membrane disease (Goodpasture syndrome)
  Dialysis independent
  Alveolar hemorrhage
  Dialysis dependent

Aplastic anemia
Autoimmune hemolytic anemia
  - Warm
  - Cold agglutinin disease (life threatening)
Catastrophic antiphospholipid Ab syndrome
Chronic focal encephalitis (Rasmussen encephalitis)
Chronic inflammatory demyelinating polyradiculopathy
Cryoglobulinemia
Focal segmental glomerulosclerosis (recurrent)
**Hemolytic uremic syndrome**
  - Complement factor gene mutations
  - Autoantibody to factor H
  - Diarrhea associated
Hypertriglyceridemic pancreatitis
**Hyperviscosity in monoclonal gamopathies**
  - Symptomatic
  - Prophylactic for rituximab treatment
**Multiple sclerosis**
  - Acute CNS demyelination unresponsive to steroids
  - Chronic progressive
Myeloma cast nephropathy
Neuromyelitis optica
<table>
<thead>
<tr>
<th>Paraproteinemic polyneuropathies</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgG/IgA</td>
</tr>
<tr>
<td>IgM</td>
</tr>
<tr>
<td>Multiple myeloma</td>
</tr>
<tr>
<td>Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS)</td>
</tr>
<tr>
<td>Phytanic acid storage disease (Refsum disease)</td>
</tr>
<tr>
<td>Posttransfusion purpura</td>
</tr>
<tr>
<td>RBC alloimmunization in pregnancy</td>
</tr>
<tr>
<td>Renal transplantation, Ab-mediated rejection</td>
</tr>
<tr>
<td>Renal transplantation desensitization</td>
</tr>
<tr>
<td>Scleroderma</td>
</tr>
<tr>
<td>Sepsis with multiorgan failure</td>
</tr>
<tr>
<td><strong>Systemic lupus erythematosus</strong></td>
</tr>
<tr>
<td>Severe complications of vasculitis</td>
</tr>
<tr>
<td>Nephritis</td>
</tr>
<tr>
<td>Thrombotic thrombocytopenic purpura</td>
</tr>
<tr>
<td>Thyroid storm</td>
</tr>
</tbody>
</table>
COMPLICATIONS OF PLASMA EXCHANGE

1) Due to the circuit exposure

- Haemolysis and thrombocytopenia
- Low fibrinogen and coagulopathy
- Hypothermia
- Complement activation
2) Due to anticoagulation

- Paraesthesia due to hypocalcemia (due to regional citrate anticoagulation)
- Bleeding complications
- HITS
3) Due to the replacement fluid

- Urticaria
- Febrile reaction to blood products
- Anaphylaxis
4) Due to the unavoidable removal of useful blood components

- Loss of useful drugs
- Immunosuppression
- Anaphylaxis
- Hypothermia
5) Due to volume loss

- Hypotension
- Vasovagal syncope
- Nausea and vomiting
How to prescribe plasma exchange
- Volume to remove
- Replacement solution given
- Machine: centrifugal or membrane
- Access
- Anticoagulation
- Frequency
Volume to remove

* depends on patient’s size and haematocrit

* 1 – 1.5x plasma volume
$y = e^{-x}$
CALCULATING TOTAL BLOOD VOLUME & PLASMA VOLUME

- Gilcher's Rule of Fives
- Blood volume (ml/kg body weight)

<table>
<thead>
<tr>
<th></th>
<th>Obese</th>
<th>Thin</th>
<th>Normal</th>
<th>Muscular</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>60</td>
<td>65</td>
<td>70</td>
<td>75</td>
</tr>
<tr>
<td>Female</td>
<td>55</td>
<td>60</td>
<td>65</td>
<td>70</td>
</tr>
</tbody>
</table>

- One plasma volume = TBV x (1 – Hct)
REPLACEMENT SOLUTIONS

- FFP
  - Full FFP replacement in TTP
  - Partial FFP replacement in diffuse alveolar haemorrhage (DAH), bleeding, procedure and severe depletion coagulopathy
  - ANCA associated vasculitis post renal biopsy or with DAH
5% Albumin

Most procedures (Myasthenia gravis, Guillain-Barre, NMDA-R encephalitis etc)

Combination of saline and albumin

Colloid should not be less than 50% of total infused, risk for hypotension
Plasma regeneration

- Patient’s own plasma is purified on line and reinfused as replacement volume
- Selective procedures/columns (LDL apheresis)
Centrifugal Plasmapheresis

Can perform separation of all blood compartments: plasmapheresis, leukapheresis, RBC exchange, platelet depletion

COBE Spectra

Fenwal Amicus

Spectra Optia
Membrane Based Plasmapheresis

Dialysis equipment that has additional functionality – PLASMAPHERESIS ONLY

PrismaFlex

NxStage
Plasmapheresis: Centrifugal Based Separation

- Kits designed to remove specified cell layer based on specific gravity
- Blood flow rates can range 10-100ml/min
- ACD-A (citrate) anticoagulant (heparin occasionally used)
- Packs RBCs to Hct of 80% or higher
  - Remove 80% or more of plasma → ~1.5xTBV processed to achieve 1.2xTPV
PLASMAPHERESIS: MEMBRANE BASED SEPARATION

- Plasma separated from other cellular components based on size.

- Whole blood flows through the hollow fibres of the filter and plasma flows through the pores (0.2 to 0.6µm) in the fibre wall

- Blood flows typically 150ml/min

- Heparin is the typical anticoagulant

- Extracts 30 – 35 % plasma, so 3 to 4 times TBV processed to achieve target plasma removal
SUMMARY

> Apheresis schedule should be determined by
  - Patient’s condition
  - Pathologic substance targeted for removal
  - Desired clinical and/or laboratory endpoint

- ASFA guidelines for TPE are divided into 4 categories based on evidence of clinical efficacy
References

- Deranged physiology
- UpToDate