Therapeutic Plasma Exchange & Red Blood Cell Exchange

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Disclosure

- I have no actual or potential conflict of interest in relation to this presentation.
TA Procedures

- Plasma exchange (TPE)
- Erythrocytapheresis/RBC exchange
- Leukocytapheresis
  - WBC reduction
  - Peripheral blood progenitor cell collection
- Plateletapheresis
- LDL Apheresis
- Extracorporeal photopheresis (ECP)
- Immunoadsorption (IA)
TA Procedures

- Plasma exchange (TPE)
- Erythrocytapheresis/RBC exchange
Basic Principles

- Substance in blood causing disease
- If you remove the substance, you will alleviate the patient’s disease
Blood Processing

- Usually process a large volume (approximately one blood volume or more for many indications)
- Separation
  - Centrifugation
  - Filtration
- Removal
- Replacement (necessary for TPE, RBCx)
- Reconstitution
- Reinfusion
Remove

- Plasma (proteins, drugs, other toxins)
- Red cells (SCD, Malaria, Babesia, Incompatible blood)
Replacement

- Patient Plasma -> Colloid (albumin, plasma, starch), crystalloid (normal saline 0.9%)
- Patient Red cells -> donor pRBC
- One compartment model
Synthesis

Lymphatic Return

Intravascular Compartment

Diffusion

Extravascular Compartment

Transmembrane Flow

Catabolism

Apheresis Device

adapted from Weinstein, 1997

Slide courtesy of Robert Weinstein, MD
TA Procedures

- Plasma exchange (TPE)
- Erythrocytapheresis/RBC exchange
Mechanism

- Replacing a substance that is lacking in the plasma
  - Patient’s plasma removed to “make room for” normal plasma (necessary to avoid volume overload)
- Removal of a substance in plasma that is causing disease (usually a protein)
- Sometimes both
Replacement of Lacking Substance

- Protein in plasma that is not able to be replaced using a commercially available product
- Possible to infuse large amounts of plasma if there is a deficiency of a plasma protein (TTP/HUS)
Removal of Pathogenic Substance

- Autoantibody (AIDP, MG, Wegener’s, Goodpasture’s, TTP)
- Alloantibody (ABO/HLA incompatible transplant, transplant rejection)
- Immune complexes
- Monoclonal Ig (Myeloma)
- Cryoglobulin (Cryoglobulinemia)
- Drugs (natalizumab)
Why is Plasma Exchange Efficacious

- **Immunosuppression reduces further production** over days to weeks
  - $T \frac{1}{2}$ of IgG = 21 days (medications will not decrease circulating antibodies for **weeks or months**)
- TPE can rapidly remove preformed antibodies
  - Indicated if antibodies are acutely toxic
- Can remove toxins and immune complexes
- Can remove light chains in myeloma associated cast nephropathy
- Possible to infuse large amounts of plasma if there is a deficiency of a plasma protein (TTP)
Kinetics

- One PV exchange will replace ~65% of pt plasma
- Two PV exchange will replace ~85% of pt plasma
- 70-85% reduction in IgG can be achieved with 5-6 plasma exchanges over 2 weeks (w/ immunosuppression)
Kinetics
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Frequency

- Daily (TTP, HUS, CAPS, Hyperviscosity/Hypertriglyceridemia if >1 TPE needed, Acute life threatening presentations of other diseases)
  - Caution if not using plasma as part of the replacement fluid
- Every other day
  - many neurological disorders, renal disorders, transplant rejection (may need daily)
- Less frequently
TA Procedures

- Plasma exchange (TPE)
- Erythrocytapheresis/RBC exchange
RBC Exchange

- Blood is removed from the body
- Separation of components
- RBC removed
- Donor RBC and patient plasma used to reconstitute whole blood
  - Removal of platelets
  - No significant depletion of coagulation factors
- Reinfusion
RBC Exchange

- Sickle Cell Disease
- Parasitemia
  - Malaria
  - Babesiosis
- ABO incompatible HSCT (Minor incompatibility)
- Removal of abnormal red blood cells
  - Improved blood flow
  - Mechanical removal of parasites and/or abnormal (or incompatible) red cells
Kinetics
Parameters of RBC Exchange

- **FCR**
  - As FCR decreases, volume of red cells needed for the exchange increases
  - Often approximately 30%
  - May need lower FCR for severe malaria

- **End Hematocrit**
  - Considerations: Pre Hct, Iron overload, Bone marrow response to anemia

- **Frequency of exchanges**
How do we know these procedures (TPE and RBCx) work?
What are the risks?
Does it really work?

- Evidence based (VS plausible mechanism)
- American Society for Apheresis (ASFA) has published guidelines on the use of Therapeutic Apheresis in Clinical Practice
  - Evidence Based Approach
  - Categorization of Indications
Does it really work?

Answer:

- For some diseases: Yes (Category I, II)
- For some diseases: Maybe, depends (Category III)
- For some diseases: No (Category IV)
New Definitions 2010

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Disorders for which apheresis is accepted as first-line therapy, either as a primary standalone treatment or in conjunction with other modes of treatment. [Example: plasma exchange in Guillain-Barre syndrome as 1st-line standalone therapy; plasma exchange in myasthenia gravis as 1st-line in conjunction with immunosuppression and cholinesterase inhibition].</td>
</tr>
<tr>
<td>II</td>
<td>Disorders for which apheresis is accepted as second-line therapy, either as a standalone treatment or in conjunction with other modes of treatment. [Example: plasma exchange as standalone secondary treatment for acute disseminated encephalomyelitis after high-dose IV corticosteroid failure; extracorporeal photopheresis added to corticosteroids for unresponsive chronic graft-versus-host disease]</td>
</tr>
<tr>
<td>III</td>
<td>Optimum role of apheresis therapy is not established. Decision making should be individualized. [Example: extracorporeal photopheresis for nephrogenic systemic fibrosis; plasma exchange in patients with sepsis and multi-organ failure].</td>
</tr>
<tr>
<td>IV</td>
<td>Disorders in which published evidence demonstrates or suggests apheresis to be ineffective or harmful. IRB approval is desirable if apheresis treatment is undertaken in these circumstances. [Example: plasma exchange for active rheumatoid arthritis].</td>
</tr>
</tbody>
</table>

*The description of the ASFA categories have been amended and simplified in comparison to the 3rd and 4th Edition of the Special Issue[1,16]. Category P, which was introduced in the 4th Edition, has been eliminated.*
# Grade of Recommendation

**TABLE III. Grading Recommendations adopted from Guyatt et al [13]**

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Description</th>
<th>Methodological Quality of Supporting Evidence</th>
<th>Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1A</td>
<td>strong recommendation, high-quality evidence</td>
<td>RCTs without important limitations or overwhelming evidence from observational studies</td>
<td>Strong recommendation, can apply to most patients in most circumstances without reservation</td>
</tr>
<tr>
<td>Grade 1B</td>
<td>strong recommendation, moderate quality evidence</td>
<td>RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies</td>
<td>Strong recommendation, can apply to most patients in most circumstances without reservation</td>
</tr>
<tr>
<td>Grade 1C</td>
<td>strong recommendation, low-quality or very low-quality evidence</td>
<td>Observational studies or case series</td>
<td>Strong recommendation but may change when higher quality evidence becomes available</td>
</tr>
<tr>
<td>Grade 2A</td>
<td>weak recommendation, high quality evidence</td>
<td>RCTs without important limitations or overwhelming evidence from observational studies</td>
<td>Weak recommendation, best action may differ depending on circumstances or patients’ or societal values</td>
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<tr>
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<td>Weak recommendation, best action may differ depending on circumstances or patients’ or societal values</td>
</tr>
<tr>
<td>Grade 2C</td>
<td>weak recommendation, low-quality or very low-quality evidence</td>
<td>Observational studies or case series</td>
<td>Very weak recommendations; other alternatives may be equally reasonable</td>
</tr>
</tbody>
</table>
Risks/Adverse Events

- Most tolerate TA well, no anesthesia or sedation is usually required
- Not uncommon
  - Fatigue
  - Hypocalcemia
  - Hypotension
  - Coagulopathy (Bleeding is uncommon)
  - Transfusion Reactions
- Vascular access
  - Peripheral (minor risks)
  - Central (risk of life threatening events)
Vascular Access

- Peripheral usually preferred
- TPE vs RBCx
  - Flow rates
  - Frequency of procedures
  - Short term vs Long term need
Vascular Access

- **TPE**
  - Higher flow rates
  - Often temporary (but usually need to perform multiple procedures per week)
  - Non-tunneled VS Tunneled VS Ports

- **RBCx**
  - Lower flow rates often acceptable
  - Non-tunneled VS Tunneled VS Ports
Recent Enhancements

- TPE performed in tandem
  - Dialysis
  - ECMO

- Isovolemic Hemodilution with RBCx
  - Automated VS Manual
  - Reduction in blood exposure for patient and cost saving for institution
  - Caution in patients with recent ischemic events
Questions???