Photopheresis

Yesterday – Today – Tomorrow
What is Photopheresis?

- Photopheresis – is a form of **apheresis** in which **blood** is treated with photoactivable drugs which are then activated with **ultraviolet light**
- During the procedure
  - **buffy coat** (**WBC** + **platelets**) are separated from the whole blood
  - cells are then treated with **8–Methoxypsoralen**
  - exposed to ultraviolet light
  - returned to the patient
Overview of Photopheresis

- **The Good:**
  - What indications we using to initiate photopheresis
  - Our treatment schedule
  - Blood Priming – indications in small children and in patients with lack of ability to tolerate fluid shifts.
  - Outcomes. – indications in small children and in patients with lack of ability to tolerate fluid shifts.

- **The Bad:**
  - Managing patients with low body weight
  - Managing patients that do not tolerate fluid shift
  - Managing the instrument when there is abnormal plasma:
    - high bilirubin/liver enzymes
    - high triglycerides
    - Receiving TPN/lipids

- **The Ugly:**
  - Managing fluid balance in small children
  - System pressure and red cell pump alarms…..Don’t give up!
What Conditions Can Be Treated By Photopheresis

BMT Indications:
As prophylaxis for transplant
  GFR ≤ 65
  Pre Week –2; week –1 then following with WBC recovery
Acute gut, liver and skin GVHD – steroid refractory
Chronic GVHD (steroid refractory) including:
  Skin
  BOOP
  Gut/Liver

Other uses:
  CTCL
  Scleroderma
  Post lung/cardiac transplant
  Crohn’s Disease
  Other Severe Skin Conditions
Methoxsalen

- Known as Uvadex
- Dosed per volume of cells collected
- Manufactured from Bishop’s Weed found along the Nile River
What Happens to the Cells Undergoing Treatment

Collected Buffy Coat

Methoxsalen

Treated cells post UVA therapy
Apoptosis is a process of programmed cell death. Apoptotic Cells produces cell fragments called apoptotic bodies that surrounding antigen presenting cells are able to engulf and quickly remove before the contents of the cell can spill out onto surrounding cells and cause damage.
Mechanisms of Action

- Decrease in Pro-inflammatory cytokines
- Increase in Anti-inflammatory cytokines
- Generation of T-Regulatory Cells

The term "cytokine" encompasses a large and diverse family of regulators produced throughout the body by cells of diverse embryological origin.
Mechanisms of Action

- ECP therapy induces immune tolerance through modulation of antigen-presenting cells as well as the induction of regulatory T cells.
- Restores immune balance

Medication

Photopheresis
Instruments

- XTS for individuals over 40kg per manufacturer’s recommendations
  - Our experience 17kg or greater OK
- CellEx –able to blood prime –no weight limits
What are the Advantages & Disadvantages of each Instrument

<table>
<thead>
<tr>
<th></th>
<th>UVAR XTS System</th>
<th>CellEx System</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Prime option ?</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Weight Limit ?</td>
<td>Minimum Approved 40 kg</td>
<td>No lower weight limit.</td>
</tr>
<tr>
<td>Treatment Cycles/Volume ?</td>
<td>6 cycles standard</td>
<td>1500mL</td>
</tr>
<tr>
<td>Treatment Time ?</td>
<td>3.5 – 4.0 hrs</td>
<td>1.5 – 3.0hrs</td>
</tr>
<tr>
<td>Ending Volemia ?</td>
<td>± 500mL</td>
<td>± 150mL</td>
</tr>
<tr>
<td>Access</td>
<td>Single site</td>
<td>Single or Dual site</td>
</tr>
<tr>
<td>Training</td>
<td>Easy to use</td>
<td>More Complex</td>
</tr>
</tbody>
</table>
Anticoagulation

- **Heparin**
  - Primarily used for all procedures
  - Anticoagulates systemically
  - Metabolized slowly (1 to 2 hours)
  - Can cause heparin-induced thrombocytopenia

- **ACD–A**
  - Citrate binds free ionized calcium to prevent blood from clotting
  - Heparin: Thrombin has been inactivated, preventing thrombus formation
Access

- Dual lumen dialysis catheter

- Triumph 1 ports
  - 7.5 or 9.6 French

- Power PICC
  - 5 or 6 French
Maintaining HCT – 28%

- Blood Prime Procedures
  - Can use some of the Red cells from the PRBC unit if patient can tolerate increased volume to maintain HCT 28% or greater.
    - We give approximately 10/kg if HCT borderline after obtaining physician order
      - Patient already exposed to unit thus limits need for d for additional transfusion

- Non–Blood Prime Procedures
  - Transfuse as needed
BMT Treatment Schedule:

- **Initiating therapy** – both pediatric and adult patients – 5 days/week x 4 weeks
- **Tapering**
  - Monthly reduction by 1 day/week
  - Never taper immunosuppression drugs the week prior to or the week after tapering photopheresis
When To Initiate Therapy

BMT:

- **First line treatment** – methylprednisolone at 1–2mg/kg.
  - Therapy effective – if there is stable disease (no progression) after 2 days of treatment and a response (improvement) after 5 days.
  - Patients with significant progression of disease after 2 days or no evidence of a response after 5 days will be considered to have steroid refractory GVHD.
  - **Note**: Recent studies have shown no benefit to higher doses of steroids in patients that have not responded to 2mg/kg.

- **Second line treatment** of steroid-refractory GVHD is MMF at 15mg/kg three times daily.
  - Patients with significant progression of disease after 3 days or no evidence of a response after 7 days will be considered to have refractory GVHD.

- **Third line treatment** of steroid-refractory GVHD is Photopheresis
  - Patients with significant progression of disease after 3 days or no evidence of a response after 7 days will be considered to have refractory acute GVHD.
Other Conditions – Treatment Schedule

- **Initiating Therapy** – both pediatric and adult patients – 2 consecutive days x 6–8 weeks
  - Looking for a response – may extend longer

- **Tapering** – 2 consecutive days every other week x 4–6 cycles
  - Followed every 3 weeks then to monthly
  - At 1 year consider discontinuing
Why Are We Aggressive?

BMT:
- Quick turn around in patient’s condition = shortened hospital stay → better outcome

Other Conditions:
- Overall improvement in disease
- Patient satisfaction – compliance to treatment plan

Example:
- CTCL patient receives treatments 2 consecutive days monthly No improvement seen for 4–6 months
- Patient becomes discouraged, seeks other means of treatment
- Aggressive upfront therapy – improves outcome reduces the need to become aggressive with other medical regimens (chemo, interferon = side effects)
Pre Treatment Instructions

- The evening before the treatment:
  - Eat a low-fat meal.
  - You should avoid foods such as high fat meats, fried foods, cheeses, eggs, butter and desserts.
  - **Reason:** High levels of fat in the blood can interfere with the cell-separation process and could result in the procedure being stopped before completion.

- The day of treatment:
  - Eat a low-fat breakfast and lunch.
  - Do not skip any meals.
  - If you are taking any medications please inform the nurse performing the procedure.
Procedure

Collecting Buffy Coat

Injecting Uvadex into the collected cell bag

Collected cells/Return Bag

Photoactivation Chamber
Blood Priming

Why?

- Low body weight – calculate patient’s total blood volume
  - determine “safe” ECV range – 10–15% of TBV
    - If exceed 15% TBV or patient does not tolerate fluid shifts
      - Prime Instrument
  - Patients that do not tolerate fluid shift – including pulmonary, cardiac or renal insufficiency patients

What do we use?

- Compatible Packed Red Blood Cell unit – 300mL volume
  - We do not dilute PRBC unit to patient HCT – but do add 100mL NS to the unit + return of prime solution
What Volume to Process?

- Non blood prime procedures
  - 1500 mL per treatment = 6 cycles on UVAR XTS

- Blood prime procedures
  - 1500 mL plus the amount processed to prime the instrument – roughly 1800 mL

- Why?
  - Validation showed that WBC counts on collected cells were significantly improved the more processed
    - With prime approximately 3–4 times patient starting WBC
    - Without prime approximately 6–8 times the patient starting WBC
Flow Rates

Non Prime Procedures
- Maximum collect rate 35 mL

Blood Prime Procedures
- During priming do not exceed 20mL
- After prime increase based on child’s size and line function 15–35 mL
Calcium Replacement

Calcium Gluconate

- 5 grams added to 50 mL Normal Saline = 100 mL volume.
  - Approximately 50 mg/mL.
- Infusion Rate initially started at 10 mL/hr (500 mg/hr).
  - Must use an infusion pump.
- Monitor ionized calcium levels:
  - Initially
  - 15 minutes
  - 30 minutes
  - Then every 30 minutes unless needed more frequently performed at bedside using i STAT®.
- Adjust infusion rate as warranted by testing results.
Post Treatment Instructions

- **Skin Protection:**
  - The medication UVADEX® used for the treatment can increase your risk of sunburn. Avoid direct sunlight including through windows.
  - Protect areas of skin including hands, face, neck, ears, etc. with sun screen (SPF 15 or greater) continuously until 24 hours after the treatment.
  - Patient that undergo treatment two days in a row must use sunscreen continuously until 24 hours after the last treatment.

- **If you experience:**
  - Difficulty breathing, chest pain or a feeling of heaviness in your chest, fever of 101°F or greater, OR other concerning symptoms following the treatment please contact your attending physician immediately.
Post Treatment Instructions

Eye Protection:
- The medication UVADEX® used for the treatment in combination with sunlight can contribute to the formation of cataracts.
- PUVA Glasses **must** be worn when the cells are reinfused and they must be worn continuously except when sleeping until 24 hours after the treatment.
- Patient that undergo treatment two days in a row must wear the PUVA glasses continuously except when sleeping until 24 hours after the last treatment.
What impacts outcome?

- The sooner treatment is initiated the better the chance of a positive outcome
- Tapering of other therapies and photopheresis treatments must be done at a different intervals otherwise impact is unknown
- Compliance with all treatment therapies
  - Following through with medications
  - Compliance with photo schedule
When Problems Exist

- Managing patients with low body weight
- Managing patients that do not tolerate fluid shift
- Managing the instrument when there is abnormal plasma:
  - high bilirubin/liver enzymes
  - high triglycerides
  - Receiving TPN/lipids
Managing Children Under 15kg

- Blood Prime instrument
- Determine if Buffy Coat to be harvested from PRBC unit or patient
  - 6–12 kg kids mainly harvest from PRBC unit
  - 12 – 15 kg dependent on how stable child is
- End Buffy Coat early – HCT no more than 16%
  - Reduces reinfusion volume
- Monitor ionized calcium levels closely until appropriate infusion rate is determined
  - Understand the instrument has an increased anticoagulant infusion at initiation and reinfusion so may need to adjust calcium gluconate infusion rate initially to be higher and then reduce during procedure unit 20 minutes prior to completion
What Do You Do If The Patient Cannot Tolerate Fluid Shifts?

- Blood Prime regardless if required by calculation of Safe ECV
- Determine maximum intake – usually set at 15% of TBV
- Watch Buffy coat harvest closely and stop once –% is reached
  - Instrument automatically stops the buffy coat harvest at 24%
    - Ending Buffy early reduces volume as well as reduces photo time
Lipemic Plasma

- Why as patient not on high fat diet
  - Drugs such as MMF and Cyclosporine cause hyperlipidemia

What can we do?

- Attempt to decrease Bowl Optic Sensor – red cell pump alarm
- We have had to plasma exchange prior to performing photopheresis
Neon Plasma

- Neon plasma linked to liver enzyme elevation especially elevated bilirubin
  - Bright yellow usually ok
  - Dark neon – usually instrument looks at it as Red Cells
    - Watch hematocrit on screen if rapidly rises to 3 – remove HCT sensor until line becomes pink and then replace sensor allowing you to collect a good buffy coat
Diet and TPN – What role does it play in the treatment?

- **TPN that contains lipids vs TPN with piggybacked in lipids**
  - Prefer piggyback lipids so we can control infusion time – following photopheresis
  - Discontinue TPN approximately 2 hours prior to treatment

- **Food during the treatment process**
  - We do not limit

- **Diets pre treatment**
  - Attempt to limit McDonald’s and high fat content foods – not always possible
System Pressure Alarms

- Frequently only option is – turn machine off
  - Wait for bowl to stop
  - Verify the tubing in the key holes is not kinked – adjust if needed
  - Restart watching for the purging of air in the return bag
  - If air not removed – stop again – tap bowl and restart
Red Cell Pump Alarms

- So Much Fun!!!
  - Adjustments to Bowl Optic Sensor
    - Schedule advanced user training with Therakos
Adverse Events

- Volume related:
  - Hypotension
  - Nausea
  - Lightheadedness/dizziness

- Skin: will have an increase in redness for approximately 24 hours after the treatment

- May have mildly elevated temp 100.5 due to treatment
Questions