Mobilization & Pre-Transplant Conditioning Regimens

Mobilization

Transplant Process

Mobilization

• A technique used to increase the number of circulating hematopoietic stem cells from the bone marrow into the bloodstream
• Only used for patients undergoing a peripheral blood stem cell transplant (not bone marrow transplant)

The premise of mobilization is based on the following...
• Progenitor cells begin rapid reproduction when depletion is recognized
• Depletion occurs by natural processes (aging/illness) and by artificial means (cell depletion by chemotherapy)
• Artificially causing depletion will result in an increase in progenitor cell counts
• Excess progenitor cells in the bone marrow will be forced into the peripheral blood
• Stem cells can be harvested, or collected, from the peripheral blood

Who gets “mobilized”?

The patient
• Auto PBSCT
• The patient IS the donor
• May receive:
  – Growth factor ONLY (in remission or autoimmune disease)
  – Chemo followed by growth factor (disease present)

The donor
• Allo PBSCT
• Family member or unrelated donor
• ONLY growth factor (because the donor has no disease)
Who doesn’t get mobilized?

- Immunotherapy patients
- These patient’s are collected with the cells in natural state and are “expanded” or “grown” after collection
- The goal of these cells are not to re-set the immune system but rather to augment and enhance the immune response

Mobilization: Growth Factor Alone

- Standard (after chemo): 300-480mcg daily until after chemotherapy nadir
- Mobilization dosing: 10-32mcg/kg QD (or divided and administered BID) until apheresis complete
- Side Effects
  - Bone Pain (reported at 86%)
  - Headache (reported at ~40%)
  - Injection-site irritation
  - Flu-like symptoms
  - Extremely Rare - Splenic rupture
  - Long-term sequelae are unknown but following healthy donors for more than 20 years has shown no greater health complications than healthy siblings

Allo Mobilization: Growth Factor Alone

- Donor scheduled in apheresis for orientation and vein check to determine appropriate access
- Check pregnancy test prior to administration of G-CSF (unsafe for pregnant women to receive G-CSF at these doses)
- Review side effects and management
- Begin injections on patient’s day -5 (after conditioning has started)
- Give injections in am (so peak effect is prior to apheresis)
- Give injections on day -1 +/- patient’s day 0, G-CSF should be given 3-4 hours before apheresis on these days
- Assess daily for bone pain, fever, allergic reactions
- G-CSF is discontinued when an adequate number of stem cells have been collected (usually ≥ 5 x 10^6/kg)
- Answer any donor questions about the collection process.

Mobilization: Chemotherapy & Growth Factor – Autologous only

- Many chemo regimens that are being used simply to treat disease have been used successfully as mobilization chemotherapy with the addition of G-CSF
- Some patients are more difficult to mobilize and may receive more than one “round” of mobilization chemotherapy
- High-dose cyclophosphamide is the most common agent used in mobilization and can be used alone, in combination with dexamethasone or in combination with other chemotherapy drugs
- Patient will be apheresed about 24 hours after the WBC has recovers to > 1,000 or when the CD34+ counts are > 5 in the peripheral blood
- Growth Factor is discontinued after final day of apheresis

Mobilization: Chemotherapy & Growth Factor

Advantages
- Additional “cell kill” for known or microscopic disease
- Additive effect for mobilization by using both chemotherapy and growth factor

Disadvantages
- Larger doses of chemotherapy may be used, placing patient at risk for complications from prolonged neutropenia
- Patient may experience fevers, mucositis, pain, nausea, vomiting, diarrhea, dehydration, malnutrition, and fatigue

Plerixafor

- Administered with GCSF to improve mobilization for patients that do not mobilize well.
- Most commonly used for patients who have had many previous rounds of chemo and marrow is slower to recover
- In a study of MM patients, patients receiving plerixafor had 3.5X higher CD34+ counts and 2.5X higher cell yield in apheresed product.
- Very expensive (around $12K per injection).
- Timing of apheresis collection important, it must be started 10-14 hours after the injection given.
- Side effect to GI tract more common, loose stool or diarrhea.
Pre-transplant Conditioning Regimens

What is Conditioning?

• “Preparative” regimens which condition or “prepare” the patient’s bone marrow to accept transplanted stem cells
• May involve high-dose chemotherapy with or without radiation therapy and/or radioimmunotherapy
• Typically lasts 4-10 days
• These are the days immediately preceding transplant and are “countdown” days

Goals of Conditioning

• Eradicate residual malignancy
• Suppress patient’s immune system to prevent graft rejection
• “Ablate” the patient’s bone marrow completely to allow space for donor stem cells (myeloablative)
• “Create space within” the patient’s bone marrow enough to allow the patient to accept the donor stem cells (non-myeloablative and immunotherapy)

Type of Regimen Depends Upon...

• Disease (malignant or nonmalignant)
• Type of transplant (autologous or allogeneic; myeloablative or non-myeloablative)
• Medical condition of patient
• Patient/provider preference
Inpatient or outpatient?

- What is the conditioning?
- What is the supportive care necessary?
- How is the patient tolerating the conditioning?
- Is there a protocol requirement?
- Does the patient have pre-existing comorbidities?
- Pediatric patients are generally admitted if under 18

**CONDITIONING CHEMOTHERAPY**

**Conditioning Chemotherapy**

- Major component of most conditioning regimens
- Single agent or combinations of agents with or without TBI and/or radioimmunotherapy

**Conditioning Chemotherapy: Agents**

- Cyclophosphamide (Cytoxan)
- Busulfan
- Etoposide (VP-16)
- Melphalan
- Thiotepa
- Carmustine
- Cytarabine
- Fludarabine

**Conditioning Chemotherapy vs standard chemotherapy**

- Doses usually significantly higher
- Often dosed in mg/kg instead of usual mg/m2
- Higher doses usually means potential toxicities are greater and require more supportive care
- Standard chemo is given in cycles
  - Conditioning chemotherapy is only given in a single cycle

**ATG**

- Anti-Human Thymocyte Globulin Equine (ATG) – ATGAM
- Anti-Human Thymocyte Globulin Rabbit (ATG) – Thymoglobulin
- Depletes T cells
- Used as conditioning for autoimmune or aplastic anemia
Anti-Human Thymocyte Globulin (ATG): Side Effects

- Sensitivity reactions, anaphylaxis
- Fever, chills, headache
- Rash
- Hyperkalemia
- Abdominal pain, diarrhea
- Weakness
- Dyspnea

Anti-Human Thymocyte Globulin (ATG): Nursing Considerations

- Skin test @ 1 hr prior to first dose of ATGAM, not Thymoglobulin
  - NO EMLA/LMX
- Anaphylaxis medications at bedside
- Premed with methylprednisolone (ATGAM only)
- Transfuse platelets after ATG infusion – ATG eats platelets

Conventional Radiation vs TBI

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<thead>
<tr>
<th>Conventional Radiation</th>
<th>Mini TBI</th>
<th>TBI</th>
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<tbody>
<tr>
<td>• Conventional</td>
<td>• Mini TBI</td>
<td>• Myeloablative</td>
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<tr>
<td>• 180 – 200/day one time a day for 4-8 weeks</td>
<td>• 200 gy one time dose</td>
<td>• TBI (150-200 gy two times a day for 3-4 days)</td>
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<tr>
<td>• Adults: May be at SCCA or UWMC</td>
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<td>• Babies: all will be at UWMC</td>
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<td>• Pedo: UWMC only</td>
<td>• Pedo: Pediatric patients under the age of 6 are sedated</td>
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TBI Pretreatment Preparation

- Consult and Simulation
  - Pretreatment planning
  - X-ray of lungs taken
  - Lead Blocks developed to shield lungs – used for 3 of 6 or 4 of 8 treatments
- Orientation to TBI and education
- Confirm orders written, signed Roadmap in place, transportation arranged if needed

TBI Pretreatment Preparation

- Purpose of TBI
- Treatment location
- Anticipated duration of treatment
- Where family members accompanying patient can wait
- Patient monitoring – no one is in the room but a camera is focused on the patient
- Anticipated side effects/management
- NO CHG baths during RT

RADIATION
### Patient Preparation Prior to TBI Transport

- Remove all jewelry, metal, tight fitting garments (check pajamas for metal)
- Remove all ointments, creams, powders, deodorants, perfumes or lip balms
- Remove contacts
- Pick out music
- Void
- Pre-hydration
- Anti-emetics and/or sedatives
- Nursing Handoff

### TBI: Side Effects

- **Fatigue**
  - Almost all patients report decrease in energy level and inability to concentrate
  - Onset of fatigue typically 3rd or 4th TBI treatment day
- **Nausea/Vomiting**
  - Usually peaks 1.5 – 2 hours after TBI
  - Prophylactic antiemetics always given before treatments
  - PRN antiemetics for breakthrough nausea and vomiting up to 48 hrs after last treatment; may be administered ATC
- **Diarrhea**
  - Onset generally within 48 hours of therapy
  - Duration – may continue for week or two after TBI – consider contribution of other conditioning agents and other causes

### TBI: Side Effects (continued)

- **Xerostomia**
  - Almost all patients experience dry mouth by 3rd or 4th treatment day
  - Dental consults prior to TBI
  - Reinforce oral hygiene programs
- **Alopecia**
  - Usually occurs gradually within 2 weeks
- **Mucositis**
  - Develops 5-7 days after treatment started
  - Tends to worsen over next week
  - Usually resolves 3-4 weeks after treatment

### TBI: Side Effects (continued)

- **Skin Reactions**
  - Mild erythema of skin common in first days following TBI
  - More common in patients receiving cyclophosphamide or thiotepa prior to TBI
  - Moist erythema may develop over elbows, heels, fingertips
  - Hyperpigmentation may occur 2-3 weeks following TBI

### TBI: Side Effects, Late

- **Gonadal Dysfunction**
  - 95–100% of females develop early menopause and sterility
  - 90–95% of males have absent spermatogenesis
  - 80% of children experience abnormal pubertal development
- **Thyroid Dysfunction**
- **Cataracts**
  - Approximately 20% of patients develop cataracts within 3 years of treatment
- **Pulmonary Damage**
  - Interstitial pneumonitis
  - Restrictive pulmonary disease
- **Neurologic complications**
  - Leukencephalopathy
  - Chronic neurologic changes
- **Secondary malignancies**
- **Growth impairment in children**

### Radioimmunotherapy

- **Biologic therapy (e.g. rituximab, tositumomab) combined with I-131 or Y-90**
- Most common with lymphoma diagnosis
- Lymphoma must be CD+ (e.g. CD20)
- Targets malignant cells, spares healthy cells
- Used in combination with chemotherapy
- Requires radiation isolation precautions
  - Varies dependent on type of radioisotope used
Conclusion

- Side effects of treatment and a patient’s course through transplant will greatly depend upon their conditioning regimen.

- Mobilization may change, Conditioning may change but the end goal will never change:

  Eradicate disease and increase event-free survival!