Troubleshooting MNC Collections in the Unmobilized vs Stimulated Donor

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Happy Nurses Week

NURSES HEAL THE WORLD!
Objectives

- Review types of leukapheresis collections available
- Discuss differences and similarities between various MNC protocols for collections
- Identify techniques and strategies to maximize efficiency and meet product specifications
Leukocyte collections in the Apheresis Program

- Many apheresis units offer numerous types of leukocyte collections
- Increase in stimulated and unstimulated MNC collections
- Drive the core business behind the scenes.
History of Leukapheresis

• Dr Carl De Laval invents hand-cranked cream separator in 1877
• Edwin J. Cohn develops centrifugal blood separator in 1951
• Emil Freireich develops NCI-IBM 2990 & IBM 2997 blood separator for use in leukemic patients in 1963 & 1973
What procedures do we perform?

**Collections**

- Stem Cell Collections (HPC)
- DLI Collections
- Dendritic Collections
- Monocyte Collections
- Photopheresis
- Granulocyte Collections
What machines do we use?

- Spectra
- Optia
- Amicus
- XTS
- Cellex
**Centrifugal Apheresis**

- **Plasma**
  - 1.025 - 1.029

- **Platelets**
  - 1.040

- **Lymphocytes**
  - 1.050 - 1.061

- **Monocytes**
  - 1.065 - 1.069

- **Granulocyte**
  - 1.087 - 1.092

- **RBC**
  - 1.078 - 1.114
Cobe

3D-Studio Max

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Types of Leukocyte Collections

**Stimulated**
- HPC Collections – auto or allo
- Cellerent - Allogeneic
- Granulocyte collections - Allogeneic

**Unstimulated Donors**
- Autologous:
  - Dendreon
  - Argos
  - DCVax
- Allogeneic:
  - DLI collections
Stem Cell Collection
“HPC”

- Leukapheresis (MNC) collections to “harvest” the cells used for BMT
- Target Cell = Pluripotent Stem Cell
- Autologous and Allogeneic
- Unrelated: National & International Marrow Donor Registries
- Allos – Cytokine stimulation
- Autos: Chemotherapy &/or mobilization agents
Dose: $2-5 \times 10^6 \text{ CD34+}/\text{kg}$
Lymphocyte Collections

- Donor Lymphocyte Infusions – usually from bone marrow donor
- Target cell: mature lymphocytes
- Goal: induce graft-versus-tumor effect (GVT) for remission of cancer
- Donors = Unstimulated
- Dose: 1 x E8 cells/kg
Target cell: Monocytes

- “raw product” used to manufacture autologous anti-cancer vaccine
- Donors/patients are unstimulated
- MNC collection is performed on blood cell separator

Dendreon: PROVENGE

- Dose: $5 \times 10^6$ million autologous CD54+ cells activated with PAP-GM-CSF
Photopheresis

- Purpose: Combination of leukapheresis with photo-chemo-therapy to promote immune balance/tolerance
- Diseases:
  - CTCL
  - BMT related GVHD
  - Solid Organ rejection
  - BOS
- Buffy coat is separated and collected by machine into large reservoir in first phase of procedure; phase two involves addition of Psoralen to leukapheresis product & initiation of UVA exposure; final phase infuses/returns the treated cells/blood product back to patient. Replacement fluid is normally not necessary
- Dose: Unknown
Technical Challenges of Leukocyte Collections

PRODUCT

• Target Cell Dose for Each Collection
  • Donor/patient’s WBC Count and Differential
  • Amount of blood processed
  • Blood Cell Separator Efficiency & Operator Proficiency

• Concurrent Plasma Collection

• Purity of product
  • Target cells vs. unwanted cells
  • Role of RBC
  • Role of Granulocytes
  • Role of Platelets
Technical Challenges of Leukocyte Collections

DONOR

• Side effects from procedure
  • Hypocalcemia from Citrate Toxicity
  • Immobility during procedures

• Side effects of pharmacologic stimulation: Neupogen or Corticosteroids
Technical Challenges of Collections as they relate to the infusion of final product

RECIPIENT

- Sterility and Potency of Product
- Manufacturing can decrease cell yield
- ABO compatibility if allogeneic
- Possibility of transfusion reactions
- Infectious Disease Risk
- Unknown risks
Regulatory Requirements of Biological Product Collections

• Guidelines versus Regulations
Challenges of Regulations and Standards

• Screening & eligibility differences among patient and donor groups and various MNC protocols
• Determining Infectious disease risk
  • Drawing IDM’s and Health History Screening
• Labeling requirements
  • ISBT
  • Conditions on degree of product risk
• Constant state of change!
So how do we manage all of this ???
Maximizing MNC Collections: Importance of Venous Access

- Minimal risk to donor/patient
  - Benefit of the procedure > risk of venous access

- Types to consider:
  - peripheral venous vs. central venous

Goal = Select Lowest risk to donor/patient
Venous Access: MNC Collections

Peripheral Veins
• Two points of venous access:
  • 17-18 gauge for draw
  • 18-20 gauge for return
• Topical or local anesthetics can be used
• Best choice: safest

Central Vascular Access
• Dialysis type dual lumen catheter
• 10.5-13 Fr
• Must have documented confirmation of proper placement from MD before use

Special Tip: At all costs protect and preserve draw and return sites!
Peripheral Veins
Short term, single use

• Advantages:
  • Safest, fewest complications
  • Easy
  • Fastest

• Disadvantage:
  • Painful to patient/donor
  • Not all patients/donors have adequate veins for apheresis use
  • temporary

Special Tip: Develop the best “phlebotomists” and take extra time to assure success!
What if CVC is not working during collection?

- Reposition patient
  - Take deep breath, turn head/neck various positions, raise corresponding arm over head, place in Trendelenburg, turn on side
- Slow down inlet rate/speed
- Assess and “re”flush catheter
- Call doctor for possible TPA admin or surgical reposition or replacement of CVC
- Does patient have an adequate peripheral vein that could be used to get through today’s procedure?
Maximizing MNC Collections: Importance of Anticoagulation, AC:WB ratios, and Inlet Flow Rate

- Slower flow rates than TPE…. 30-80 ml/min
- Depending on BCS, dwell time in centrifuge may be critical to meeting product yields
- Clumping is not good…. 
- Majority of anticoagulant goes back to donor/patient, hypocalcemia can be a significant Problem for some donors!
Anticoagulation

- Citrate versus Heparin
- Heparin is sometimes used in conjunction with ACDA
- Advantages of heparin: systemic effects vs. NO hypocalcemia!
  - MOA – Binds AT III – inactivates Thrombin & Factors Xa & Thrombin (IIa)
- Advantages of ACDA: superior anticoagulant extracorporeal anticoagulation only!
  - MOA – binds Ca++
Maximizing MNC Collections: Importance of Minimizing Alarms & Procedure Stops

- What is causing the alarms?
- If alarms are flow related, slow down inlet rate/speed
- Assess and “re”flush catheter needles sites
- If CVC, correct the problem: Call doctor for possible TPA admin or surgical reposition or replacement of CVC
- Does patient have an adequate peripheral vein that could be used to get through today’s procedure?
- Procedure stops: bathroom breaks, eating, not “squeezing”
- Remember our goal & priority?
What if donor/patient is having a hypocalcemic reaction during collection?

Remember the causes of hypocalcemia during Apheresis

- ACDA reinfused to patient
- How do we know when a donor/patient is having a hypocalcemia reaction?
  - Close monitoring of Vital Signs
    - Baseline for comparison
    - Changes from baseline in any VS
  - Changes in behavior
    - Pursing lips
    - Changes in demeanor

Prompt recognition & intervention:

- Pause procedure & assess donor/patient & Stay PAUSED…
- Consider Calcium supplementation: PO, IV drip, IV slow push
- Prophylactic Ca++ replacement may be needed for next procedure
What if donor/patient is having a vasovagal reaction during collection?

• Change or shift in vital signs
• Changes in behavior
• Change in temperature: cold → hot

Prompt recognition & intervention:
• Pause procedure & assess donor/patient
• Lower head – Trendelenberg
• Start fluid bolus
• Wet cold cloth or pack to head, neck, and chest
• Keep donor/patient talking & eyes open
• Keep legs uncrossed
• Consider combination hypocalcemia/vagal reaction
What can donors/patients do during MNC Collection?

• Can donor/patient eat during procedure?
• What activity level can donor/patients maintain during procedure?
• Can family members be present during collection?
• Can donor/patient get out of chair/bed during procedure?
• What if donor/patient needs to go to bathroom during collection?
Maximizing MNC Collections: Importance of Collection Efficiency and Meeting Target Yield

- Target Cell Dose for Each Collection
  - Donor/patient’s WBC Count and Differential, donor’s target cell counts
  - Amount of blood processed: Fixed volume of blood or amount of time, vs. x donor’s total blood volume, or predictive equation
  - Blood cell separator efficiency & Operator Proficiency
- Concurrent Plasma Collection for product storage
- Purity of product
  - Target cells vs. unwanted cells – protocol specific
  - Role of RBC – usual goal to minimize
  - Role of Granulocytes – usual goal to minimize
  - Role of Platelets – usual goal to minimize for product & donor benefit
What if collection yields poor results?

- Review previous procedure:
- Number of pump stops
- Adequacy of venous access:
  - If CVC was used - Rule out recirculation of catheter, and/or formation of fibrin sheath
  - If Peripheral venous access was used, evaluate needle gauge and choice of veins
- Presence of clumping or clotting
- Amount of blood processed – consider an increase volume of blood processed for next procedure
General Tips

Pre-procedure:
• If patient has CVC, educate referring facility and patient for best practices to assure catheter is patent on day of collection
• Hydrate, hydrate, hydrate
• Increase oral intake of calcium
• Void immediately before procedure no matter what patient says
• Wear appropriate clothing to allow for easy venous access & urination during procedure
• Referring MDs instruct patient to take baby ASA if their platelet count is high (Argos)
General Tips

• Procedure: decrease inlet flow to increase dwell time in centrifuge to improve efficiency of collection
• AC ratio will be adjusted if clumping is noticed during collection
• Periodically stop and flush the lines with saline if frequent access alarms are encountered
• Use lower AC:WB ratios in this patient group due to higher platelet counts (Argos)
• Have patient take ASA prior to next procedure, if not contraindicated
Summary

• Beneficial to develop help tools for each MNC collection protocol
  • “cheat sheet” or decision tree
• Utilize resources from research sponsors & blood cell separator vendors
• Educate apheresis operators about research study, science behind the collections, and disease indications
• Utilize quality monitors to evaluate effectiveness of collection
• Investigate all product failures and non-conformances
Thank you!

QUESTIONS?

Proud to be an Apheresis Nurse!

Be nice to me... I may be your nurse someday!!!!
Remember...catheters and needles come in sizes that I choose!!!!!