Transfusion Options for the Patient Refractory to Platelet Transfusions

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Overview:

- Testing algorithms for patients
- Strategies for product selection
- Challenges and obstacles
- What lies ahead
Acknowledgments

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“Support Options for the Patient Who is Refractory to Platelet Transfusion”

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Acknowledgments

Platelet Testing: ASHI/AABB Joint Program
AABB Annual Meeting, October, 2011

- Patricia Kopko, MD, Blood Source, Mather, CA
  “Strategies for Platelet Support of the Refractory Patient”

- Lesley Kresie, MD, Carter BloodCare, Bedford, TX
  “Clinical Outcomes Using HLA Matched Platelets”

- Karen Nelson, PhD, D.ABHI, Puget Sound Blood Center, Seattle WA
  “Survey Results: HLA Antibody Testing for Platelet Selections”
What testing are we talking about?

- Testing available at ARC SED:
  - Platelet Crossmatching
  - HLA antigen typing
  - HLA antibody screening and identification
  - HPA antigen typing
  - HPA antibody screening
Platelet Crossmatching

- Performed via commercially available kit
- Donor units selected from those already in inventory
- Can detect anti-HLA or –HPA, minor ABO
- TAT can be quicker as products are in inventory
- Can utilize the plasma from same sample sent for HLA antigen typing
HLA antigen typing

- Only necessary to test HLA-A, B (Class I)
- Test methods have substantially changed in last decade (molecular-based)
- Can utilize the buffy coat from same sample sent for Platelet Crossmatching
- Longer product TAT as matched donor must be recruited and scheduled; product must undergo processing prior to release
HLA antibody screening and identification

- Cause of refractoriness usually HLA antibodies
- HLA allo-antibodies can form within 2-4 weeks
- PRA can be gained and lost
- Identification of abs specificities aids in selection of matched platelets
- Test sensitivity - are all abs identified by Luminex based testing clinically relevant?
HPA testing

ELISA based screening for HPA antibodies but limited to those associated with GPIIb/IIIa, GPIa/IIa, GP1b/IX and GPIV

ELISA based screening limited to pooled HLA Class I

Platelet genotyping addresses HPA antigens 1-6 and 15. Currently best predictor of PLA-1 phenotype
Which Testing to Choose?

Three suggested strategies:

1. HLA/HPA antibody screen via ELISA
2. Platelet Crossmatch via SPRCA
3. HLA type and screen via Luminex

What do these tests tell me?

1. HLA or HPA antibody presence
2. Incompatibility rate
3. Antigens to match; Antibodies to avoid
Suggested Testing Algorithm

ELISA Ab screen

+ HLA Ab scr
- HPA Ab scr

- HLA Ab scr
+ HPA Ab scr

+ HLA Ab scr
+ HPA Ab scr

- HLA Ab scr
+ HPA Ab scr

- HLA Ab scr
- HPA Ab scr

HLA/HPA Antibody Specificity and / or PLT XM

Try 1 HLA or PLT XM Product

Inc
Continue
HLA/XM

Inc = or
Give
Random Plts

HLA Matched

HLA Antibody ID

- PLT

HLA or HLA Ag Neg & XM Compatible

Crossmatch Compatible or PLA-1 Negative

HLA or HLA Antigen Negative

HLA Matched

HLA Antibody ID

- PLT

HLA or HLA Antigen Negative

Inc = or
Give
Random Plts
Suggested Testing Algorithm

8 Unit PLT XM

- Incompat 8/8
  - HLA Matched
  - HLA type
    - HLA Antibody ID
      - HLA Antigen Negative
    - + HLA - PLT
    - + HLA + PLT
  - - HLA + PLT

- Strong Incompat
  - HLA or HPA Antibody Specificity and / or Differentiation
    - + HLA + PLT
    - + HLA - PLT
    - - HLA + PLT

- Wkly Incomp
  - Crossmatch Compatible or PLA-1 Negative

- All Comp
  - Try 1 XM Product
    - Inc = or Give Random Plts
    - Inc Continue XM

HLA or HLA Ag Neg & XM Compatible

HLA or HLA Antigen Negative

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Suggested Testing Algorithm

HLA type and screen

- HLA Ab detected
  - Determine HLA Ab specificity
    - Select "Antigen Neg" donors
      - Ask center to re-recruit Donor whose units pt responds
    - Select HLAM Donors Exclude those w Corresponding ab spec

- HLA Ab Not detected
  - Try I HLA Product
    - Inc = or Give Random Plts
    - Continue HLAM
      - Inc

Strategy 1 - Unit selection:

**HLA type only**

Search of unrelated donors for identical HLA-A&B - most centers have some type of computerized donor base search or search of inventory; isn’t necessary to repeat HLA

>35% have no match in most donor bases; >80% no match in inventory

Matching donor must be recruited and scheduled; product must undergo manufacturing process = longer TAT

Matching includes blanks and cross-reactive or CREG antigens; if no HLA ID has been performed CCl can be affected

**Has 30-75% (~50%) success rate depending on the grade of match**

*Ralph R Vassallo; “Support Options for the Patient Who is Refractory to Platelet Transfusion”*
Strategy 2 - Unit selection: Platelet Crossmatching

Best option for STAT

Best TAT for products as units are selected from inventory

Can be $$$ for those patients with ↑ PRA

Must resubmit sample for XM following any sensitizing event

Testing must be repeated for each day of desired transfusion

Has 50-75% (~55%) success rate

Ralph R Vassallo; “Support Options for the Patient Who is Refractory to Platelet Transfusion”
Strategy 3 - Unit selection: HLA Type with Screen/ID

Better TAT because if no matching HLA type in inventory then unit can be selected to avoid antibody specificities

Use of “Antigen Negatives” ↑ likelihood of compatible units particularly for patients with “rare” HLA types or extensive antibodies to avoid

Can be difficult to stay in-group ABO; can still require donor recruitment which can ↑ TAT

Has 60-75% (~70%) success rate

Ralph R Vassallo; “Support Options for the Patient Who is Refractory to Platelet Transfusion”
Obstacles

Refractoriness-Immune and non-immune
Need good assessment of patient status

TAT from request to receipt of product-
HLA matched and platelet crossmatched are not “shelf” products

Effectiveness Monitoring- the “PlaDo” study
Post-transfusion platelet counts key

Logistics-
Testing involves getting patient samples to lab

Expense-
Resistance to additional testing due to costs
What lies ahead?

Advances in testing methods

“Complement (C1q) fixing solid-phase screening for HLA antibodies increases the availability of compatible platelet components for refractory patients” Magali J. Fontaine, Jenny Kuo, Ge Chen, Susan A. Galel, Evelyn Miller, Flavia Sequeira, Maurene Viele, Lawrence T. Goodnough, and Dolly B. Tyan

TRANSFUSION, Volume 51, December 2011, 2611-2618
What lies ahead?

Improved Donor Selection methods: 

*HLAMatchmaker*

Rene Duquesnay improved his original concept of CREG-matching criteria for a computerized selection method based on shared immunogenic amino acid epitopes.
References


- The Trial to Reduce Allo-immunization to Platelet Study Group. *NEJM* 1997; 337: 697-729
Questions?