Current and emerging selection criteria for HLA supported platelet transfusions

Delordson Kallon
H&I, National Blood Service, NHSBT, England
Number of HLA Selected Platelets Issued

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Will cover…

- Reasons for using HLA Selected Platelets – Platelet Refractoriness
- Guidelines for Management of Refractory Patients
- Current Matching Strategies – HLA Antigen Matching
- Emerging Matching Strategies – HLA Epitope Matching
Reasons for using HLA Selected Platelets
Thrombocytopenia

- Platelet count less than $140 \times 10^9/l$
- Haemorrhage occurs $10-30 \times 10^9/l$
- Petechiae (pinpoint haemorrhage)
- Ecchymoses (bruising)
- Easy bruising, gum and nose bleeds, haematuria and prolonged menses
- GI blood loss can lead to Iron deficiency and anaemia
- Intracranial Haemorrhage $< 5 \times 10^9/l$
Pooled Platelets (20%)
Apheresis Platelets (80%)
Platelet Refractoriness

Corrected Count Increment (CCI) of less than between 3,000 – 5,500 per μL per m² per \(10^{11}\) platelets 1 hour post transfusion.

\[
\text{Platelet Count Increment (}/\mu\text{L}) \times \text{Body Surface Area (m}^\text{2}) \times \text{Platelets Transfused (}/10^{11}\text{)}
\]

Practical Definition

Increase in patient’s platelet count of $<10 \times 10^9/l$ between 1 and 24 hours after the transfusion of an adult dose of ABO compatible apheresis platelets on two separate occasions.
**Types of Patients**

Matched Platelet Patients

- Chronic Leukaemia’s 4%
- Kidney Disease 2%
- Lymphoma 3%
- Acute Lymphoblastic Leukaemia (ALL) 4%
- Aplastic Anaemia 10%
- Acute Leukemia 11%
- Platelet Disorders 8%
- Non Hodgkins Lymphoma 1%
- Hodgkins Lymphoma 1%
- Acute Myeloid Leukaemia (AML) 39%
- Myelodyplastic Syndrome (MDS) 17%

Current and emerging selection criteria for HLA supported platelet transfusions
Causes of Platelet Refractoriness

Non Immune (80%)
- Bleeding
- Old platelets
- Splenomegaly, hepatomegaly
- DIC
- Infection and its treatment especially amphotericin B
- Fever

Immune (20%)
- Platelet alloantibodies
  - anti HLA (class I - >95%)
  - anti HPA (<5% HPA + HLA, HPA only <1%)
- Other antibodies
  - Autoantibodies
  - Drug-dependent antibodies
  - ABO antibodies
- Immune complexes
Guidelines for Management of Refractory Patients
Current and emerging selection criteria for HLA supported platelet transfusions

Guidelines

1. Patient likely to receive multiple transfusions
   - Consider prospective HLA typing
   - Assess transfusion response to random platelets

2. Poor response > twice
   - Test for anti HLA antibodies

3. HLA antibody results
   - POS: Use HLA selected platelets
   - NEG: Reconsider non immune factors

4. Consider trial use of HLA selected if no test results available
Guidelines cont.

Current and emerging selection criteria for HLA supported platelet transfusions

- **Review increments**
  - **GOOD**
    - Continue with HLA selected platelets
    - Retest serum monthly during transfusion
  - **POOR**
    - Provide 'A' grade ABO compatible if possible
    - If response still poor test for anti HPA antibodies

- **HPA results available**
  - **POS**
    - Provide HLA and HPA selected
  - **NO**
    - Review matches. Consider non immune factors
    - Discuss with H&I Consultant Clinical Scientist

- **Non immune factors absent**
  - Consider trial of HLA selected platelets

- **Non immune factors present**
  - Treat non immune cause
  - Base transfusion support on clinical status
Not off the shelf Products

• HLA type of patient
  A1,A2 B8,B44 – 597 in 10,000 donors compatible
  A33,X B58,X - 0 in 10,000 donors are fully matched

• HLA Antibody profile
  – More HLA antibodies = fewer mismatched antigens can be selected

• Additional donation requirements – e.g. CMV negativity reduces donor field by approx 50%

• Repertoire of current stock
Current Matching Strategies – Antigen Matching
Historical HLA Matching

- Platelets were matched at the HLA-A and B Loci
- ‘A’ match grade = complete match
- ‘BU’ grade = homozygous donor who nevertheless has no HLA antigens not present in the patient
- ‘B1X’ – ‘B4X’ grades = donor with one to four same CREG mismatches
- ‘C’ grade = donor with one or more HLA antigen and CREG mismatches
Current HLA Matching

- Platelets are matched at the HLA-A and B Loci
- ‘A’ match = complete match (36%)
- ‘B1’- ‘B4’ match = mismatched for between 1 and 4 HLA antigens (64%)
Match grade ‘A’ examples

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*homozygous donor
Match grade ‘B’ match examples

**B1 match**

- donor: A1, A2; B8, B27
- patient: A1, A68; B8, B27

**B2 match**

- donor: A1, A66; B7, B27
- patient: A1, A68; B8, B27
Case Study 1 – Role of HPA

- Female AML patient (38yrs)
- Post chemo with 70% cRF

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- Tested for HPA: HPA-1b Pos

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Case Study 2 – Importance of Antibody Monitoring

- Male MDS patient (65yrs)
- No antibody samples or increments provided for 12 months

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- Tested HLA and new specificities found

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Emerging Matching Strategies – HLA Epitope Matching
HLA Matching

- HLA selected platelets are currently provided on the basis on counting the number of serologically defined mismatched HLA antigens the donor has with the patient at HLA-A and HLA-B.
- Can matching at the epitope level allow donors to be used who would otherwise have been considered a serological mismatch?
What is an Epitope?

- The antibody makes contact with 15-20 amino acid residues on the antigen
- Substitution studies show only 2-5 AA’s confer specificity
Traditional vs. Epitope Matching

Epitope matching provides a new means of assessing donor patient matching. Consider a platelet patient with HLA type A2, 30; B42, 53 and two potential donors D1 and D2 with types as listed.

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### Current and emerging selection criteria for HLA supported platelet transfusions

**ePlatelets**

![ePlatelets interface](image)

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Prospective Clinical Trial

• NHSBT and King's College Hospital joint prospective clinical trial underway
• Preliminary data to be evaluated soon
Thank you