GUIDELINES FOR THE MANAGEMENT OF PATIENTS REFRACTORY TO PLATELETS

REASON FOR ISSUE: Address two DCRs relating to change in terminology to Matched Platelets and revise current practice in provision of matched platelets with respect to blood bankers role. Rewording of certain aspects of the document.

1. PURPOSE

The purpose of this document is to define how patients who are truly refractory to platelet transfusions should be managed. It is based on reviews of the literature and currently accepted practice.

2. BACKGROUND

When a patient does not have a satisfactory response to platelet transfusions it is important to find out why and in particular whether or not the failure is due to immunological or non-immunological (e.g. clinical) causes. For example, in recent years clinical factors such as sepsis, DIC, splenomegaly have largely surpassed alloimmunisation as the major cause of refractoriness.

Identifying patients with white cell (HLA) or platelet (HPA) antibodies is important since the use of HLA-matched (or HPA-matched) platelet components may result in improved transfusion responses. Similarly the identification of patients with other allo- and (rarely) autoantibodies is also important as it may be possible to find serologically (‘crossmatch’) compatible platelets in these situations.

However in deciding how to treat a refractory patient there may be a number of appropriate strategies for improving the response to platelet transfusions such as matching for HLA or HPA, identifying donors based on antibody specificity prediction (single antigen matching) and very rarely resorting to cross-match compatible platelets.

3. DEFINITIONS

- **Alloimmunisation** is defined as the development of HLA or HPA antibodies
- **HLA antibodies** are antibodies to HLA antigens (only HLA class I antibodies are considered in platelet refractoriness).
- **HPA antibodies** are antibodies to Human Platelet Antigens
- **Refractoriness** is a failure to obtain a satisfactory response to transfusion of random donor platelets on two or more occasions. A poor platelet response is defined by a platelet increment of <10x10^9/L or (more accurately) a Corrected Count Increment (CCI) of <5000/uL
- **Platelet increment** is the difference between pre- and post transfusion platelet counts. This may be a reasonable measure of refractoriness or used to calculate the CCI (see below). The post transfusion platelet count should be performed 10 to 60 minutes after the transfusion.
- **Corrected Count Increment** is determined using the following formula (where BSA represents the patient’s Body Surface Area):

\[
CCI = \frac{\text{Platelet Increment (10}^9/L) \times BSA (m^2)}{10^{11} \text{ platelets transfused}}
\]

- **Body Surface Area** is determined using the following formula (also known as the ‘Mosteller’ formula):

\[
BSA = \sqrt{\frac{\text{Height (cm)} \times \text{Weight (Kg)}}{3600}}
\]
4. **KEY RESPONSIBILITIES**

**NZBS TMS (or MO)**  
Liaison with the patient’s physician. Initiates the request for ‘special platelets’ and coordinates the provision of suitable platelet components.

**DHB Clinicians**  
Responsible for the patient and ensuring that the correct samples and tests are requested.

**NZBS National Tissue Typing Laboratory**  
HLA and/or HPA typing of potential platelet recipients; testing for the presence of HLA and/or HPA antibodies; and the identification of suitable platelet donors.

**NZBS Donor Services staff**  
Calling in and bleeding the appropriate platelet donors as identified by the National Tissue Typing Laboratory.

**NZBS Manufacturing Services**  
Processing of the collected platelet donation.

**NZBS Logistics and Customer Services**  
Ensuring that the appropriate platelet components are sent to the relevant location (e.g. hospital blood bank).

**Blood Bank staff**  
Blood Bank staff may be required to locate matched platelets using the HAPU application on cornerstone.

5. **RELATED DOCUMENT(S)**

- 111M034 Request For Matched Platelets
- 111F034 Matched Platelet Requisition and Record Form

6. **POLICY**

6.1 **Request for Platelets**  
The first point of contact with NZBS will be a TMS (or MO). Samples may have been received by the Tissue Typing Laboratory without prior consultation. This will still necessitate communication between the TMS/NZBS MO and treating clinician.

6.1.1 Ascertain whether or not the patient is refractory i.e. has had a poor response to random donor platelets on two or more occasions (refer to figure 1: Algorithm To Determine If Patient Is Refractory To Platelets).

6.1.2 Determine the nature and urgency of the request in discussion with the patient’s physician.

6.1.3 Discuss with the treating physician as to what testing of the patient is required and what samples should be collected.

6.1.4 Initiate and coordinate investigation(s) to determine whether the refractoriness is due to immunological or non-immunological causes.
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6.1.5 Liaise with the National Tissue Typing Laboratory regarding provision of appropriate platelets. Refer to document Requests For Matched Platelets (111M034).

6.2 Management Of Refractory Patients

6.2.1 Refer to figure 2: Algorithm For Management Of Patients Refractory To Platelets.

6.2.2 Depending on whether or not test results are available, the options shown below in (table 1) for managing the patient should be considered:

Table 1: Options For Managing Patients Refractory To Platelets

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Patient’s HLA (‘tissue type’) not known and serum sample(s) not yet available</td>
<td>Consider transfusing ABO-compatible, single donor platelets</td>
</tr>
<tr>
<td>b. Patient serum samples are available</td>
<td>Platelet antibody screen should be performed and serum sample retained for further testing</td>
</tr>
<tr>
<td>c. Patient’s HLA type is known, and HLA-matched platelet donors are available</td>
<td>These should be considered particularly if HLA immunisation is suspected as the most likely cause of refractoriness</td>
</tr>
<tr>
<td>d. The patient has HLA and/or HPA antibodies</td>
<td>HLA-matched (and/or HPA matched) platelets or matching based on antibody specificity should be selected for transfusion. Cross-matching is rarely done. Further antibody testing should be considered every 3 to 6 months or if refractoriness returns</td>
</tr>
<tr>
<td>e. The patient does not have HLA or HPA antibodies</td>
<td>The TMS (or MO) will advise the treating physician accordingly Consideration should be given to non-immunological causes for which the TMS (or MO) may advise suitable management options.</td>
</tr>
</tbody>
</table>

6.3 Follow-up Post Transfusion

Following transfusion the TMS (or MO) will:

6.3.1 Ascertain the patient’s response to the platelet transfusion by requesting the treating physician to obtain a post transfusion platelet count (10-60 minutes post transfusion).

6.3.2 Discuss with the Tissue Typing laboratory the patient’s response to possibly assist in future selection of appropriate donors.
6.3.3 If the response to matched platelets is poor, the TMS (or MO) will determine what further investigations are required in consultation with the treating clinician.

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**Consult NZBS TMS**

**Is the patient truly refractory?**
**i.e.** Poor response to random donor platelets on two or more occasions.

**Perform platelet count**
using EDTA sample
collected 10 mins - 1 hour post infusion
or calculate the 1 hour CCI

**Has patient had an adequate response to platelet transfusion(s)?**

- **Yes**
  - **Adequate response**
    - >10x10⁹/L increment post infusion
    - or a CCI >5000/μL
    - **Continue support with non-matched ABO-compatible platelets**

- **Inadequate response**
  - <10x10⁹/L increment post infusion
  - or a CCI <5000/μL
  - **Patient Refractory**

- **No**
Patient Refractory

Consult NZBS TMS

Serum sample(s) available?

Yes

Send sample(s) to the National Tissue Typing Laboratory

No

Has patient been HLA Class I typed?

Yes

Check availability of HLA-matched platelet donors

No

No

Send sample(s) to the National Tissue Typing Laboratory

Perform an antibody screen

HLA Class I type patient

Testing complete?

Yes

HLA matched donors available?

No

No

Continue support with fresh ABO-compatible single donor platelets

Yes

Are HLA/HPA antibodies present?

No HLA/HPA antibodies present

Is patient’s response to compatible platelets adequate?

Bad Response

Consider 1. HLA compatibility
2. Non-immune consumption
3. HPA antibodies
4. ABO antibodies

Consider further serological testing
Discuss with NZBS TMS

Adequate Response

Continue with Matched platelets

Make decision about further platelet support

Are non-immune causes suspected (e.g. sepsis, DIC, medications, splenomegaly)?

Yes

Consult NZBS TMS

No

Retest for HLA antibodies every 3 - 6 months or if refractoriness returns

Good Increment Observed

Nature of Increment Observed

Good Increment Observed

Consideration may be given to use Grade A or B match donor(s) if available

Evidence not compelling

Consult NZBS TMS

Two Poor Responses

Stop HLA matched platelets

Two Poor Responses

Use HLA/HPA-matched apheresis platelets or matching based on antibody specificity

Are non-immune causes suspected (e.g. sepsis, DIC, medications, splenomegaly)?

Retest for HLA antibodies

No

Retest for HLA antibodies

Consult NZBS TMS

Adequate Response

Continue with Matched platelets

Retest for HLA antibodies every 3 - 6 months or if refractoriness returns

Nature of Increment Observed

Two Poor Responses

Stop HLA matched platelets

Nature of Increment Observed

Two Poor Responses

Good Increment Observed

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Two Poor Responses

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