

BLOOD ISSUES

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A Transfusion Medicine Newsletter

Implementation of Routine Antenatal Prophylaxis with Anti-D immunoglobulin in New Zealand

In August 2009 the Director General of Health wrote to all DHB CEOs outlining his expectations regarding implementation of routine antenatal prophylaxis with RhD immunoglobulin. Planning has already commenced for a pilot implementation. This will be undertaken by MidCentral Health. The Ministry will then be requesting all DHBs to progress implementation in early 2010 based on guidelines published by the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG).

RhD Immunoglobulin (Anti-D) Antenatal Prophylaxis - The Rationale

In RhD-negative individuals exposure to RhD-positive red cells can lead to the production of anti-D (sensitisation). Blood Services aim to avoid transfusion of RhD-positive red cell and platelet components to RhD-negative recipients. Particular care is taken in RhD-negative women of child bearing age or younger. Sensitisation can also occur during pregnancy and this is now the most frequent cause of anti-D in the female population.

Sensitisation can occur any time during pregnancy, but is most common in the third trimester and during childbirth. Sensitisation can follow events in pregnancy known to be associated with foeto-maternal haemorrhage (FMH), such as medical interventions (chorionic villus sampling, amniocentesis or external cephalic version), terminations, late miscarriages, antepartum haemorrhage and abdominal trauma. It can also occur in the absence of an observed potentially sensitising event.

In the absence of antenatal and postpartum anti-D prophylaxis, the risk of sensitisation following a single ABO-compatible RhD incompatible pregnancy is about 16%, but it is only 2% if the mother and foetus are ABO incompatible. About 80% of pregnancies are ABO compatible which means that the overall risk of sensitisation, without prophylaxis is approximately 13% of at risk pregnancies. In most of these women the initial sensitisation would have occurred during the first pregnancy/childbirth.

Following the introduction of routine post-natal anti-D prophylaxis the proportion of RhD-negative women found by routine antenatal testing to have demonstrable anti-D within 6 months of delivery of their first RhD-positive ABO-compatible pregnancy fell from 4-9% to 0.1-0.5%, and the proportion with demonstrable anti-D by the end of their second RhD-positive ABO-compatible pregnancy fell from 16% to 1.5%.

Without routine antenatal anti-D prophylaxis (RAADP), the majority of those primigravidae who are sensitised before delivery in the absence of an identifiable sensitising event appear to be sensitised in the third trimester. A New Zealand study found that 87% (14/16) of primigravidae did so in the third trimester, compared with only 27% of multigravidae (7/26). This is compelling data to suggest that many women who develop antibodies early in their second pregnancy have actually been sensitised late in the first pregnancy.

The evidence from clinical trials shows that the use of RAADP reduced the rate of sensitisation in primigravidae and multigravidae who are RhD-negative. RAADP is now considered by most experts to be an effective intervention. It is further considered that the benefits of RAADP are much greater than the risks, and that the use of anti-D immunoglobulin, including routine prophylaxis, provides reassurance for pregnant women who are RhD-negative.

Recommendations for Antenatal anti-D Prophylaxis

- Universal anti-D prophylaxis is recommended for pregnant women who are RhD-negative with no preformed anti-D antibodies.
- Anti-D in the form of 625 IU NZBS RhD immunoglobulin, should be offered at 28 weeks and again at 34 weeks, to all RhD-negative women with no preformed anti-D antibodies.
- It is absolutely essential that women be screened again for pre-existent anti-D and that a sample is taken before the first routine prophylactic injection is given at 28 weeks. The result of the test does not need to be available before the administration.
- No repeat screening is necessary before the second administration at 34 weeks.
- Potentially sensitising events occurring around the time of RAADP still require to be managed with additional doses of anti-D and Kleihauer testing.

NZBS Role in Implementation of Routine Antenatal Prophylaxis in New Zealand

NZBS can play an important role in supporting implementation by the DHBs.

1. Supplies of RhD Immunoglobulin

Full implementation of antenatal prophylaxis will likely lead to a 2-3 fold increase in the use of RhD immunoglobulin. Current stocks in New Zealand are good and at this stage we do not anticipate any constraints on supply. Information provided by DHBs will be important to NZBS production planning in this area.

2. Tools to Support Implementation

NZBS has updated the guidelines on the 'Use of RhD Immunoglobulin during pregnancy and the post partum period'. The revised guideline is consistent with the RANZCOG guideline. The document is available on the NZBS website (www.nzblood.co.nz).

Routine antenatal prophylaxis has been in place in Australia for some years. NZBS has access to the various educational tools developed by the Australian Red Cross Blood Service (ARCBS) and CSL Bioplasma. New Zealand versions of these various tools have been developed – these include pocket booklets containing frequently asked questions.

3. Laboratory Protocols

The experience in Australia indicates that implementation of routine antenatal prophylaxis will impact significantly on laboratories undertaking routine antenatal screening. In particular there will be an increased frequency of positive antibody screens due to the presence of passive anti-D. NZBS provides guidance on the appropriate investigation of such samples. Reporting protocols will also be updated. These will be based on recommendations contained in the 'ANZSBT Guidelines on Blood Grouping and Antibody Screening in the Antenatal and Perinatal setting'. The ANZSBT Guidelines are freely available on the Society website (www.anzsb.org.au).

4. Supply Logistics

The international experience indicates that timely access to supplies of RhD Immunoglobulin will be important for successful implementation. A careful balance between access and traceability will be required. In many instances however it is likely that additional stockholding facilities will need to be established. This will apply particularly in geographically large DHBs. NZBS has developed a policy and procedures for stock holding of fractionated blood products outside of the Blood Bank. This can be accessed on the NZBS website.

An Audit of the Appropriateness of Red Cell Usage for Three Surgical Procedures in Seven New Zealand Hospitals

Transfusion of blood components has played an important role in the development of modern medicine. Blood transfusion undoubtedly save lives, but transfusions also carry risks of harm. Accordingly, the decision to transfuse needs to be a considered one and viewed similarly as with other risk/benefit decisions common in medical practice. Guidelines are in existence to promote a consistent approach that puts the patient's best interest first and reduces the pressure on blood supplies. New Zealand Blood Service has endorsed the National Health and Medical Research Council (NHMRC) guidelines for appropriate use of blood components that were published in October 2001.

Red cells are the most frequently prescribed blood component in New Zealand. It is important to understand how clinicians use this precious resource and whether current transfusion practice meets published guidelines. International studies have demonstrated wide variations in transfusion practices not just between countries and regions but also between hospitals in the same region. Despite having a red cell transfusion rate of 125,000 per year, little has been published about red cell use in New Zealand or the extent to which alternatives such as autologous pre-donation and cell salvage are in use.

Therefore a prospective audit of three common surgical procedures (first time coronary artery bypass graft, first time total hip replacement, and total abdominal hysterectomy) within seven main centres in New Zealand was undertaken. The aim was to assess the appropriateness of red cell usage during the surgical procedures and the following post-op period as measured against the NHMRC guidelines. The hospitals chosen were the main public hospitals in Auckland, Manukau, Hamilton, Palmerston North, Wellington, Christchurch and Dunedin. The audit focussed on "arranged" surgical procedures (i.e. elective, booked or non-emergency cases but including urgent and in-hospital acute). Emergency procedures were excluded from the audit.

The audit commenced from the time of admission and concluded on day seven post operatively, on discharge (if before day seven), on redo surgery, or on death of the patient whichever came first. Only adult patients were included in the audit. The look-back period for pre-operative investigation of anaemia went back as far as four years.

A target was set of at least twenty operations for each of the three surgical procedures per site. The results were collected by seven Transfusion Nurse Specialists and reviewed by two Transfusion Medicine Specialists.

This audit was the first multi-centre audit to look at red cell usage within New Zealand and as such, provides a suitable baseline for clinicians to compare practice, and against which to measure future improvements.

The results from this audit show that 32% of all red cell units transfused were inappropriate. This compares with other studies showing rates of inappropriate transfusion ranging from 3% to 35%.

The initial decision to transfuse was generally in line with published guidelines, with 84% of patients transfused receiving at least one transfusion assessed as appropriate. However, in only 38% of patients transfused were **all** units transfused assessed as appropriate, indicating a significant level of over-transfusion.

The majority of patients received at least two units before the haemoglobin level was rechecked. This may be due to the historical practice of prescribing a minimum of two units of red cells which was once considered best practice, however this is no longer the case.

Studies conducted in patients undergoing CABG have shown increased mortality and morbidity associated with red cell use in a dose dependent fashion. Although the studies need to be confirmed, clinicians should use the absolute minimum number of transfusions required to obtain the relief of symptoms, and therefore for top-up transfusions, the patient's symptom control or haemoglobin level should be checked after each unit. It was noted that some orthopaedic units aim for a Hb level of 100g/L: this is considered controversial and there is evidence that a restrictive transfusion practice is safe for most patients including those with heart disease.

Variation in transfusion practices was apparent across the country. For example, patients having a CABG receiving the correct dose (all units were assessed as appropriate) ranged from 29% to 100% per DHB. Likewise, hip replacement patients, the proportion ranged from 0% to 44%.

Discharge haemoglobin (Hb) values are often taken as surrogate markers for appropriateness of transfusion practice with high discharge haemoglobin levels a marker of inappropriate transfusion. The results of this audit demonstrate that the average discharge Hb value was 9g/L higher amongst the inappropriately transfused group compared with the appropriately transfused group, validating the assessment technique.

It was noted that a pre-transfusion haemoglobin level was available for all units transfused, although in many cases no haemoglobin level was available between units. While the majority of transfusions (76%) fell within the NHMRC categories suggesting transfusion was likely to be appropriate, the correlation between NHMRC category and clinical assessment of appropriateness, which took other factors into account, was not strong for pre-transfusion haemoglobin levels above 70 g/L. A significant part of this was the length of time between the haemoglobin measurement and the transfusion, with one in five haemoglobin measurements occurring before surgery and the transfusion at or after surgery, making the haemoglobin measurement of less use.

Transfusion sparing techniques such as intra-operative cell salvage, drain reinfusion and acute normovolaemic haemodilution, did not appear to be universally used ranging from 43% to 90%. Almost all cases where such techniques were used occurred in cardiac bypass surgery, with cell salvage and return of pump blood widely used. One hospital used normovolaemic haemodilution prior to cardiac surgery. The variation from the audit results suggests that transfusion practices would be responsive to clinical education.

Pre-operative anaemia was identified in 15% of patients. However only 32% of this group had any evidence of investigation into the causes of their anaemia and only 13% of anaemic patients were treated with haematinics. Anaemia is common in the elderly population and especially so in pre-operative patients, with around a third of these readily treatable.

Treating anaemia with haematinics is a much safer alternative to blood. A low haemoglobin prior to surgery puts the patient at increased risk of receiving a transfusion.

Preoperative transfusion is generally not an accepted practice and it was reassuring to see that only 1.2% (n=5) of patients received red cells (13 units) before their operation. However, eight of these units were deemed inappropriate. As there are safer alternatives to preoperative transfusions, such as oral or intravenous iron supplements, it would seem difficult to argue for preoperative transfusions in this group of elective surgery patients.

Although this is the last topic discussed, the first step in the transfusion process is the decision to use blood. The clinician responsible for this decision should be clear what s/he is trying to achieve and should document this. In this audit, the indication was recorded in 46%, less than in other studies showing over 60%. It has been suggested that poor documentation correlates with inappropriate transfusion, and a trend towards this was seen in this audit.

Recommendations From Audit

This audit has identified several areas which could be responsive to appropriate education. These include:

- The optimum dose of red cells should be more closely assessed to avoid over transfusion.
- Routine prescribing of two red cell units to top patients up should be avoided.
- Each site should investigate any barriers to implementing transfusion sparing techniques e.g. intra-operative cell salvage or acute normovolaemic haemodilution.
- Each site should investigate strategies to improve identification and treatment of anaemic patients before their surgery.
- Documentation around blood transfusion, notably the indication for transfusion and blood loss in theatre, should be improved.

Revised NZBS Forms for Documenting Transfusion Requirements and Managing Adverse Transfusion Reactions

The New Zealand Blood Service (NZBS) is committed to providing standardised processes across its vein to vein service to enhance safety and efficiency. In the clinical arena measures taken by NZBS included the introduction of a national request form and adverse transfusion reaction notification form, which are in use at the majority of clinical settings across the country. As part of the on-going quality improvement initiatives of NZBS, updated forms will soon be available for the clinical setting.

Request for Blood Bank Tests & Blood Components or Products

The request form is forwarded by clinical staff to their local Blood Bank when they require any serological tests to be performed and when blood is required for a patient. The request form is available in the community setting as well as within hospitals to communicate to Blood Banks what service is required. A blood specimen accompanies the request form and this underpins the pre-transfusion requesting process. National guidelines are in place to inform clinical staff on the correct method of specimen collection and requesting. To ensure the right blood is administered to the right patient the pre-transfusion requesting process is strictly monitored.

The NZBS National Haemovigilance Programme, which was established in 2005, monitors and analyses adverse events that have been reported during the transfusion chain. Errors which occur in specimen collection can be traced back to the initial request form and failure to follow the correct process. These findings as well as feedback from clinical staff and changes in recommended best practice have provided NZBS with the impetus to review the current request form.

The new request form has been designed to reinforce safe transfusion practice by the development of a four-step requesting system. This streamlines and clarifies the sequential considerations before forwarding requests to Blood Banks. These steps are:

1. Clearly identify the patient.
2. Document why the transfusion is required and the relevant patient diagnosis and history.
3. Indicate what tests or blood the patient requires.
4. Then, collect the pre-transfusion specimen, or other tests necessary, to accompany the form.

Other features have been incorporated in the new design to meet the needs of both clinical staff and Blood Banks. These include: the ability to link the mother's details to their babies specimen; tick-boxes to indicate which test or blood is required to simplify and rationalise requests; advice on specimen validity; a proposed date of surgery field to improve planning; and a section on the prior history of anti-D administration which will be useful for Blood Banks when the routine use of anti-D is introduced across NZ during 2010.

Transfusion-related Adverse Reaction Notification Form

The reaction form is utilised after a patient has an adverse reaction during or following a transfusion, and ensures a standardised method for reporting. The reaction form is completed by the clinical staff attending the patient and forwarded to the Blood Bank who commence a serological investigation and notify their local Transfusion Safety Officer (TSO).

The TSO, (who is either the Team Leader of the Blood Bank or the Transfusion Nurse Specialist), undertakes a review of the reaction, and notifies the National Haemovigilance Programme. This ensures that transfusion reactions are able to be analysed and monitored on both a local and national level.

A robust and successful National Haemovigilance Programme depends upon clinical staff reporting failures in the transfusion chain. The reaction form is the first step in ensuring adverse transfusion reactions are reported and managed appropriately.

A recent transfusion audit undertaken by NZBS in eight NZ hospitals demonstrated that only 60% of transfusion reactions were reported to Blood Bank for investigation. The new reaction form has been redesigned after consultation with clinical staff and the National Haemovigilance Office with the primary aims of improving reporting compliance and ensuring the management guidelines provided are current and easy to follow. The new form is sequential in nature, clearly identifying four main issues:

1. Who is the patient?
2. What is the patients transfusion and medical history?
3. What signs and symptoms were evident during the reaction?
4. What interventions occurred?

Clinical prompts have been clearly defined in the new form to streamline and encourage reporting. The most common presentations of febrile or allergic reactions lead the prompt list. Findings from the National Haemovigilance Programme have demonstrated that approximately 75% of reactions reported each year are either febrile or allergic in nature.

Clinical Guidelines for Management of Adverse Transfusion Reactions

Clinical guidelines for the management of reactions are provided on the reverse of the notification form to assist clinical staff. The guidelines provide appropriate measures to manage either mild transfusion reactions or moderate to severe transfusion reactions, including adjunct treatments. During the review of the reaction form these guidelines were updated to reflect changes in both NZ and international best practice.

To support clinical practice the clinical management guidelines from the form have been made into an educational poster. During the introduction of the new reaction form the poster will also be made available.

2008 Annual Haemovigilance Report

The 2008 annual Haemovigilance report is now available on the NZBS website (www.nzblood.co.nz). The report contains information on adverse events associated with transfusion in New Zealand during 2008. Hard copies can be obtained on request (jillian.sinden@nzblood.co.nz)