Pathogen inactivation of platelets

The primary methods of reducing the risk of an infection being transmitted via blood transfusion are careful selection of blood donors and testing of the donated blood. Pathogen inactivation is a technology to reduce further any transfusion-transmissible infections in platelets.

A systematic review was carried out to assess whether such pathogen inactivation reduces the clinical efficacy of the platelets (stopping/preventing bleeding, increasing platelet count, affecting the need for further transfusions) or their safety (any difference in the rate of death following transfusion, or side effects). The findings were published on 28th March this year.

A summary is attached.

NOTE
The full systematic review is published at
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009072.pub2/abstract;jsessionid=C918EB18BB83E43072DB06DDCAD274BA.f01t01

SaBTO is asked whether it agrees that a Working Group should be established, under the chairmanship of Dr Lorna Williamson, to review the findings of the systematic review, and European data on pathogen inactivation technologies; and to consider whether pathogen inactivation would be an appropriate risk reduction measure to be introduced by the UK Blood Services.

Background

Pathogen Inactivation technology is of interest to the blood services as despite improvements in donor screening and laboratory testing, a small risk of viral, bacterial or protozoal contamination of platelets remains. There is also an ongoing risk from newly emerging blood transfusion-transmitted infections (TTIs) for which laboratory tests may not be available at the time of initial outbreak.

Pathogen Inactivation involves photochemical pathogen reduction, a process by which pathogens are either inactivated or significantly depleted in number, thereby reducing the chance of transmission. This process might offer additional benefits, including platelet shelf-life extension, and negate the requirement for gamma-irradiation of platelets. Although current pathogen-reduction technologies have been proven significantly to reduce pathogen load in platelet concentrates, a number of published clinical studies have raised concerns about the effectiveness of pathogen-reduced platelets for post-transfusion platelet recovery and the prevention of bleeding when compared with standard platelets.

SaBTO previously reviewed the topic in 2009. At that time, concern was expressed that PI platelets might have reduced effectiveness in either preventing or treating bleeding, or result in increased side-effects. Therefore, SaBTO requested a systematic review of clinical trials of pathogen-reduced platelets for the prevention of bleeding. This was undertaken by Professor Mike Murphy and colleagues at the UK Blood Services Systematic Review Initiative in Oxford, and published by the Cochrane Collaborative in March 2013.

The objective of the review was to assess the effectiveness of pathogen-reduced platelets for the prevention of bleeding in patients requiring platelet transfusions.

Main results of the review

The review considered 10 trials comparing pathogen-reduced platelets with standard platelets. Two licenced technologies were included, Intercept and Mirsaol. Nine trials assessed Intercept pathogen-reduced platelets and one trial Mirasol pathogen-reduced platelets. Two were randomised cross-over trials and the remaining eight were parallel-group RCTs. In total, 1422 participants were available for analysis across the 10 trials, of which 675 participants received Interceptand 56Mirasol platelet transfusions. Four trials assessed the response to a single study platelet transfusion (all Intercept) and six to multiple study transfusions (Intercept (N = 5), Mirasol (N = 1)) compared with standard platelets.

Primary outcomes were mortality, ’any bleeding’, ’clinically significant bleeding’ and ’severe bleeding’, and were grouped by duration of follow-up: short (up to 48 hours), medium (48 hours to seven days) or long (more than seven days).

Meta-analysis of data from five trials of multiple platelet transfusions reporting 'any bleeding' over a long follow-up period found an increase in bleeding in those receiving pathogen-reduced platelets compared with standard platelets using the fixed-effect model; however, this meta-analysis showed no difference between treatment arms when using the random-effects model.

There was no evidence of a difference between treatment arms in the number of patients with 'clinically significant bleeding' (reported by four out of the same five trials) or 'severe bleeding' (reported by all five trials).

The review found no evidence of a difference between treatment arms for all-cause mortality, acute transfusion reactions, adverse events, serious adverse events and red cell transfusion requirements in the trials which reported on these outcomes.

No bacterial transfusion-transmitted infections occurred in the six trials that reported this outcome.

Although the definition of platelet refractoriness differed between trials, the relative risk of this event was 2.74 higher following pathogen-reduced platelet transfusion.

Participants required 7% more platelet transfusions following pathogen-reduced platelet transfusion when compared with standard platelet transfusion, although the interval between platelet transfusions was only shown to be significantly shorter following multiple Intercept pathogen-reduced platelet transfusion when compared with standard platelet transfusion.

In trials of multiple pathogen-reduced platelets, analyses showed the one- and 24-hour count and corrected count increments to be significantly inferior to standard platelets. However, one-hour increments were similar in trials of single platelet transfusions, although the 24-hour count and corrected count increments were again significantly lower.

Review Conclusions

The review found no evidence of a difference in mortality, 'clinically significant' or 'severe bleeding', transfusion reactions or adverse events between pathogen-reduced and standard platelets.

For a range of laboratory outcomes the results indicated evidence of some benefits for standard platelets over pathogen-reduced platelets. These conclusions are based on data from 1422 patients included in 10 trials.

Results from ongoing or new trials are required to determine if there are clinically important differences in bleeding risk between pathogen-reduced platelet transfusions and standard platelet transfusions.

Comment

Intercept platelets are now used in an increasing number of blood centres in Europe; it is estimated that 1 million doses have now been transfused. Thus the data from these relatively small trials will gradually be supplemented by larger datasets from field trials as well as routine haemovigilance data.