The effect of plasma transfusion on morbidity and mortality: a systematic review and meta-analysis


CRD summary
The review concluded that very low-quality evidence suggested that plasma transfusion was associated with a reduction in risks of death and multi-organ failure in patients undergoing massive transfusion; there was an increase in acute lung injury. The review was well conducted. The authors’ conclusions are suitably cautious and appear appropriate.

Authors’ objectives
To evaluate the benefits and harms of plasma transfusion in common clinical settings.

Searching
MEDLINE, CINAHL, Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science, SCOPUS and EMBASE (to August 2009) and Science Citation Index were searched. Search terms were reported. Reference lists of retrieved articles and reviews were searched. Experts in the field were contacted.

Study selection
Randomised controlled trials (RCTs) and controlled observational studies of plasma transfusions versus control in adult patients were eligible for inclusion. The control group could be medical management without plasma transfusion, a lower dose of plasma, or a lower plasma:red blood cell transfusion ratio. Relevant outcomes included death, nonfatal myocardial infarction, stroke, acute lung injury, multi-organ failure, blood loss and red blood cell transfusion requirements. Studies were excluded if the control group received whole blood or autologous platelet rich plasma. Studies in patients who received plasma for plasmapheresis were excluded.

The included studies compared plasma transfusions (generally one to 10 units) with no treatment, lower plasma doses/ratios, red blood cells, saline, albumin, standard care and other solutions in adult patients with various conditions such as burns, cardiac surgery, liver transplant and trauma. Mean age of patients ranged from 24 to 76. The proportion of females ranged from 1% to 66%. Most studies did not use anti-coagulation or have liver disease.

Paired reviewers independently performed study selection and disagreements were resolved by consensus.

Assessment of study quality
Paired reviewers independently assessed study quality factors such as blinding, randomisation, loss to follow-up and allocation concealment.

Data extraction
Pairs of reviewers independently extracted data on mortality, acute lung injury and other adverse events onto a standardised extraction form and used these data to calculate odds ratios (ORs) and 95% confidence intervals (CIs). Authors of studies were contacted for missing data.

Methods of synthesis
A random-effects meta-analysis (DerSimonian and Laird) was undertaken to calculate pooled odds ratios and 95% CIs. Statistical heterogeneity was assessed using the Q test and the I² statistic. Subgroup analysis was undertaken for patients who underwent massive transfusions, surgery without massive transfusion, anticoagulation use, study design, therapeutic versus prophylactic use and medical patients. Meta-regression was undertaken using effect size as the dependent variable and follow-up as the independent variable. Sensitivity analysis was undertaken excluding studies in which assumptions were made.

Results of the review
Thirty-seven studies were included in the review (n=12,421 patients): 13 RCTs and 24 observational studies. Trial
sample size ranged from 18 to 4,546 patients (median=94). Follow-up varied from one day to 68 months (median seven days). The quality of evidence was deemed low to very low: five trials used allocation concealment; six blinded patients; and one had adequate randomisation. High levels of survival bias were noted in some observational studies.

Compared with lower plasma ratios, there was a statistically significantly reduced risk of mortality in patients who underwent surgery with massive transfusion with higher plasma ratios (OR 0.38, 95% CI 0.24 to 0.60, $I^2=85\%$; 10 studies).

Compared with control, plasma had a statistically significantly increased risk of acute lung injury (OR 2.32, 95% CI 1.46 to 3.71, $I^2=38\%$; seven studies) and a statistically significantly reduced risk of multi-organ failure (OR 0.40, 95% CI 0.26 to 0.60, $I^2=0\%$; four studies).

There was no statistically significant difference in mortality in patients who underwent surgery without massive transfusions (seven studies). There was no statistically significant difference between groups in trials in patients with liver disease (three studies).

Sensitivity analysis did not explain the high levels of heterogeneity in massive transfusion mortality.

**Authors’ conclusions**

Very low-quality evidence suggested that plasma transfusion was associated with a reduction in risks of death and multi-organ failure in patients who underwent massive transfusion; there was an increase in acute lung injury.

**CRD commentary**

Inclusion criteria for the review were clearly defined. Several relevant databases were searched without language restrictions. Publication bias was not assessed and could not be ruled out. Attempts were made to reduce reviewer error and bias throughout the review process. Quality assessment was not conducted using a standard checklist, although the quality criteria identified by the authors were appropriate and the authors’ ascertainment that the quality of evidence was very low seemed reasonable given the study information presented. Trials were pooled using random-effects meta-analysis. Reasonable measures were taken to assess and explore statistical heterogeneity.

The review was generally well conducted. The authors’ conclusions are suitably cautious and appear appropriate.

**Implications of the review for practice and research**

Practice: The authors did not state any implications for practice.

Research: The authors stated that further RCTs were needed. These should select patients with clear pre-transfusion bleeding risk and indications for transfusion and seek to determine the best plasma:red blood cell ratio and timing of transfusion.

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