Appropriateness of fresh-frozen plasma usage in hospital settings: a meta-analysis of the impact of organizational interventions

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CRD summary
This review assessed the impact of organisational interventions aimed at reducing inappropriate fresh-frozen plasma (FFP) usage in hospital settings and concluded that organisational interventions showed a positive impact on the reduction of rates of inappropriate FFP transfusion episodes. The breadth of interventions considered made the validity of the conclusion unclear.

Authors’ objectives
To produce a quantitative synthesis of the impact of organisational interventions on appropriate fresh-frozen plasma (FFP) usage in hospital settings aimed at reducing inappropriate transfusion episodes.

Searching
Eight databases, which included PubMed and EMBASE, were searched until July 2008. Search terms were specified, but language restrictions were not. Additional handsearching of references in retrieved articles was conducted and experts contacted in order to identify further appropriate studies.

Study selection
Experimental or comparative studies were considered eligible for inclusion if they focused on comparison between levels of inappropriate FFP transfusion episodes before or after an intervention. Studies were excluded if they focused on red blood cells or other blood components, were descriptive studies that reported results of retrospective audits or were studies of low quality.

Study publication dates ranged from 1990 to 2006. Countries included Australia, Hong Kong, India, Taiwan, USA, Italy, Pakistan and Finland. Most hospitals were teaching or university hospitals. Physicians were the main targeted population. All study were before-after designs. Duration of controls and duration of interventions ranged from two to six months. Types of intervention included new request forms, prospective monitoring audits, educational programmes and computerised audits. Seven of the 10 included studies had equal duration pre- and post-intervention periods; in the three remaining studies the ratio of post- to pre-intervention durations varied from 2:1 to 1:3.

It was unclear how many reviewers performed the search and selection process and how this process was performed.

Assessment of study quality
Two reviewers independently assessed studies in terms of: allocation to study groups; data analysis; presentation and comparability of baseline characteristics; outcome measures used and assessor blinding; and follow-up. For each criterion, each study was assigned a grade between zero (criterion not met) and 2 (criterion fully met); grades were summed to produce an overall quality assessment score of between zero and 10. Studies that scored less than 6 were excluded from further analysis.

Kappa scores were calculated to assess agreement between reviewers. Disagreements were resolved by consensus or with a third reviewer.

Data extraction
Two reviewers independently extracted data required to calculate risk ratios (RRs), with 95% confidence intervals (CIs), of inappropriate episodes of FFP transfusion (defined as a transfusion of FFP that did not conform with at least one of the hospital’s stated criteria). Discrepancies were resolved by consensus.

Methods of synthesis
Risk ratios with 95% CIs were pooled using a random-effects model. Heterogeneity was assessed using the $X^2$ test and considered significant if $p<0.05$.

Sensitivity analysis was conducted by considering the effect on the pooled estimate of excluding the most influential studies and stratifying results according to date of study publication (until 1999 and between 2000 and 2006). A fail-safe number was calculated using an established approach to assess whether the results appeared robust to the file-drawer problem.

**Results of the review**

Ten studies ($n=7,149$ FFP transfusion episodes, range 50 to 2,786 FFP transfusion episodes) were included in the review. All studies received study quality scores of either 6 or 7 out of 10. Study scores for individual criteria were not reported. Inter-reviewer agreement was rated as good ($\text{kappa}=0.75$, 95% CI 0.58 to 0.91). No studies were excluded due to poor study quality (score of less than 6).

Overall, pooled results indicated a statistically significantly lower rate of inappropriate FFP episodes (RR 2.02, 95% CI 1.44 to 2.84) after interventions compared with before interventions.

Subgroup analysis by publication date was conducted and no significant differences were found between older and newer studies, but results were not reported. Statistically significant heterogeneity was identified ($I^2=95\%$). The number of unpublished studies required to invalidate the pooled risk ratios was judged to be very large (564 studies; more than 50 times the number of included studies), which indicated that publication bias was not a substantial issue.

**Authors’ conclusions**

The authors concluded that organisational interventions showed a positive impact on the reduction of rates of inappropriate FFP transfusion episodes.

**CRD commentary**

This review addressed a relatively clear research question supported by relevant inclusion and exclusion criteria. The search strategy was clearly defined; however, it was unclear how many reviewers performed the search and selection process and how this process was performed, so the possibility of error and bias at this stage could not be ruled out. Quality assessment was conducted in duplicate, which reduced risks of error and bias, and used as a criterion for exclusion of poor quality studies; however, only aggregate quality scores were reported (rather than details of how each study was assessed according to each criterion), which made interpretation of the quality assessment more problematic. A range of primary study details were provided, but these excluded details about hospital patient characteristics and hospital size, which may have affected comparability between studies and, in the case of smaller hospitals, the validity of results based on a short duration of observation. A high level of both clinical and statistical heterogeneity was observed, which raised challenges to the pooling of such diverse interventions; given the reviewers’ intention to pool results from these studies the choice of a random-effects model seemed appropriate. Given that trials were (necessarily) non-blinded and of varying characteristics and duration, there were a number of reasons why an organisational intervention of the type assessed may not be as effective as the pooled result indicated, and so the validity of the conclusion is unclear.

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

**Practice:** The authors stated that systemic organisational interventions should be implemented to different levels of decision-making to improve appropriate and safe FFP usage.

**Research:** The authors stated that economic evaluations of the the impact of organisational interventions on FFP usage were needed.

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