Transfusion of older stored blood and risk of death: a meta-analysis

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CRD summary
That authors concluded that use of older stored blood for transfusion was associated with a significantly increased risk of death. This conclusion reflects the evidence presented but clinical and methodological differences between the studies and the possibility of missed relevant studies mean that the reliability of this conclusion is undecided.

Authors' objectives
To compare the effect of older versus newer transfused blood on mortality.

Searching
PubMed, EMBASE and SCOPUS were searched to May 2011 for publications in English; search terms were reported.

Study selection
Studies that compared survival rates among patients who received transfusions of blood stored over longer versus shorter durations of days were eligible for inclusion. The primary outcome of interest was mortality; a priori secondary outcomes included severe adverse events.

Studies were published between 2001 and 2011. Most study populations were cardiac surgery or trauma patients. New blood age ranged from 1.6 days to 21 days; old blood age ranged from nine days to 42 days. More than two-thirds of the studies reported that blood was wholly or partially leukoreduced. The mean volume of blood transfused per patient ranged from 1.2 to 10.6 units. Definitions of mortality varied across the studies.

The authors did not state how many reviewers selected studies for inclusion.

Assessment of study quality
The authors did not report any quality assessment.

Data extraction
Two reviewers independently extracted data (count data, adjusted hazard ratios or risk ratios) to calculate odds ratios with 95% confidence intervals for mortality or severe adverse events with transfusion of older versus newer blood. Where studies had multiple methods for division, the method that provided the greatest age gap between old and new stored blood was used. Where more than one cut-off value was used to divide the two stored blood groups, the cutoff closest to 21 days was used. For studies that compared each transfused group with a third group, the comparison of oldest versus newest blood was calculated. Where the estimated effect was based on a continuous blood age, the estimated effect size of third-quartile blood age was compared with first-quartile blood age. Adverse events were reported if they were significant and combined, where appropriate, when they were reported in at least two studies.

Any discrepancies in data extraction were resolved by a third reviewer.

Methods of synthesis
Odds ratios and 95% confidence intervals were pooled using a random-effects model. Heterogeneity was assessed using Q and I² statistics (I²≤30% indicated low heterogeneity). Subgroup analyses were performed according to study population (subgroups of primary diagnosis types, adults and paediatric patients) and severe adverse events. Publication bias was assessed using a funnel plot and Egger's regression test. Overall mortality estimates for count data versus adjusted results from the same studies were compared using the exact Wilcoxon matched-pairs signed-rank test.

Results of the review
Twenty-one studies were included in the review and meta-analysis (409,966 patients): three randomised controlled trials (126 patients, range 17 to 57), six observational prospective studies (6,295 patients, range 34 to 4,933) and 12 observational retrospective studies (403,545 patients, range 176 to 387,130).
Mortality: The odds of mortality were statistically significantly increased with transfusion of older stored blood compared with newer stored blood (OR 1.16, 95% CI 1.07 to 1.24; 21 studies; I²=3.7%). Subgroup analyses for adult patients, trauma patients, cardiac surgery patients and non-cardiac and non-trauma patients revealed similar results. The number needed to treat to save one life with use of only new blood was 97. No statistically significant difference in the odds of mortality was found between studies with count data (16 studies) and those with adjusted mortality results (five studies) (p=0.55).

Severe adverse events: Transfusion of older blood was related to statistically significantly increased odds of multiple organ dysfunction syndrome (OR 2.26, 95% CI 1.56 to 3.25; three studies; I²=0%) and pneumonia (OR 1.17, 95% CI 1.08 to 1.27; three studies; I²=0%), compared with transfusion of newer blood. Two studies demonstrated a non-significant increase in incidence of acute respiratory distress syndrome with transfusion of older blood (OR 1.03, 95% CI 0.84 to 1.28; I²=0%). The authors reported no meta-analysis for renal dysfunction and sepsis due to significant statistical heterogeneity between the individual studies involved.

No evidence for publication bias was found. Further results were reported in the paper.

Authors' conclusions
Based on available data, use of older stored blood for transfusion was associated with a significantly increased risk of death.

CRD commentary
The review question was clear. Broad but reproducible inclusion criteria were reported. Relevant databases were searched but the restriction to studies in English increased the risk that relevant studies were missed. Efforts were made to minimise reviewer error and bias during data extraction but it was unclear whether such efforts were made during study selection. No quality assessment was reported and this made it difficult to ascertain levels of within-study bias that may have influenced the review findings. Study details were presented. Clinical differences between the studies and variability in their study designs made the appropriateness of the synthesis methods unclear. Subgroup analyses explored some clinical and statistical differences between the studies but the subgroups relating to clinical differences were very broad and it was difficult to know whether the patients within these subgroups were suitably similar for meta-analysis. The authors warned that findings may not be generalisable to the general population given that most of the included studies had populations of critically or seriously ill patients.

The authors' conclusion reflects the evidence presented but a lack of study quality information, clinical and methodological differences between the studies and the possibility of missed relevant studies mean that the reliability of this conclusion is undecided.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that well-designed multicentre randomised controlled trials with adequate statistical power were required to confirm the findings.

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