

Does blood transfusion increase risk of postoperative complications ?

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Since in several countries transfusion surveillance systems are in place, the incidence of immediate and severe side effects of blood transfusion is known and estimated approximately 1 in 100.000 transfusions. The largest risk of a severe transfusion complication is as a result from clerical errors leading to transfusion of the wrong product, acute haemolytic transfusion reaction. Other well-known side effects are bacterial contamination of blood products, transfusion-induced acute lung injury (TRALI) caused by antibodies in the donor, immune antibodies in the recipient leading to haemolytic or febrile transfusion reactions and the potential risk of transmission of an infectious disease from the donor to a patient.

But, transfusions can also cause complications that are either not immediate or not obviously associated with transfusions. Such complications must be sought in well-designed clinical studies and will never emerge from survival studies. An example of unexpected transfusion effects, is the beneficial effect of pre transplantation blood transfusions on cadaver kidney graft survival, discovered by multivariate analysis of factors associated with graft surveillance (1).

This observation that blood transfusions suppressed the immune response against an allograft, initiated a large number of in-vitro studies investigating the immune response after blood transfusions, animal experiments and clinical analysis. In-vitro studies showed that blood transfusions down-regulate T cell immune responses and natural killer cells. More than 100 observational studies addressed the effect of pre-operative transfusions on recurrence of cancer, post operative infections and mortality.

Peri-operative transfusions are in retrospective, prospective and randomised studies associated with increase of postoperative infections, (multiple) organ failure, wound dehiscence, length of stay in hospital and the intensive care unit, cancer recurrence and even with mortality. An unsolved question however is whether blood transfusions have a causal role aggravating postoperative com-

plications or that the indication for transfusion is the real risk factor. This problem can only be unravelled by randomized studies. Ideally in such studies, matched patient groups with a similar indication for transfusion (or "transfusion trigger") are assigned to receive or not to receive blood transfusions. Unfortunately, such studies are rare in general and not available for surgical interventions.

Indirect evidence of a causal role of peri-operative blood transfusions on postoperative complications may be obtained from randomised studies comparing different blood products. Another acceptable approach to estimate the contribution of transfusions among other factors leading to postoperative complications, is by multivariate regression analysis from prospective studies. We searched the literature for both types of surrogate studies. Randomised clinical trials, comparing allogeneic blood products or autologous versus allogeneic blood usage, reveal that blood transfusions are associated with a small increased risk for postoperative complications. On the other hand, multivariate regression analysis suggests that transfusions substantially contribute to postoperative complications.

Yet, it remains doubtful whether these relationships are causal. Unidentified risk factors may still be responsible for a deleterious transfusion effect. One of such factors, which is in most studies not analysed, is blood loss. Studies comparing patients treated with surgical techniques or pharmacological drugs to reduce bleeding with patients treated with placebo should not only address the question of costs and reduction of allogeneic transfusions but also the incidence of postoperative complications now attributed to blood transfusions.

References

1. Opelz G., *et al.*, LANCET, **22**, 868-71, 1972.

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