

EVIDENCE BASE FOR TRANSFUSION: COLLEGE HOSTS MEETING OF SIGN GUIDELINE DEVELOPMENT GROUP AND THE INTERNATIONAL STUDY OF PERIOPERATIVE TRANSFUSION (ISPOT)*

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Transfusion – and avoiding transfusion – is much in the news these days so there is great interest in all the alternatives to transfusion, especially for patients undergoing planned surgery.

The ISPOT project was established with a grant from the International Society for Assessment of Technologies in Health Care (ISATHC) and with funding from PPP Medical Trust to evaluate the evidence, attitudes and practices relating to the use of alternatives to perioperative allogeneic blood transfusion. These alternatives include pharmaceuticals (aprotinin, desmopressin, tranexamic acid, amino-caproic acid and erythropoietin), pre-operative autologous donation of blood (PAD), cell salvage, and acute normovolaemic haemodilution (ANH).

ISPOT has been lead by Professor Andreas Laupacis, Director of the Loeb Medical Research Institute in Ottawa. The project has involved ten countries including Scotland. The project's final workshop was held in the College with generous support from both the College and Fresenius-NPBI.

Part of the workshop was directed to a meeting with the recently-constituted SIGN Guideline Development Group on effective management of perioperative anaemia in elective surgery, chaired by Dr Pat Tansey, Consultant Haematologist, Victoria Infirmary, Glasgow.

The sharing of information and ideas emphasised the evolving views based on many studies that transfusion can often be minimised by attention to all the details of management (pre-, intra-, and post-operative). A corollary is that the real outcome benefits of special technologies such as auto-transfusion are probably restricted to a small proportion of cases.

The SIGN Guideline Group will be making use of a number of the publications from the ISPOT project: these are summarised below. A further legacy of the project is the establishment of a set of Cochrane reviews on surgical transfusion issues: these will initially be placed with the Cochrane Injuries Group with leadership from the Ottawa group, Dr Brian McClelland (SNBTS) and Dr David Henry (Perth, Australia).

PUBLISHED PAPERS

- Laupacis A, Fergusson D, for the International Study of Perioperative Transfusion (ISPOT) Investigators. Drugs to minimise peri-operative blood loss in cardiac surgery – Meta analyses using perioperative blood transfusion as the outcome. *Anesth Analg* 1997; 85:1258-67.

*A report based on a meeting held in the College on 17 June 1999

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- Laupacis A, Fergusson D, for the International Study of Perioperative Transfusion. The efficacy of technologies to minimise perioperative allogeneic transfusion. *Alternative approaches to Human Blood Resources in Clinical Practice. Proceedings of the 22nd International Symposium on Blood Transfusion, Groningen 1997.* Smit Sibinga CT, Fratantoni JC (eds). Kluwer Academic Publishers, 1998.

This meta-analysis summarised all the evidence from randomised controlled trials regarding the efficacy of aprotinin, tranexamic acid, amino-caproic acid and desmopressin. The largest amount of evidence concerns aprotinin, which clearly decreases the likelihood of perioperative transfusion. There is less evidence for tranexamic acid, but this agent also appears to be effective. A trend toward benefit is observed with amino-caproic acid, but a very small number of patients were studied.

- Graham I, Fergusson D, Dokainish H *et al.* Autologous versus allogeneic transfusion: patients' perceptions about predonation of autologous blood. *CMAJ* 1999; 160:989-95.

This study determined the perceptions of patients regarding pre-operative autologous donation, and found that patients who had pre-donated were generally very satisfied with the experience and did not suffer adverse consequences in terms of their quality of life. The study documented, once more, that patients who pre-donate autologous blood are more likely to receive transfusion than those who do not.

- Fergusson D, van Walraven C, Coyle D, Laupacis A. Economic evaluations of technologies to minimise perioperative transfusion: a systematic review of published studies. *Transfus Med Rev* 1999; 13(2):106-17.

This systematic review summarised all of the published economic evaluations of technologies to minimise perioperative transfusion. The highest quality studies concerned pre-operative autologous donation and they generally found that PAD did not meet conventional criteria for cost-effectiveness. The methodological quality of the studies for most of the other technologies was poor.

- Bryson GL, Laupacis A, Wells G for the International Study of Perioperative Transfusion (ISPOT) Investigators. Does acute normovolaemic haemodilution reduce perioperative allogeneic transfusion? A meta-analysis. *Anesth Analg* 1998; 86:9-15.

This meta-analysis of all randomised controlled trials of acute normovolemic haemodilution found that there is no clear evidence that ANH is effective, particularly when low quality randomised controlled trials are excluded from the analysis.

- McAlister FA, Clark HS, Wells PS, Laupacis A. Perioperative allogeneic blood transfusions do not cause adverse sequelae in oncologic patients. A meta-analysis of unconfounded studies. *Br J Surg* 1998; 85:171-8.

This meta-analysis could find no convincing evidence that exposure to perioperative allogeneic blood increases the risk of mortality or cancer recurrence in cancer patients.

- Laupacis A, Fergusson D, for the International Study of Perioperative Transfusion (ISPOT) Investigators. Erythropoietin to minimise perioperative blood transfusion. Four meta-analyses of randomised trials. *Transfus Med* 1998; 8:309-17.

This meta-analysis included all randomised controlled trials of the perioperative use of erythropoietin, both used on its own and to augment PAD. Erythropoietin appeared to be effective in both cardiac and orthopaedic surgery in decreasing exposure to allogeneic blood transfusion, although the number of patients studied was too small to reliably exclude a small but clinically important increase in the risk of side-effects.

- Bryson G, Laupacis A. *Evidence-based resource in anaesthesia and analgesia: A collection of systematic reviews*. BMJ Books.

This is a chapter in the first 'evidence-based' textbook of anaesthesiology, summarising the various ISPOT systematic overviews.

- Forgie M, Wells P, Laupacis A, Fergusson D. Pre-operative autologous donation decreases allogeneic transfusion but increases exposure to all red cell transfusion – Results of a meta-analysis. *Arch Intern Med* 1998; 158:610-16.

This meta-analysis of all published randomised controlled trials and high-quality cohort studies of PAD showed that PAD is effective at decreasing exposure to allogeneic blood transfusion. However, there is a considerable increase of exposure to any transfusion (allogeneic and autologous), presumably because of a lower pre-operative haemocrit in patients who pre-donate, as well as a different transfusion threshold.

- Faught C, Wells P, Fergusson D, Laupacis A. Adverse effects of methods of minimising perioperative allogeneic transfusion – A review of the literature. *Transfus Med Rev* 1998; 12(3):206-25.

This paper systematically reviewed the literature regarding the adverse effects associated with the various methods of minimising exposure to perioperative allogeneic blood transfusion.

- Rubens FD, Fergusson D, Wells PS *et al*. Plateletpheresis in cardiac surgery: a meta-analysis of the effect on transfusion requirements. *J Cardiovasc Thoracic Surg* 1999; 116:641-7.

The results of this meta-analysis of plateletpheresis in cardiac surgery were inconclusive regarding the efficacy of this technique.

PUBLICATIONS IN PRESS

- Clark H, Wells G, Huet C *et al*. Assessing the Quality of Randomised Trials: Reliability of the Jadad Scale. *Control Clin Trials*.

This methodological paper reviews the operating characteristics of the Jadad Scale, a commonly-used scale to assess the quality of randomised controlled trials. It found that there can be considerable intra-observer variability in the interpretation of this scale.

- Fergusson D, Blair A, Henry D *et al*. for the ISPOT Investigators. Technologies to minimise blood transfusion in cardiac and orthopaedic surgery: Results of a practices' variation survey in nine countries. *Int J Technol Assess Health Care*.

This survey of the use of technologies to minimise blood transfusion found a large variation in the use of these technologies within and among countries.

- Huet C, Salmi LR, Fergusson D *et al*. for the International Study of Perioperative Transfusion (ISPOT) Investigators. A meta-analysis of the effectiveness of cell salvage to minimise perioperative allogeneic blood transfusion in cardiac and orthopaedic surgery. *Anesth Analg*.

This meta-analysis of the effectiveness of cell salvage to minimise perioperative allogeneic transfusion found that it appeared to be effective for orthopaedic surgery, but much less effective for cardiac surgery and this trend was not statistically significant. Desmopressin appeared to be ineffective. The number of patients studied for all interventions was too small to definitely exclude a small but clinically important increase in side-effects.

PAPERS SUBMITTED

- Grant FC, Laupacis A, O'Connor A *et al*. Evaluation of a decision aid for autologous pre-donation for patients before open-heart surgery. *BMJ*.

As part of the ISPOT project, a decision aid was developed to help patients undergoing cardiac surgery decide whether or not they wish to pre-donate autologous blood. This paper describes the experience of the very first 59 patients given this decision aid in Ottawa, Canada. In general, patients were very enthusiastic about the decision aid. The decision aid markedly increased patients' knowledge and evidence-based expectations.

IN PREPARATION

- Fergusson D for the ISPOT Investigators. Meta-analysis of therapies to prevent blood transfusion: An exploration of methodological issues.

This study uses the data from the various ISPOT meta-analyses to explore important methodological issues regarding the conduct of meta-analyses.

Other manuscripts in the preparatory stage:

- Influences on the use of blood transfusion technologies: an overview study of national and institutional stakeholders.
- Factors instituting the uptake of technologies to minimise allogeneic transfusion in eight Ontario hospitals.
- Alternatives to allogeneic blood transfusion: a comparison of influences on uptake in Australia and Canada.
- Influences of uptake on preoperative autologous donation: a comparison of participating ISPOT countries.
- Influences on the uptake of cell-salvage and acute normovolemic haemodilution: a comparison of eight countries in the ISPOT study.
- Multi-disciplinary cross-cultural qualitative studies: a commentary on issues of collaboration, methodology, analysis and publication.

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