Autologous transfusion: a reasonable measure under the principles of health economics

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The use of postoperative autologous blood transfusion versus allogeneic blood transfusion, following elective surgery.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort, of composite gender and race, made up of 65-year-old patients undergoing elective total hip replacement surgery.

Setting
The setting was secondary care. The economic study was conducted in the USA.

Dates to which data relate
The effectiveness data were derived from studies published between 1979 and 2001. The costs were derived from literature published between 1995 and 2001. The costs were adjusted to 2000 prices.

Source of effectiveness data
The effectiveness data were derived from a review or synthesis of completed studies.

Modelling
A Markov simulation model was used to compare the two types of transfusion in terms of their costs and outcomes. A hypothetical cohort of 65-year-old patients underwent autologous or allogeneic blood transfusion, following elective total hip replacement surgery, was considered. The model included possible health states following transfusion. For example, transfusion reaction, postoperative bacterial infection, HIV infection and acquired immune deficiency syndrome (AIDS), as well as hepatitis B, C and non-A non-B non-C (fulminant, acute and chronic), potentially followed by cirrhosis and hepatocellular carcinoma. The time horizon of the model was the remainder of the patients' lives. The model was a modification of a published model (Sonnenberg et al. 1999, see "Other Publications of Related Interest" for bibliographic details).

Outcomes assessed in the review
The outcomes assessed in the review included:
the probabilities of transfusion and units of blood needed for patients undergoing total hip replacement;

the probabilities and units of additional allogeneic blood required for autologous patients;

the probabilities of transfusion reactions with autologous and allogeneic blood;

the risk of postoperative infections due to transfusion or operation (including HIV, hepatitis B, hepatitis C, non-A non-B non-C hepatitis, and bacterial infections);

the transition probabilities between the health states of the model;

the excess mortality rates at these health states; and

the age-specific mortality rates for patients of composite gender and race.

**Study designs and other criteria for inclusion in the review**
Transition probabilities were derived from the multi-centre AIDS Cohort Study. The probability of transfusion and quantity of transfusion were obtained from a Mayo Clinic Study of 332 patients undergoing hip replacements for degenerative joint disease. Two randomised trials of autologous versus allogeneic transfusion (475 patients and 120 patients in each study), both published in 1993, were used to estimate the excess risk of bacterial infection following blood transfusion. The designs of the other studies included in the review were not stated.

**Sources searched to identify primary studies**
Not reported.

**Criteria used to ensure the validity of primary studies**
Not reported.

**Methods used to judge relevance and validity, and for extracting data**
Not reported.

**Number of primary studies included**
Approximately 15 primary studies were included in the review.

**Methods of combining primary studies**
The results of the primary studies were combined by narrative means. In some cases, when the results of the primary studies differed, an average value was estimated and used in the model.

**Investigation of differences between primary studies**
Potential differences between the primary studies were not discussed in the analysis.

**Results of the review**
The probabilities pertaining to blood transfusion and complications were:

for transfusion in elective hip replacement, 0.89;

for additional allogeneic transfusion to autologous patients, 0.36;
for minor and major allogeneic transfusion reactions, 0.0039 and 0.000113, respectively;
for minor and major autologous transfusion reactions, 0.0013 and 0, respectively; and
for postoperative bacterial infection without transfusion, 0.037.

The relative risk of postoperative bacterial infection after allogeneic transfusion was 1.85.

The average transfusion requirement was 2.8 units of allogeneic blood, 2.4 units in patients receiving only autologous blood, and 1.1 units of allogeneic blood for autologous patients receiving additional blood.

The risk of infection per unit of screened blood was 1.9 x10^-6 for HIV, 1.6 x10^-5 for hepatitis B, 9.7 x10^-6 for hepatitis C, and 9.6 x10^-7 for hepatitis non-A non-B non-C.

The transition probabilities related to viral infection were:
for hospitalisation for post-transfusion hepatitis B or C, 0.033 and 0.025, respectively;
for fulminant hepatitis if hospitalised for hepatitis B or C, 0.047 and 0.20, respectively; and
for chronic hepatitis after acute hepatitis B or C, 0.075 and 0.85, respectively.

The annual rates of developing disease were:
for cirrhosis following chronic hepatitis B or C, 0.054 and 0.011, respectively;
for hepatocellular carcinoma following chronic hepatitis B or C, 0.0033 and 0.0009, respectively; and
for AIDS after HIV infection, 0.006 (after a 3-year period of zero risk).

The mortality rate was 0.005 with elective hip arthroplasty, 0.005, 0.75 with fulminant hepatitis, and 0.26 with postoperative infection.

The excess annual mortality rate due to chronic hepatitis was 0.028, cirrhosis 0.117, hepatocellular carcinoma 0.56, and AIDS 0.285.

Age-specific all-cause mortality rates were not presented.

Methods used to derive estimates of effectiveness
Some estimates of effectiveness were based on author’s assumptions.

Estimates of effectiveness and key assumptions
The following assumptions were made in the structure of the model:
the type of transfusion did not affect operative mortality;
patients receiving autologous blood after total hip replacement had donated 3 units preoperatively;
patients who acquired HIV infection as a result of postoperative transfusion began in the most favourable prognostic category and did not undergo treatment until they developed symptomatic AIDS;
if chronic hepatitis developed, it would occur during the first year after acute hepatitis;
all deaths from hepatitis occurred among patients hospitalised for fulminant hepatitis B or C; and
the mortality rate from postoperative infection was calculated on the basis of mortalities of specific postoperative infections (i.e. pneumonia, bacteraemia, deep wound infection), assuming that the relative proportions of postoperative specific infections in the model were the same as those reported for patients in four New Jersey hospitals.

Measure of benefits used in the economic analysis
The outcome measure used was the number of quality-adjusted life-years (QALYs) associated with each strategy assessed. The utility weights were derived from published literature.

Direct costs
The direct costs consisted of health care service costs. These comprised the costs of transfusion (autologous and allogeneic), transfusion reaction and bacterial infection, acute and chronic hepatitis (treatment and hospitalisation), care for cirrhosis and hepatocellular carcinoma, and AIDS treatment. The quantities and the unit costs were not reported separately. The costs were based on data reported in the published literature or in hospital administrative databases. The total costs were derived using modelling. Discounting was carried out at an annual rate of 3%, which was appropriate as the study estimated the long-term costs resulting from transfusion. All of the costs were adjusted to 2000 prices.

Statistical analysis of costs
The costs were treated deterministically. No statistical analysis of the costs was undertaken.

Indirect Costs
The indirect costs were not included in the analysis.

Currency
US dollars ($).

Sensitivity analysis
A sensitivity analysis was carried out to investigate whether the variability in input parameters had any impact on the results of the economic analysis. The parameters examined included the cost-difference between autologous and allogeneic blood, the relative risk of infection with allogeneic transfusion, and mortality and the costs of infection. Also examined were the risk of death and morbidity of autologous transfusion, the age of patients, and the discount rate. One-way, two-way and threshold sensitivity analyses were performed. The threshold analysis was used to demonstrate cases in which the incremental cost-effectiveness ratio (ICER) reached $50,000/QALY, a value below which the intervention was deemed cost-effective. The range of values used in the other forms of sensitivity analysis was based on author's assumptions and values reported in the literature.

Estimated benefits used in the economic analysis
The total benefits of each intervention were not presented separately. Only the incremental benefits were shown. Autologous transfusion resulted in 0.0523 additional QALYs per patient over allogeneic transfusion. The benefits were discounted at an annual rate of 3%, and were estimated over the patient's lifetime.

Cost results
The average total cost per patient was $1,395 for allogeneic transfusion and $1,539 for autologous transfusion.

Autologous transfusion incurred an additional (incremental) cost of $144 per patient.

The total costs were discounted at 3% annually and referred to the lifetime of the patient.
Synthesis of costs and benefits
The costs and benefits were combined in the form of ICERs. The ICER of autologous versus allogeneic transfusion was $2,750/QALY (i.e. autologous transfusion was more effective and incurred an additional cost of $2,750 per additional QALY gained).

Sensitivity analysis showed that the ICER was sensitive to the cost-difference between autologous (more expensive) and allogeneic blood. Autologous transfusion became dominant (more effective and less costly than allogeneic transfusion) when its additional cost per unit was less than $13 (base-case $66). Its ICER exceeded $50,000/QALY when it cost $652 per unit more than allogeneic blood.

The ICER was also highly sensitive to the relative risk of bacterial infection with allogeneic transfusion; if this was 1.0, then the ICER would become $2,545,000/QALY. The threshold analysis showed that if the relative risk exceeded 1.10, then the ICER would be lower than $50,000/QALY. If the ratio exceeded 2.39, then autologous transfusion would dominate. In addition, autologous transfusion would be cost-effective (ICER < $50,000/QALY) if the mortality of infection exceeded 0.012, even if the additional cost of infection were $0. If the cost of infection exceeded $19,600, then autologous transfusion would dominate.

The results were sensitive to the risk of death or morbidity of autologous transfusion. However, the threshold values above which the ICER would exceed $50,000/QALY were well above the likely range for these values. The results were not significantly affected by patient age or discount rate.

Authors’ conclusions
Autologous transfusion was a cost-effective intervention, demonstrating an incremental cost-effectiveness ratio (ICER) well below the acceptable threshold of $50,000 per quality-adjusted life-year (QALY). Postoperative bacterial infection was by far the most significant determinant of cost-effectiveness of autologous transfusion, or any other allogeneic transfusion sparing strategy.

CRD COMMENTARY - Selection of comparators
Although a justification for the comparators used was not explicitly given, it was apparent that both interventions represented alternative forms of current practice in the USA. Allogeneic transfusion seems to have been routine practice initially, eventually being replaced by autologous transfusion (where applicable), owing to strong concerns about the risks of infection after allogeneic transfusion. You should consider whether any of the comparators represents widely used practice in your own setting.

Validity of estimate of measure of effectiveness
The author did not state that a systematic review of the literature had been undertaken. The effectiveness estimates were combined using narrative methods. In cases where the results of the primary studies differed, an average value was estimated and used in the model. The author reported in detail the methods used to derive estimates of effectiveness, but potential differences between the primary studies were not investigated. However, the range of specific parameter values derived from the review was subjected to a sensitivity analysis.

Validity of estimate of measure of benefit
The estimation of benefits was modelled. The Markov model used was appropriate for this purpose, as it included all potential health states following blood transfusion and enabled the calculation of benefits over the lifetime of the patients. The measure of health benefits used in the economic analysis was QALYs. These are appropriate for comparing the results of this study with those of different interventions. The future benefits were discounted using an appropriate discount rate, which was varied in the sensitivity analysis. In the present study, the author did not report how the quality of life was estimated: by the use of patients’ preferences (which is the more appropriate approach) or experts’ opinion. This fact may limit the relevance of the QALY measurements.
Validity of estimate of costs
The perspective of the study was not stated, but it appears to have been consistent with that of the health care system. All the relevant costs to this perspective were included in the analysis. The costs and the quantities were not reported separately, which hinders the generalisability of the results. A sensitivity analysis of the costs was conducted for specific cost components, such as the cost-difference between autologous and allogeneic blood, and the cost of postoperative bacterial infection. Discounting was carried out, which was appropriate as the costs were incurred during the patients' lifetime. The year to which the prices referred was reported, and this improves the reproducibility of the results.

Other issues
The author made appropriate comparisons of his findings with those from other studies. However, the issue of the generalisability of the results to other settings was not addressed. The results of the analysis were adequately reported and the author's conclusions reflected the scope of the analysis. The author did not report any further limitations of his study.

Implications of the study
Based on the study results, it can be inferred that, in terms of cost-effectiveness, postoperative autologous transfusion could replace allogeneic transfusion following elective surgical procedures. According to the analysis, the issue of relative risk of postoperative bacterial infection is crucial to the cost-effectiveness of autologous blood transfusion and, at the time of publication, had still not definitely been resolved. The author suggested that his analysis could be used as a framework for evaluating novel treatments designed to spare allogeneic blood transfusion, such as haematopoietic growth factors or blood substitutes.

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