The efficacy and cost of aprotinin in children undergoing reoperative open heart surgery

D’Errico C C, Shayevitz J R, Martindale S J, Mosca R S, Bove E L

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
Aprotinin in children with congenital heart disease undergoing repeat open heart surgery (OHS).

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
Children older than 1 month undergoing reoperative OHS.

Setting
The practice setting was a children's hospital in the United States. The economic study was carried out in the United States.

Dates to which data relate
Effectiveness and resource use data was collected during the period July 1993 to October 1995. The price year was not stated.

Source of effectiveness data
The evidence for final outcomes was derived from a single study.

Link between effectiveness and cost data
The costing was undertaken prospectively on the same patient sample as that used in the effectiveness study.

Study sample
61 patients admitted to a single centre for repeat OHS for congenital heart disease were recruited. The study was stopped after enrolment of 61 patients (prior to completion of the planned 165 patients) because preliminary examination of the results from patients ineligible for this study indicated significant differences in blood loss between patients who received aprotinin and those who did not. Four of the original 61 patients enrolled were excluded from the analysis: one had antithrombin III deficiency, 2 patients experienced surgical bleeding requiring mediastinal re-exploration and one patient could not be separated from cardiopulmonary bypass (CPB).

Study design
The study was a single centre, randomised controlled trial. Patients were randomised in a double-blind fashion to receive either ALD, ASD or P. The surgical procedures were each performed by one of two surgeons.

**Analysis of effectiveness**
The analysis of the clinical study was based on treatment completers only. The primary health outcomes used were the amount of postoperative blood loss (not significantly different across groups) and the need for transfusion of banked blood components (significantly lower for both aprotinin groups compared to placebo: p=0.005 for ASD and p=0.006 for ALD). There were no significant differences among the groups with respect to CPB, aortic cross-clamp, and deep hypothermic circulatory arrest durations, volume of packed red blood cells used in the CPB circuit prime, and the volume of perfusate infused at the end of the CPB. Significantly more female patients were randomised to the P group.

**Effectiveness results**
The volume of blood loss in the operating room and over the first 24 postoperative hours was not significantly different between the groups of patients:

- **ALD**, 2.3 +/- 1.8 mL/kg and 27 +/- 19 mL/kg;
- **ASD**, 2.4 +/- 2.0 mL/kg and 35 +/- 28 mL/kg;
- and **P**, 5.9 +/- 10.2 mL/kg and 44 +/- 39 mL/kg;

(p=0.15 and p=0.26, respectively).

Over the first 24 postoperative hours, fewer patients in the ALD and ASD groups received packed red blood cells than P patients (ALD 53%, ASD 89% and P 95%, p=0.001). ALD (median 1, range: 0 - 13) and ASD (median 2, range: 0 - 12) patients had significantly fewer exposures to banked blood component units than P patients (median 6, range: 0 - 11; p=0.001).

**Clinical conclusions**
The results demonstrated that the use of aprotinin in children undergoing OHS was associated with a decrease in both the proportion of patients receiving banked blood component transfusions and the number of exposures to different units of banked blood components over the first 24 postoperative hours. The groups did not differ significantly with respect to the overall number of complications (including mortality).

**Measure of benefits used in the economic analysis**
No single measure of benefit was produced within the economic evaluation. The effectiveness analysis revealed that aprotinin was more advantageous compared to placebo.

**Direct costs**
Local charges at the clinical centre were used in cost estimation. Costs were not discounted. Price dates were not given. Hospital direct costs were considered including: drugs, OR time, blood products, hospital stay charges. Quantities were not reported separately and were measured during the trial (1993-1995).

**Currency**
US dollars ($).

**Sensitivity analysis**
Sensitivity analysis was not carried out.
Estimated benefits used in the economic analysis
Not applicable.

Cost results
The total charges were $5,318.99 for ALD, $5,006.12 for ASD, and $8,893.86 for P. The blood product charge for each patient who received aprotinin was $634 (+/- 609) or for placebo was $2,371 (+/-4350; p=0.02). Aprotinin patients spent on average 15 minutes less in the OR, received fewer units of blood products, but incurred the additional charge for aprotinin. They accrued $2,236 less on average in OR, blood component, and drug charges overall (p=0.015) than the placebo patients.

Synthesis of costs and benefits
Synthesis was not undertaken by the authors because it was not relevant since clinical outcomes were superior for the aprotinin groups and charges were less when compared to placebo.

Authors' conclusions
For a specific group of children, namely those undergoing reoperative OHS, aprotinin can provide a cost-effective means of limiting banked blood unit transfusions and, thereby, decrease the risks associated with exposures to multiple blood components.

CRD COMMENTARY - Selection of comparators
It is not clear why a placebo was used as the comparator, nor do the authors provide a justification for this choice.

Validity of estimate of measure of benefit
The authors noted that the number of patients was too small to draw conclusions about the safety of aprotinin.

Validity of estimate of costs
Inadequate detail was provided on the methods of cost estimation.

Source of funding
Supported in parts by grants from Miles Pharmaceuticals Inc and Metronic Hemotec Inc.

Bibliographic details

PubMedID
8942585

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Aprotinin /administration & dosage /economics /therapeutic use; Cardiac Surgical Procedures /economics; Child; Child,
Preschool; Cost Savings; Cost-Benefit Analysis; Double-Blind Method; Erythrocyte Transfusion/adverse effects/economics; Female; Hemostatics/administration & dosage/economics/therapeutic use; Hospital Charges; Hospitalization; Humans; Infant; Length of Stay; Male; Operating Rooms/economics; Placebos; Plasma; Platelet Transfusion/adverse effects/economics; Postoperative Complications; Prospective Studies; Reoperation; Risk Factors; Time Factors

AccessionNumber
21997000023

Date bibliographic record published
30/11/1998

Date abstract record published
30/11/1998