An economic analysis of amiodarone versus placebo for the prevention of atrial fibrillation after open heart surgery


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 study evaluated prophylaxis with oral amiodarone in patients undergoing open heart surgery. The doses used are described in the 'Study Sample' field.

Type of intervention
Prophylaxis, (primary prevention).

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised elderly patients (at least 60 years old) and pre-specified sub-groups (i.e. sub-groups in which amiodarone was more beneficial, see 'Effectiveness Results' section) undergoing open heart surgery.

Setting
The setting was secondary care (an urban academic hospital). The economic study was carried out in Connecticut, USA.

Dates to which data relate
The dates to which the effectiveness and resource use data related were not reported. The price year was 2000.

Source of effectiveness data
The effectiveness data were derived from a single prospective study. The effectiveness analysis was published elsewhere (Giri et al., see 'Other Publications of Related Interest' below for bibliographic details). This paper reported the outcome results briefly and the cost analysis in more detail.

Link between effectiveness and cost data
The costing was carried out prospectively on the same sample of patients as that used in the effectiveness study.

Study sample
Power calculations were reported. A sample size of 100 patients per group was needed to assure 0.80 power in the detection of a 50% difference in postoperative atrial fibrillation rate, with an anticipated 33% rate in the placebo group.

A total of 220 patients (168 men, 52 women) were included in the study, with an approximate 10% drop-out rate
anticipated after selection. Of these, 120 (74 men) were assigned to the amiodarone group (receiving amiodarone plus beta-blockers) and the remaining 100 (94 men) to the placebo group (receiving beta-blockers alone). The mean age of the patients was 72.5 years in the amiodarone group and 72.7 years in the placebo group.

Patients who were enrolled less than 5 days before surgery were given amiodarone 400 mg 4 times daily on preoperative day 1, 600 mg twice daily on the day of surgery, and 400 mg twice daily on postoperative days 1 to 4. Patients who were enrolled at least 5 days before surgery were given amiodarone 200 mg 3 times daily for 5 days before surgery, 400 mg twice daily on the day of surgery, and 400 mg twice daily on postoperative days 1 to 4.

Study design
This was a prospective, double-blinded, randomised study that was carried out in a single centre. The duration of follow-up was until discharge. The authors did not report any loss to follow-up.

Analysis of effectiveness
It appears that the analysis of the clinical study was conducted on an intention to treat basis. The primary health outcome used was the frequency of atrial fibrillation. The secondary health outcomes were:

- beta-blocker tolerance,
- the frequency of stroke,
- the frequency of ventricular tachycardia,
- the occurrence rates of adverse effects (bradycardia, heart block, nausea and hypotension),
- the levels of thyroid-stimulating hormone and aminotransferase, and
- the length of stay.

The baseline characteristics of the groups were generally similar except for a higher percentage of patients who had experienced a myocardial infarction in the amiodarone group, (p=0.005). The surgical characteristics were also generally similar. The exceptions were fewer patients in the amiodarone group required defibrillation to restore sinus rhythm after aortic cross-clamp release, (p=0.04) and the pump heart rate pre- and post cardiopulmonary bypass.

Effectiveness results
The overall risk of atrial fibrillation was reduced by 41% with amiodarone (frequency with amiodarone 23% versus 38% with placebo; p=0.01).

Postoperative beta-blockers were tolerated in a similar percentage of patients in the amiodarone and placebo groups (70% versus 64%; p=0.758).

Amiodarone was more beneficial in the following sub-groups:

- patients with no tolerance to preoperative beta-blockers,
- those with normal left atrial size,
- those with no history of atrial fibrillation or heart failure, and
- those older than 70 years.

Amiodarone significantly lowered the frequency of cerebrovascular accident and ventricular tachycardia (frequency with amiodarone 2% versus 7% with placebo; p=0.04 for each).
The occurrence rates of adverse effects were similar in the two groups, although there was a trend toward more nausea with amiodarone (27% versus 16%; p=0.056).

Thyroid-stimulating hormone and aminotransferase levels were similar in the two groups.

The mean length of stay in the intensive care unit was 2.4 (+/- 1.1) days in the amiodarone group versus 2.5 (+/- 1.2) days in the placebo group (difference non significant).

The total length of stay was not significantly different between the amiodarone and the placebo groups (9.2 +/- 8.2 days versus 9.4 +/- 7.8 days; p=0.86).

**Clinical conclusions**

Routine prophylaxis with amiodarone, in addition to standard care with beta-blockers, was more effective than standard care alone in patients undergoing open heart surgery.

**Measure of benefits used in the economic analysis**

No summary benefit measure was used in the economic evaluation. In effect, a cost-consequences analysis was conducted.

**Direct costs**

A hospital perspective was adopted. The categories of costs included in the analysis were general ward, intensive care unit, operating room medical and surgical supplies pharmacy, laboratory, intravenous therapy, anaesthesia, respiratory, cardiac catheterisation, radiology, physical therapy, electrocardiography, vascular laboratory, haemodialysis, computer tomography, nuclear cardiology, gastrointestinal service, speech therapy, electroencephalography, pulmonary function testing, recovery room and emergency room. Professional fees were not included. The costs were determined from the day of surgery until hospital discharge. Charges were obtained from the Hartford hospital Claims management database, and then converted to costs using hospital-derived cost-to-charge ratios. The unit costs and the quantities of resources used were not presented separately. The price year was 2000. The resource use data were derived from actual data coming from the sample of patients involved in the effectiveness study. Discounting was not relevant as all the costs were incurred during less than one year.

**Statistical analysis of costs**

The costs were presented as mean values with standard deviations. A statistical test (non-parametric Mann-Whitney test) was carried out to compare the costs observed in the study groups. A multivariate analysis was conducted to determine whether specific preoperative factors were predictors of total cost, (preoperative beta-blockers use, age older than 70 years and no history of heart failure).

**Indirect costs**

The indirect costs were not included.

**Currency**

US dollars ($).

**Sensitivity analysis**

One-way sensitivity analyses were performed on the efficacy of amiodarone using 95% confidence intervals (95% CI: 3.4% - 27.6%) and on the cost of amiodarone per 200-mg tablet ($0.44 - $1.31), with the lower limit representing the cost of generic oral amiodarone.
Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The costs in all departments were similar between the amiodarone and placebo groups, (p>0.05 for all comparisons).

The mean total cost was $15,565 (+/- 9,832) in the amiodarone group versus $16,126 (+/- 8,043) in the placebo group (difference $561/patient; p=0.12).

In the one-way sensitivity analysis, the findings remained robust to changes in the effectiveness and cost of amiodarone.

Synthesis of costs and benefits
A synthesis of the cost and effectiveness data was not relevant since amiodarone was the dominant strategy (the costs between the amiodarone and placebo groups were similar, but amiodarone was more effective than placebo).

Authors' conclusions
Routine prophylaxis with amiodarone in addition to standard care with beta-blockers is cost-effective, compared with standard care alone, in patients undergoing open heart surgery.

CRD COMMENTARY - Selection of comparators
The choice of the comparator (beta-blockers alone) was justified as it represented the standard prophylaxis to prevent postoperative fibrillation in patients undergoing open heart surgery. The authors mentioned other possible interventions that were not included in the analysis. You should decide whether the comparator used represents a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
A prospective double-blinded randomised study was performed, which was appropriate for the study question. Power calculations were carried out and these justified the size of the sample used in the study. The study groups were comparable at baseline, thus confounding factors are probably low. The investigators were blinded to the allocation of patients to the study groups; therefore, few assessment biases may have occurred. The data came from a single centre and this may hinder the generalisability of the results to other settings. Relevant statistical analyses were undertaken to compare health outcomes between the groups.

Validity of estimate of measure of benefit
No summary benefit measure was used in the analysis so, in effect, a cost-consequences analysis was carried out. Please refer to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

Validity of estimate of costs
The perspective of the study (hospital) was stated. It appears that all the relevant categories of costs have been included in the analysis. The professional fees were omitted from the analysis since physicians and surgeons were not employed by the hospital. No justification was provided for the exclusion of costs after the initial hospitalisation. Since there was a significant reduction in the frequency of stroke, these costs might have differed between the two groups and, therefore, the omission might have biased the results in favour of the placebo group.

Details on the unit costs and resource quantities were not reported, which limits the transferability of the economic analysis to other settings. The authors acknowledged that the costs incurred might have been protocol driven and these trials have low external validity. The authors reported a cost-to-charge ratio mechanism to derive costs which is
methodologically superior to the reporting of charges only. Discounting was not carried out as the costs were incurred during less than 2 years. Statistical tests of the costs were performed when the cost estimates were compared. Sensitivity analyses were performed on the costs to test the robustness of the results.

Other issues
The authors compared their results with other published studies and found consistent results. They did not address the issue of the generalisability of the study results to other settings. The results were not reported selectively and the conclusions reflected the scope of the study. The authors reported limitations of the cost analysis (highlighted already). Sensitivity analyses were performed to take variability in the cost or effectiveness data into consideration.

Implications of the study
The authors recommended that future studies should be conducted to examine the cost-effectiveness of selective prophylaxis, while primary cost-effectiveness studies should be conducted to validate these findings.

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Bibliographic details

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Other publications of related interest


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