Low-dose oral amiodarone prophylaxis reduces atrial fibrillation after pulmonary resection

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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 low-dose oral amiodarone (LDOA) as prophylactic treatment for atrial fibrillation (AF) after pulmonary resection. LDOA comprised 200 mg by mouth every 8 hours. Treatment was started after recovery from general anaesthesia and was discontinued at dismissal.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients undergoing pulmonary resection by thoracotomy.

Setting
The setting was a hospital. The study was carried out at the Mayo Clinic, Scottsdale, AZ, USA.

Dates to which data relate
The effectiveness and resource use data were collected between October 1 1998 and March 31 2001. The cost data may have related to the same period. The price year was not reported.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was undertaken retrospectively using the same patient population as that used in the effectiveness analysis.

Study sample
No power calculations were performed in the planning phase of the study to assure a certain power. Patients that underwent pulmonary resection by thoracotomy at the hospital were analysed. The final sample size comprised 83 patients. Of these, 31 were treated by the same doctor and received LDOA, while 52 were treated by other, different doctors and did not receive LDOA. The median age was 74 years (age range: 60 - 83) in the LDOA group and 71 years (age range: 61 - 86) in the no-prophylaxis group. Patients that underwent thorascopic resections were excluded because, as the authors stated, the incidence of postoperative AF was less well defined in that population. The authors did not report any evidence that the study sample was appropriate for the study question.
Study design
This was a retrospective cohort study that was performed at a single centre. The duration of follow-up was not specifically reported, although it may have been up to 6 weeks (i.e. the treatment period for AF). The authors did not report any loss to follow-up.

Analysis of effectiveness
The basis used for the effectiveness analysis was not reported, although it seems to have been intention to treat. The primary health outcomes assessed in the clinical study for both the LDOA and no-prophylaxis patients were:

- the overall incidence of AF and the odds ratio (OR) for LDOA patients in comparison with no-prophylaxis patients;
- the incidence of AF by type of surgical procedure (i.e. pneumonectomy, intrapericardial dissection, extended resection, lobectomy, wedge resection, segmentectomy, metastasectomy, and thymectomy with lung resection);
- the number and proportion of patients developing AF that received electrical cardioversion;
- the number and proportion of patients experiencing complications related to AF;
- the number and proportion of admissions to the intensive care unit (ICU) that were related to AF; and
- the number and proportion of patients experiencing complications, in general, and the type of complication experienced.

The authors also reported the following:

- the number and proportion of LDOA patients with AF that experienced nausea as a side effect of LDOA;
- the time to AF postoperatively;
- the time to achieve a heart rate of less than 110 beats per minute;
- the total duration of AF;
- the time to recurrent AF;
- the duration of recurrent AF; and
- the number of days of hospitalisation for both groups of patients.

Moreover, univariate and multivariate logistic regression models were used to assess the association of postoperative AF with the use of LDOA. These models considered potential confounding factors such as age, prior arrhythmias, heart medication, heart disease, prior cardiac operation or angioplasty, abnormal preoperative electrocardiogram, hypertension, diabetes, prior myocardial infarction and pulmonary risk factors. The authors reported that there was no association between the two groups and preoperative risk factors such as preoperative risk heart rate, preoperative ejection fraction, age, forced expiratory volume, predicted diffusion capacity of the lung for carbon monoxide, and preoperative oxygen desaturation with exercise.

Effectiveness results
In total, 3 patients receiving LDOA (9.7%) and 17 patients not receiving LDOA prophylaxis (33%) developed postoperative AF (OR 0.221; 95% confidence interval, CI: 0.059 - 0.829).

The median total duration of AF was 18 hours (range: 8 - 186) in the no-prophylaxis group and 2 hours (range: 0.5 - 12) in the LDOA prophylaxis group.

The median hospital stay was 7 days (range: 3 - 17) in the no-prophylaxis group and 6 days (range: 3 - 22) in the LDOA
prophylaxis group.

The only significant differences between patients receiving and not receiving LDOA prophylaxis, in terms of the development of AF by type of surgical procedure, were found among patients that underwent intrapericardial dissection or lobectomy. Of those that underwent intrapericardial dissection, 4 of the 5 no-prophylaxis patients (80%) developed AF versus 1 of the 6 LDOA patients (17%), (p=0.08). Of those that underwent lobectomy, 11 of the 37 no-prophylaxis patients (30%) developed AF versus none of the 21 LDOA patients (0%), (p=0.0046).

Of the patients experiencing AF, 2 of the 17 no-prophylaxis patients (11.7%) required electrical cardioversion versus none of the 3 LDOA patients (0%).

Four of the 17 no-prophylaxis patients (23.5%) experienced AF-related complications versus none of the 3 LDOA patients (0%).

Two of the 17 patients in the no-prophylaxis group (11.7%) were admitted to the ICU in relation to AF versus none of the 3 patients in the LDOA group (0%).

In general, 23 of the no-prophylaxis patients and 9 of the LDOA patients experienced complications. The complications in the no-prophylaxis group were prolonged air leak (7), pneumonia (3), atelectasis requiring bronchoscopy (3), respiratory failure requiring ventilatory support (2), renal failure (2), gastrointestinal tract bleeding (2), re-exploration for bleeding (2), myocardial infarction (1) and pericarditis (1). The complications in the LDOA group were renal failure (4), postoperative deaths due to myocardial infarction (1) and bronchopleural fistula (1), urinary retention (1) and physical deconditioning (1).

None of the confounding factors considered at analysis were found to be associated with AF.

Clinical conclusions
The risk of developing AF was significantly lower among those patients receiving LDOA than those not receiving LDOA prophylaxis. The median duration of AF was also shorter in the LDOA group and the number of complications lower. However, it seems worthwhile to remark that there were 2 postoperative deaths due to general complications among the LDOA patients versus none in the no-prophylaxis group.

Measure of benefits used in the economic analysis
No summary measure of benefit was used in the economic analysis. The study was therefore categorised as a cost-consequences analysis.

Direct costs
Only days of hospitalisation were reported separately from the costs. The direct costs included in the economic analysis appear to have been those of the hospital, as hospital charges were used to estimate the costs. The source of the costing was the patients' records, thus the costing was based on actual data. Discounting was not performed, but it was irrelevant since the costs were incurred in less than 2 years. The study reported the median hospital charges, which appear to have been the median hospital charges per patient, although the authors did not specify this clearly. The price year was not stated.

Statistical analysis of costs
A regression model was used to compare the hospital charges according to the number days of hospitalisation for both the LDOA and no-prophylaxis patients.

Indirect Costs
No indirect costs were considered in the economic analysis.
Currency
US dollars ($).

Sensitivity analysis
No sensitivity analyses were performed.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
No significant differences were found in the median hospital charges when patients with and without LDOA prophylaxis were compared. The median hospital charges were $30,800 (range: 20,400 - 96,900) for patients not receiving LDOA prophylaxis versus $26,700 (range: 11,000 - 55,900) for patients receiving LDOA prophylaxis, (p>0.05). The median hospital charges for patients in general were $28,600 (range: 11,000 - 96,100).

The results of the regression model showed that patients receiving LDOA prophylaxis had lower incremental charges per day of hospital stay, compared with patients not receiving LDOA prophylaxis, when the number of days of hospitalisation was 5 or more.

The costs of adverse events may have been considered in the economic analysis.

Synthesis of costs and benefits
Not applicable due to the cost-consequences analysis undertaken.

Authors' conclusions
Low-dose oral amiodarone (LDOA) significantly reduced the incidence of atrial fibrillation (AF) following pulmonary resection and may be a cost-effective strategy.

CRD COMMENTARY - Selection of comparators
Although no explicit justification was given for the comparator used (no LDOA prophylaxis treatment), it appears to represent current practice in the authors' setting (besides the health technology under analysis). You should decide whether this comparator represents current practice in your own setting.

Validity of estimate of measure of effectiveness
The analysis used a retrospective cohort study. The authors stated that the results might have been biased because of the retrospective nature of the study and because the patients were not randomly assigned to each one of the groups. The authors did not show that the study sample was representative of the study population. The fact that the patients were recruited from only one site may make it unlikely that the study sample would be representative of the study population. The patient groups were shown to be comparable at analysis for some important risk factors (e.g. hypertension, diabetes and prior myocardial infarction). However, some risk factors such as hyperthyroidism and heavy alcohol use were not considered, which may have influenced the outcomes obtained. Regression analyses were used to take account of confounding factors.

Validity of estimate of measure of benefit
The authors did not derive a summary measure of health benefit. The analysis was therefore categorised as a cost-consequences analysis.
Validity of estimate of costs
The perspective adopted was not reported, although it appears to have been that of the hospital. It cannot be stated clearly whether all the relevant costs were considered in the economic analysis since hospital charges, and not categories of costs, were included in the economic analysis. The hospital charges were used to estimate the costs, which may not reflect the true opportunity costs of the interventions considered at analysis. The resource quantities and the costs were not reported separately and the price year was not reported. All these factors introduce uncertainty into the reliability of the costing and hinder reflation exercises to other settings. A regression analysis was used to compare the hospital charges for both interventions. The cost estimates were specific to the study setting and no sensitivity analyses were performed.

Other issues
The authors made appropriate comparisons of their findings with those from other studies. They reported that the estimated incidence of AF was similar to that observed in other evaluations. LDOA prophylaxis was also found to be effective for other surgical interventions such as cardiac operations.

Implications of the study
The authors suggested that a prospective randomised controlled trial should be performed.

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None stated.

Bibliographic details

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Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
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& control; Confidence Intervals; Cost-Benefit Analysis; Humans; Middle Aged; Odds Ratio; Pneumonectomy;
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