Pharmacologic prophylaxis for postoperative atrial tachyarrhythmia in general thoracic surgery: evidence from randomized clinical trials
Sedrakyan A, Treasure T, Browne J, Krumholz H, Sharpin C, van der Meulen J

CRD summary
This review assessed the effectiveness of anti-arrhythmic medications in reducing post-operative atrial tachyarrhythmia (AT) in general thoracic surgery. The authors concluded that calcium-channel blockers and beta-blockers both reduce post-operative AT, but evidence does not support the use of digitalis. This was generally a well-conducted review and the authors’ conclusions are likely to be robust.

Authors’ objectives
To assess the effectiveness of anti-arrhythmic medications in reducing post-operative atrial tachyarrhythmia (AT) in patients undergoing general thoracic surgery (GTS).

Searching
MEDLINE, EMBASE and the Cochrane Controlled Trials Register were searched from 1980 to 2003; the search terms were reported. No language restrictions were applied. The reference lists of RCTs and reviews were checked for additional studies.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Studies that compared the prophylactic use of anti-arrhythmic medications with placebo were eligible for inclusion. The studies were required to use no additional experimental medications or devices. The included studies used calcium-channel blockers, beta-blockers, magnesium, digitalis, flecainide and amiodarone.

Participants included in the review
Studies of patients undergoing GTS were eligible for inclusion. Studies of patients undergoing heart-lung transplantation or paediatric operations were excluded. The participants in the included studies had a mean age of 63.2 years (reported in 9 studies), 41.3% were female (reported in 4 studies) and 20.9% were undergoing pneumonectomy.

Outcomes assessed in the review
The review assessed arrhythmia, bradycardia, hypotension, severe pulmonary complications, myocardial ischaemia and mortality. The criteria used to define these outcomes were reported.

How were decisions on the relevance of primary studies made?
Two reviewers independently selected studies.

Assessment of study quality
Validity was assessed and scored using the Jadad scale, which considers the reporting and handling of randomisation, blinding and handling of withdrawals. The maximum possible score was 5 points. It appears that one reviewer extracted validity data. It was unclear whether these data were independently confirmed by a second reviewer.

Data extraction
One reviewer extracted the data and a second reviewer independently confirmed the number of events and the number
randomised to treatment groups. Any discrepancies were resolved through discussion among all reviewers. The authors of all selected studies were contacted for details of missing information. Unspecific reports of 'no major complications' were counted as missing data rather than zero events.

**Methods of synthesis**

How were the studies combined?
The studies were grouped according to the class of medication and combined using a fixed-effect meta-analysis, with weighting by the inverse of the variance. Pooled risk ratios (RRs) with 95% confidence intervals (CIs) were calculated. Risk differences were also calculated and used to estimate the number of events averted or induced per 100 procedures, with 95% CI.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the chi-squared statistic.

**Results of the review**

Eleven RCTs (n=1,294) were included.

The quality scores ranged from 2 to 5. No statistically significant heterogeneity was found.

Calcium-channel blockers (4 RCTs, n=618) significantly reduced the risk of AT compared with placebo (RR 0.50, 95% CI: 0.34, 0.73). For every 100 patients treated, 11 episodes of AT were averted (95% CI: -17, -5). Calcium-channel blockers carried a slightly greater risk of adult respiratory distress syndrome (ARDS) than placebo, but this difference was not statistically significant (RR 1.31, 95% CI: 0.46, 3.72).

Beta-blockers (2 RCTs, n=129) significantly reduced the risk of AT compared with placebo (RR 0.40, 95% CI: 0.17, 0.95). For every 100 patients treated, 14 episodes of AT were averted (95% CI: -26, -2). Beta-blockers increased the risk of pulmonary oedema, although this was not statistically significant (RR 2.15, 95% CI: 0.74, 6.23).

Magnesium (1 RCT, n=194) significantly reduced the risk of AT compared with placebo (RR 0.40, 95% CI: 0.21, 0.78). For every 100 patients treated, 16 episodes of AT were averted (95% CI: -27, -5). No information on severe pulmonary complications with magnesium was reported.

Digitalis (3 RCTs, n=285) significantly increased the risk of AT compared with placebo (RR 1.51, 95% CI: 1.00, 2.28). No data on severe pulmonary complications with digitalis were reported.

The one RCT (n=30) of flecainide found no statistically significant difference between flecainide and placebo for AT (RR 0.16, 95% CI: 0.01, 2.89). No severe pulmonary complication events were reported.

The one RCT (n=62) of amiodarone found no statistically significant difference between amiodarone and placebo for AT (RR 0.14, 95% CI: 0.02, 1.10). There was a greater risk of ARDS in the amiodarone group than the placebo group, but this difference was not statistically significant (RR 7.00, 95% CI: 0.38, 130.26).

Further analyses of the outcomes hypotension, bradycardia, myocardial ischaemia and mortality were presented.

**Authors’ conclusions**

Calcium-channel blockers and beta-blockers both reduce post-operative atrial tachyarrhythmia. Treatment should be individualised and the potential harms of beta-blockers taken into account. Evidence does not support the use of digitalis in patients undergoing GTS.

**CRD commentary**

The review question was clear in terms of the study design, intervention, participants and outcomes. Three relevant databases were searched and attempts were made to minimise language bias. Methods were used to minimise bias and...
errors in the study selection and data extraction processes, although not all data were extracted in duplicate. Validity was assessed using appropriate criteria, but the quality of the individual studies was not reported. Statistical heterogeneity was assessed and the studies were appropriately combined in meta-analyses. This was generally a well-conducted review and the authors’ conclusions are likely to be robust.

**Implications of the review for practice and research**

Practice: The authors stated that the potential adverse effects of beta-blockers should be taken into account when selecting a prophylactic agent for patients undergoing GTS.

Research: The authors stated that there is a need to examine the effectiveness of magnesium as an addition to a main prophylactic regimen.

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