Adverse effects of low dose amiodarone: a meta-analysis
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Authors’ objectives
To assess the odds of experiencing adverse effects with low-dose amiodarone therapy when compared with placebo.

Searching
MEDLINE was searched through 1996 for trials published in all languages. Manual searches of references and review articles were also carried out.

Study selection
Study designs of evaluations included in the review
Double-blind placebo-controlled trials of maintenance amiodarone with a mean follow-up of at least 12 months [A: and presence of an explicit description of adverse effects in both intervention and placebo groups] were included. Crossover designs were excluded.

Specific interventions included in the review
Maintenance amiodarone (dose of less than or equal to 400 mg/day) and placebo.

Participants included in the review
The majority of participants were men, aged 56 to 66 years, who all had underlying heart disease; this included post-myocardial infarction, symptomatic heart failure or asymptomatic ventricular arrhythmia.

Outcomes assessed in the review
Adverse effects of the following types were assessed: hepatic, gastrointestinal, pulmonary, thyroid, neurologic, skin, eye, Bradycardia or conduction disturbance, and drug discontinuation.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The authors do not state that they assessed validity.

Data extraction
The data were independently extracted by two authors.

Methods of synthesis
How were the studies combined?
The odds ratios (OR) and 95% confidence intervals (CIs) were calculated to estimate the likelihood of adverse effects of treatment with low-dose amiodarone, compared with placebo. A weighted average of the ORs (pooled OR) for each adverse effect was calculated using the Mantel-Haenszel method, as modified by Yusuf et al. (see Other Publications of Related Interest).

How were differences between studies investigated?
The homogeneity of treatment effect across trials was assessed using a chi-squared test.
**Results of the review**

Four double-blind placebo-controlled trials with 1,465 patients (738 and 727 in the amiodarone and placebo groups, respectively) were included.

There was a higher likelihood of experiencing other adverse effects as a result of treatment with low-dose amiodarone. The OR was 4.2 (95% CI: 2.0, 8.7) for thyroid (p=0.001), 2.0 (95% CI: 1.1 to 3.7) for neurologic (p=0.02), 2.5 (95% CI: 1.1, 6.2) for skin (p=0.05), 3.4 (95% CI: 1.2, 9.6) for ocular (p=0.02), and 2.2 (95% CI: 1.1, 4.3) for bradycardiac (p=0.02) effects.

The odds of discontinuing the drug in the amiodarone group were approximately 1.5 times that of the placebo group (OR 1.52, 95% CI: 1.2, 1.9, p=0.003).

Similar hepatic and gastrointestinal adverse effects were found in the amiodarone group and control groups: the ORs were 1.2 (95% CI: 0.4, 3.3, p=0.7) and 1.1 (95% CI: 0.7, 1.9, p=0.678), respectively. There was a trend towards increased odds of pulmonary toxicity (OR 2.0, 95% CI: 0.9, 5.3, p=0.07).

**Authors’ conclusions**

Compared with placebo, there was a higher likelihood of experiencing adverse effects with exposure to low daily doses of amiodarone. Thus, although low-dose amiodarone may be well tolerated, it is not free of adverse effects.

**CRD commentary**

The objectives, the inclusion criteria for the primary studies, and the study details were clearly presented. The search was adequately described, and attempts were made to locate non-English language articles. However, limiting the electronic search to one database (MEDLINE) suggests that relevant studies may have been missed. The validity of the included studies does not appear to have been assessed. The authors’ conclusions appear to be supported by the evidence presented. However, it is unclear how generalisable the findings of this review are, as most patients included in the four trials were older and male. Adverse effects of amiodarone may be different in other patient groups.

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**Other publications of related interest**


**Indexing Status**

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.