Amiodarone-associated proarrhythmic effects: a review with special reference to torsade de pointes tachycardia

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Authors' objectives
To assess the incidence of amiodarone-mediated aggravation of ventricular tachyarrhythmias or the development of new arrhythmias, in particular torsade de pointes.

Searching
MEDLINE and Current Contents (Clinical Medicine) were searched from 1973 to June 1993 for English language papers, using keywords such as ‘amiodarone’, ‘torsade de pointes’, ‘proarrhythmia’ and ‘aggravation of arrhythmia’. Manual searches of references in review articles were performed similarly.

Study selection
Study designs of evaluations included in the review
Case reports, retrospective studies with at least 50 patients and a follow-up of at least 6 months, and controlled studies with an English summary documenting the use of amiodarone. Studies without complete data on the type of arrhythmias or the amiodarone-associated proarrhythmic effects, and those without clear descriptions of the methods used or of the efficacy and side-effects of amiodarone, were excluded.

Specific interventions included in the review
The antiarrhythmic agent amiodarone.

Participants included in the review
Patients treated with amiodarone (for cardiac rhythm disorders).

Outcomes assessed in the review
Amiodarone-associated proarrhythmic events, especially Torsade de Pointes Tachycardia.

How were decisions on the relevance of primary studies made?
Two independent investigators read the reports.

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

Data extraction
Two independent investigators read the reports.

Methods of synthesis
How were the studies combined?
Studies were combined by a qualitative review estimating the overall complication rates.

How were differences between studies investigated?
Complication rates were calculated separately for case reports, uncontrolled studies and controlled trials.

Results of the review
Six individual case reports (in addition to the 59 already identified in a 1989 review), 17 observational studies and 7
placebo-controlled trials.

In many cases of torsade de pointes with amiodarone, other predisposing factors were also present. Of the 2,878 patients in uncontrolled studies, 2% developed a proarrhythmic event including the 0.7% with torsade de pointes. In the 7 placebo-controlled trials, amiodarone was not associated with the development of a proarrhythmic event.

**Authors' conclusions**
Amiodarone appears to be associated with a low incidence of proarrhythmic events, with torsade de pointes developing in less than 1% of cases. Thus, amiodarone is useful in treating patients at high risk of sudden death.

**CRD commentary**
The variety of study designs, durations of follow-up and patient mix make it difficult to derive an overall estimate of adverse events. This ranged from 2 to 0% but was difficult to attribute to amiodarone because of the use of other agents. Whilst adverse events appear low, the effectiveness of amiodarone in reducing risk of death is still being evaluated in prospective trials.

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