Propafenone for the treatment of supraventricular tachycardia and atrial fibrillation: a meta-analysis

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Authors' objectives
To determine propafenone’s effectiveness in terminating and suppressing supraventricular arrhythmias using meta-analytic techniques.

Searching
MEDLINE (1974-1997) and PaperChase (1974-1997) were searched electronically for relevant studies and abstracts of data still to be published in full text. Both English and non-English publications were considered.

Study selection
Study designs of evaluations included in the review
All study designs were considered eligible. Studies had to report the dose, frequency and route of propafenone administration, and discuss the duration of follow-up or end point assessment. Data from trials using reduction in frequency, severity, or duration of episodes as end points in paroxysmal AF, were included in the text of the review but not formally combined. Randomised and non-randomised controlled trials were included in the review.

Specific interventions included in the review
Intravenous (2mg/kg initial bolus +/- infusion) and oral (450,600,900 mg/day) propafenone.

Participants included in the review
Patients with supraventricular tachycardia or atrial fibrillation, including paroxysmal AF (as defined by recurrent episodes lasting <72hrs) and chronic AF (as defined by a fixed pattern of AF lasting >72hrs). Studies reporting on atrioventricular (AV) reentrant tachycardias (Wolff-Parkinson-White) were excluded from the review. Patient exclusion criteria also varied across studies but in general patients with major conduction abnormalities, bradyarrhythmias, active cardiac ischaemia, recent myocardial infarction, or uncontrolled heart failure were excluded from participating in the studies. Patients with significant electrolyte, hepatic, renal or other metabolic abnormalities were also excluded from most of the trials.

Outcomes assessed in the review
Chronic suppression (9-12mths follow-up) and acute termination of arrhythmia; chronic suppression (6 and 12mths follow-up) and acute termination (1, 2, 4, 8, 12, 24 and 48hrs after initiation of therapy) of AF; efficacy of therapy for paroxysmal AF (as defined by a significant reduction in the frequency, severity, or duration of episodes of arrhythmia).

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
Data from each of the studies was extracted under the following headings:

1. Trial design (randomised vs non-randomised).

2. Goal of treatment (termination vs suppression).
3. Type of arrhythmia (supraventricular tachycardia; paroxysmal AF vs chronic AF).

4. Dosing regimen (dose, intravenous vs oral, duration).

5. Time of follow-up or endpoint.

6. Efficacy (number of people in sinus rhythm as compared with the total population at risk). Efficacy rates from trials designed to assess the acute termination of AF were calculated based on time from the initiation of therapy. Data were pooled at 1, 2, 4, 8, 12, 24 and 48 hours after the initiation of therapy and data at intermediate times were analysed at the next longer time point, e.g. 3hr efficacy data were analysed with 4hr data. For randomised comparisons between propafenone and placebo, the rate difference (RD) was calculated (i.e. the difference between the proportion of patients in sinus rhythm in the propafenone and control arms).

**Methods of synthesis**

**How were the studies combined?**

Pooled estimates of the percentage of patients converting to or remaining in sinus rhythm were calculated, with 95% CIs and p values. Variances were calculated using Greenwood's formula (see Other Publications of Related Interest). Rate differences (RD) from randomised studies were combined in a weighted average RD using the methods described by Cochran, and DerSimonian & Laird (see Other Publications of Related Interest). The statistical significance of the pooled RD was calculated by a z value. Comparisons between different dosing routes and trial designs were also made by calculating z and the results given as the mean percentage of patients in sinus rhythm along with 95% CIs. P values <0.05 were interpreted as statistically significant.

**How were differences between studies investigated?**

The authors do not state how differences between the studies were investigated.

**Results of the review**

Sixty studies in total, including acute termination of supraventricular tachycardia n=8 studies, n=153 patients; chronic suppression of supraventricular tachycardia n=6 studies, n=214 patients; acute termination of AF n=27 studies, n=1843 patients; and suppression of AF n=25 studies, n=1105 patients.

Propafenone successfully terminated 83.8% (95% CI: 78.1, 89.7%) of supraventricular tachycardias and the proportion of patients remaining in sinus rhythm without recurrent arrhythmia at 1yr was 64.6% (95% CI: 58.1, 71.1). The likelihood of converting a paroxysm of atrial fibrillation increased over time, with 76.1% (95% CI: 72.8%, 79.4%) of patients in sinus rhythm 24hrs after the initiation of therapy. Patients receiving intravenous therapy were more likely to convert to sinus rhythm in the first 4hrs after drug administration. The treatment benefit of propafenone versus placebo in converting sinus rhythm was greatest in the first 8hrs after treatment (treatment benefit at 4hrs 31.5%, 95% CI: 24.5, 38.5; at 8hrs 32.9%, 95% CI: 24.3, 41.5, p<0.01). This treatment benefit decreased to 11.0% (95% CI: -0.6, 22.4) after 24hrs. Propafenone was effective in suppressing recurrences of AF in 55.4% (95% CI: 51.3%, 59.7%) of instances at 6mths and 56.8% (95% CI: 52.3, 61.3) at 12mths.

**Authors' conclusions**

Propafenone is effective in terminating supraventricular tachycardias and AF in the vast majority of patients. Suppression of arrhythmia recurrences is feasible in most patients, although its effectiveness decreases over time.

**CRD commentary**

This review focuses on a question with clearly defined inclusion and exclusion criteria. The review is based on an adequate literature search of two electronic databases. The authors provide little information about review methods, including the study selection process and assessment of study quality. Detailed data tables were used to extract the study information, however these were not published. A tabulated summary of the main study details would have been helpful.
Implications of the review for practice and research
The authors state that ‘propafenone is effective in terminating supraventricular tachycardias and AF in the vast majority of patients. Suppression of arrhythmia recurrences is feasible in most patients, although its effectiveness decreases over time. The decision to use propafenone in a patient should be based on an assessment of its net benefit’.

Bibliographic details

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Anti-Arrhythmia Agents /administration & dosage /therapeutic use; Atrial Fibrillation /drug therapy; Propafenone /administration & dosage /therapeutic use; Research Design; Tachycardia, Supraventricular /drug therapy; Time Factors

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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.