Efficacy and safety of vernakalant in recent-onset atrial fibrillation after the European medicines agency approval: systematic review and meta-analysis

CRD summary
The authors concluded that, compared with control, vernakalant was effective and safe, for rapid conversion of recent-onset atrial fibrillation, but one unpublished trial was discontinued due to safety concerns. The authors acknowledged the limitations of the included trials, such as small samples, and their suggestion that the findings should be interpreted with caution, seems appropriate.

Authors' objectives
To assess the efficacy and safety of vernakalant for patients with recent-onset atrial fibrillation.

Searching
PubMed and EMBASE were searched for relevant studies, published in English, from 2000 to May 2011. Search terms were reported. The website of the European Medicines Agency (EMA) and ClinicalTrials.gov were searched for any reports or studies involving vernakalant. The references of all relevant studies were scanned.

Study selection
Randomised controlled trials (RCTs) were eligible for inclusion if they compared intravenous vernakalant as a first treatment, versus placebo or another antiarrhythmic drug, for cardioversion in patients with recent-onset atrial fibrillation. Patients with atrial flutter were excluded from the analyses. The primary outcomes were the cardioversion rate (within 90 minutes of drug administration) and serious adverse events.

Most of the included trials used intravenous vernakalant, at an initial dose of 3mg/kg, followed by 2mg/kg when necessary. The trials included patients with recent-onset atrial fibrillation (three to 72 hours), short-duration atrial fibrillation (three hours to seven days), long-duration atrial fibrillation (eight to 45 days), or symptomatic atrial fibrillation (three to 48 hours). Most trials compared vernakalant with placebo.

Two reviewers independently selected the trials. Disagreements were resolved through consensus or by involving a third reviewer if necessary.

Assessment of study quality
Two reviewers independently assessed trial quality, using the Cochrane risk of bias tool and the Jadad scale (maximum score 5).

Data extraction
Data were extracted to calculate relative risks and their 95% confidence intervals. Two reviewers were involved in data extraction. Trial authors were not contacted for additional information.

Methods of synthesis
The pooled relative risks and 95% confidence intervals were calculated using a random-effects model. Statistical heterogeneity was assessed using $I^2$ and $T^2$. Publication bias was not assessed, as there were too few included trials. For the evaluation of efficacy, only the data on patients with atrial fibrillation of short duration (less than seven days) were included.

Results of the review
Five trials were included in the review (1,099 participants). The trials were of high quality: four had a Jadad score of 4, and one scored 5.

The pooled analysis showed that vernakalant was associated with significantly more cardioversion, than the control ($RR = 8.43, 95\% CI 4.38$ to $16.26; I^2 = 50\%; five trials$). No statistical significant difference was found in the serious adverse
events, between patients on vernakalant and those on control (placebo or amiodarone; RR 0.91, 95% CI 0.60 to 1.36; I²=11%; five trials).

**Authors' conclusions**
Compared with controls, vernakalant was effective and safe, for rapid conversion of recent-onset atrial fibrillation, but one unpublished trial was discontinued due to safety concerns.

**CRD commentary**
The review addressed a clear question and was supported by appropriate inclusion criteria. Relevant sources were searched, but trials in languages other than English were not sought, so relevant trials may have been missed. Appropriate methods to reduce reviewer error and bias were used. The quality of the included trials was assessed, but the full results were not reported. Appropriate methods were used to pool the data and assess heterogeneity.

The authors acknowledged the limitations of the trials (small samples, the possible duplication of data, which may have overestimated the treatment effects, and possible selection bias), and their suggestion that the findings should be interpreted with caution, seems appropriate.

**Implications of the review for practice and research**
**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that cost-effectiveness analysis and comparison with other antiarrhythmic drugs, including those in class I, were needed, along with the assessment of treatment in the emergency department.

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