Comparison of efficacy and safety of dabigatran, rivaroxaban and apixaban in patients with atrial fibrillation using network meta-analysis

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CRD summary
All-cause deaths were equivalent for each treatment, but apixaban and dabigatran 110mg seemed to prevent more strokes, with least risk, for patients with non-valvular atrial fibrillation; dabigatran 150mg seemed better for patients at high risk of embolism. The review was generally poorly reported. The indirect comparisons and potential for confounding mean that the conclusions may not be reliable.

Authors' objectives
To compare the efficacy and safety of dabigatran, rivaroxaban, and apixaban, for patients with atrial fibrillation.

Searching
EMBASE and MEDLINE were searched, and search terms were reported. ClinicalTrials.gov was searched and regulatory documents were sought. The reference lists of identified articles were screened.

Study selection
Prospective randomised controlled trials (RCTs) of dabigatran, rivaroxaban, or apixaban, in patients with atrial fibrillation, were eligible for inclusion. Trials had to report strokes, systemic embolisms, intracerebral haemorrhages, myocardial infarctions, and deaths. The control groups had to be treated with a vitamin K antagonist (usually warfarin), adjusted to an international normalised ratio of two to three. Trials that did not report all the outcomes were excluded.

The included trials were of dabigatran 110mg or 150mg twice daily, rivaroxaban 20mg once daily, or apixaban 5mg twice daily, compared with warfarin, for patients with atrial fibrillation and a mean age ranging from 70 to 73 years. The percentage of female patients ranged from 35 to 40. The use of aspirin ranged from 31 to 40%. Trials were published between 2009 and 2011. The percentage of patients with a CHADS2 score of three or more, ranged from 30 to 87, where reported.

The authors did not state how many reviewers selected the trials.

Assessment of study quality
The authors did not state that they assessed trial quality, but they did discuss the quality of blinding and randomisation.

Data extraction
The data were extracted for stroke, systemic embolism, intracerebral haemorrhage, myocardial infarction, and death. These were used to calculate odds ratios, with 95% confidence intervals. The authors did not state how many reviewers extracted the data.

Methods of synthesis
Network meta-analysis was performed, but the methods were not described. Pooled odds ratios and 95% confidence intervals were calculated. Statistical heterogeneity was assessed, for some analyses, using Cochran's Q.

Results of the review
Three RCTs were included in the review (50,578 patients). The trials ranged from 14,264 to 18,201 patients. One trial was open label for warfarin and blinded for the dose of dabigatran; two trials were double blind and double dummy.

Dabigatran 150mg was associated with a statistically significantly reduced risk of ischaemic stroke or systemic embolism, compared with dabigatran 110mg (OR 1.38, 95% CI 1.02 to 1.88) and rivaroxaban (OR 0.74, 95% CI 0.56 to 0.98). Apixaban was associated with a statistically significantly reduced risk of major bleed, compared with dabigatran 150mg (OR 1.35, 95% CI 1.10 to 1.66) and rivaroxaban (OR 1.48, 95% CI 1.21 to 1.81). There was no statistically significant difference between the agents for mortality. The results for other outcomes were presented.
Authors' conclusions
The number of deaths was the same for every treatment. Apixaban and dabigatran 110mg seemed to provide the most benefit with the least risk, for stroke prevention in patients with non-valvular atrial fibrillation. Dabigatran 150mg might be better for patients at a high risk of embolism.

CRD commentary
The inclusion criteria for the review were deliberately very strict and potentially relevant papers, such as those that reported some, but not all the outcomes, may have been excluded. Two relevant databases were searched. The search dates and any language restrictions were not reported. Publication bias was not assessed and cannot be ruled out. It was not clear if any attempts were made to reduce reviewer error and bias throughout the review.

Quality assessment was not reported, which makes it difficult to assess the reliability of the evidence, but all three trials were randomised and at least partly blinded. The data were combined using a network meta-analysis, but the methods were not fully reported. The authors noted a number of potential confounding factors in the evidence, such as the patients' CHADS2 scores.

The review was generally poorly reported. The indirect comparisons and the potential for confounding mean that the authors' conclusions may not be reliable.

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

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