Network meta-analysis of oral anticoagulants for primary prevention, treatment and secondary prevention of venous thromboembolic disease, and for prevention of stroke in atrial fibrillation

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Background
Warfarin is an effective oral anticoagulant for stroke prevention in atrial fibrillation (AF), but anticoagulation is underused in clinical care (Lee et al., 2011). The risk of venous thromboembolic (VTE) disease during hospitalisation can be reduced by low molecular weight heparin (LMWH): warfarin is the most frequently prescribed anticoagulant for treatment and secondary prevention of VTE. Warfarin-related bleeding is a major reason for hospitalisation for adverse drug effects (Pirmohamed et al., 2004). Novel oral anticoagulants (NOACs) have a more rapid onset and offset of action than warfarin and more predictable dosing requirements (Garcia et al., 2010).

Objectives: Determine the best oral anticoagulant/s for prevention of stroke in AF and for primary prevention, treatment and secondary prevention of VTE.

Methods

Participants: Patients eligible for anticoagulation with • AF and VTE treatment or secondary prevention: warfarin. • Primary prevention of VTE: LMWH.

Results display: for each review, we provide • Network plots for one of the main outcomes. • Mean ranks for licensed interventions reflecting their effectiveness to reduce the risk of several key adverse outcomes (smaller ranks are better).

Results: Stroke prevention in AF • 23 trials • 27 interventions • 94,656 patients (97% from phase III studies)

Mean ranks for licensed interventions

Results: VTE primary prevention • 35 interventions • 77,563 patients (88.9% from phase III studies) • Hip surgery: 18 trials • Knee surgery: 17 trials • Medical: 7 trials • Comparisons of efficacy outcomes were imprecisely estimated

Mean ranks for licensed interventions

Results: VTE secondary prevention • 10 all phase III trials • 9 interventions • 10,390 patients • Comparisons for many outcomes were imprecisely estimated

Mean ranks for licensed interventions

Conclusions
• NOACs have advantages over warfarin in patients with AF. Of the available NOACs, apixaban 5mg bd offers the best balance between efficacy and safety.
• We found no strong evidence that they should replace warfarin or LMWH in primary prevention, treatment or secondary prevention of VTE.
• No strong evidence that NOACs should replace post-operative LMWH in primary prevention of VTE in patients undergoing hip or knee surgery.
• NOACs offer no efficacy advantage over warfarin in the acute treatment of VTE, but have a lower rate of bleeding complications.
• If secondary prevention after 3-6 months of anticoagulation for a first episode of VTE is to be considered (this is not currently established practice), NOACs provide no efficacy advantage over warfarin, but have a lower rate of bleeding complications.

References


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