A meta-analysis to determine the effect of anticoagulation on mortality in patients with blunt head trauma

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CRD summary
This review estimated the effect of warfarin anticoagulation on mortality in people with head injuries. The authors concluded that warfarin anticoagulation was associated with an increased risk of death. The lack of validity assessment, presence of considerable heterogeneity and need to rely on case-control studies implies that the authors’ conclusions should be treated with some caution.

Authors' objectives
To estimate the effect of warfarin anticoagulation on mortality rates in people with head injuries.

Searching
MEDLINE (to November 2011) and EMBASE (to October 2010) were searched (search terms provided) without language restrictions. Reference lists of included studies were examined for further relevant papers. The authors did not search for unpublished data. Studies published only in abstract form were excluded. Studies had to be published in peer reviewed journals.

Study selection
Case-control studies or cohort studies with a nested case-control group that allowed mortality rates of head injury patients on warfarin to be compared with those not on warfarin were eligible for inclusion. Studies of trauma patients on anticoagulants were included if they provided data to enable consideration of a subset analysis of mortality rates in the head injury group. Studies that examined the effect of antiplatelet agents were excluded. Also excluded were studies of patients with minor head injury (Glasgow Coma Scale 15) and those in which the subgroup of patients on warfarin could not be distinguished from those who took other agents (such as aspirin or clopidogrel). No lower sample size limits were applied.

Studies included patients with various types of head injury, some requiring confirmation on computed tomography and others applying certain ICD-9 (International Classification of Diseases 9) codes as inclusion criteria. Most studies did not report the injury composition of included patients. Mean age of patients was 70.2 to 81.9 years in the warfarin group and 54 to 81.7 years in the non-warfarin group. Mean ratings on the Glasgow Coma Scale and injury severity scores were similar between groups (range 11 to 14.13 and 10.4 to 24.9). The mean international normalised ratio (INR) ranged from 2.3 to 3.3. Where reported, INR was corrected using fresh frozen plasma (FFP) with or without vitamin K.

The search was conducted by one author. Full papers were reviewed by another author.

Assessment of study quality
No formal validity assessment was undertaken as the authors judged that all studies were likely to be relatively small ‘non-powered studies.

Data extraction
There was no contact with authors of any study. The review authors did not state how many reviewers performed data extraction.

Methods of synthesis
A statistical synthesis was performed. No details of the method of synthesis employed were given. Q and I² tests for heterogeneity were presented as were fixed-effect and random-effects meta-analysis of odds ratios (OR). There was a narrative description of study heterogeneity.

Results of the review
Eleven studies (5,756 participants, range 40 to 2,791) were included: seven nested case-control and four case control studies.

Mortality was found to be considerably higher in patients who took anticoagulant medication (fixed-effect OR 2.01, 95% CI 1.63 to 2.47 and random-effects OR 2.25, 95% CI 1.49 to 3.38). Ten of the 11 studies had an odds ratio greater than one and seven of these had confidence intervals that did not overlap one so the authors’ judged the fixed-effect model to be the preferred model. Studies were found to be highly heterogeneous ($I^2=63.53\%$).

**Authors' conclusions**
The authors concluded that patients using warfarin anticoagulant medication and who suffered blunt head trauma appeared to have an increased risk of death compared to a similar cohort not using warfarin.

**CRD commentary**
The aim and inclusion criteria for this review were stated clearly. The electronic literature search covered two major databases (search terms provided) without language restrictions. There was no search for grey literature so there was a risk of publication bias. The review methods (including study selection) were not clearly reported so reviewer bias was a possibility. The lack of validity assessment meant that the relative reliability of individual study results could not be judged.

Study details were generally adequate but lack of detail on sources and characteristics of cases and controls was a concern given the multiple biases associated with case-control designs. The statistical synthesis appeared appropriate. Some investigation of possible causes of heterogeneity would have been useful.

The lack of validity assessment and of investigation of reasons for heterogeneity compounded with the need to rely on case-control studies implies that the authors’ conclusions should be treated with some caution.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice

**Research:** The authors stated that further work was needed to compare the effect on mortality of newer anticoagulant agents such as dabigatran in patients with blunt head trauma.

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