Bleeding risk of combined oral anticoagulant and antiplatelet therapy in cardiovascular disease

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Authors' objectives

To assess the safety of combining oral anticoagulant and antiplatelet therapy.

Searching

EMBASE was searched from 1960 to 1994. [A: The search strategy was not defined. Only papers written in the English language were included].

Study selection

Study designs of evaluations included in the review

Clinical trials, of which most were randomised, were included.

Specific interventions included in the review

Combinations of anticoagulants and antiplatelet therapy, compared with either intervention alone or with placebo, namely: acenocoumarin (alone and with aspirin), warfarin (alone or with placebo, aspirin or dipyridamole), aspirin (alone and with warfarin), double placebo.

Participants included in the review

Patients with artificial heart valves; patients with unstable angina or non-Q myocardial infarction; healthy high-risk men.

Outcomes assessed in the review

Reduction in thrombotic phenomena (myocardial (re)infarction, stroke, valve thrombosis and thromboembolism).

Bleeding complications, categorised as either major bleeding (requiring hospital admission and/or blood transfusion) or minor bleeding (defined as other bleeding).

How were decisions on the relevance of primary studies made?

The author does not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality

[A: All studies which combined oral anticoaguant and antiplatelet therapy were included, provided cardiovascular disorders were treated]. The author does not state how the papers were assessed for validity, or how many of the reviewers performed the validity assessment.

Data extraction

The author does not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.

Methods of synthesis

How were the studies combined?

The studies were combined by a narrative review.

How were differences between studies investigated?

The author does not state how differences between the studies were investigated.

Results of the review

Intra-cardiac thrombosis (4 trials: acenocoumarin plus aspirin (65 patients) versus acenocoumarin alone (57 patients);

warfarin plus 500 mg aspirin (75 patients) versus warfarin alone (73 patients);

warfarin plus 250 mg aspirin (170 patients) versus warfarin plus 100 mgdipyridamole (181 patients) versus warfarin alone (183 patients); and

warfarin plus slow-release aspirin (186 patients) versus warfarin plus placebo (184 patients).

Unstable angina or non-Q myocardial infarction (1 trial): 162.5 mg aspirin plus warfarin (105 patients) versus 162.5 mg aspirin alone (109 patients).

High-risk men (1 trial): warfarin plus 75 mg aspiring (911 patients) versus warfarin plus placebo (917 patients) versus 75 mg aspirin plus placebo (907 patients) versus double placebo (932 patients).

Combined therapies. High-intensity oral anticoagulation plus high-dose aspirin: 609 person-years; 7.2 major bleedings per 100 person-years (95% confidence interval, CI: 5.1, 9.3, p=0.06).

High-dose aspirin, high-intensity oral anticoagulation plus low-dose aspirin: 282 person-years; 8.5 major bleedings per 100 person-years (95% CI: 6.0, 11.0, p=0.02).

Low-intensity oral anticoagulation plus low-dose aspirin: 1,022 person-years; 5 major bleedings per 100 person-years (95% CI: 3.7, 6.3, p>0.05).

Reference therapies. High-intensity oral anticoagulation: 1,222 person-years; 3.3 major bleedings per 100 person-years (95% CI: 2.3, 4.3, p=0.62).

Low-intensity oral anticoagulation: 1,020 person-years; 3.6 major bleedings per 100 person-years (95% CI: 2.5, 4.7, p=0.28).

Low-dose aspirin: 1,070 person-years; 2.2 major bleedings per 100 person-years (95% CI: 1.3, 3.1, p=0.62).

Placebo: 1,057 person-years; 2.5 major bleedings per 100 person-years (95% CI: 1.5, 3.5, p=0.62).

Authors' conclusions

The safety of combined oral anticoagulant and antiplatelet therapy is probably acceptable, provide the antiplatelet therapy is given in a low dose.

CRD commentary

Important methodological details are absent from the review: there is no indication of how studies were selected; the validity of each included study was not assessed; specific trial design of the individual studies is not mentioned; data regarding patient characteristics are lacking (e.g. age, sex ratio, underlying conditions).

The literature search was limited to EMBASE, and the search strategy is not provided.

These are important methodological issues which are highly relevant to the validity of the review considering the small number of studies included.

Implications of the review for practice and research

The trials reviewed here may indicate that combined therapy is 'probably' acceptable, although one should be cautious of the results considering the lack of methodological rigour. Further large randomised clinical trials are needed to provide conclusive evidence.

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