Antithrombotic therapy in patients treated with oral anticoagulation undergoing coronary artery stenting. An expert consensus document with focus on atrial fibrillation

CRD summary
The authors concluded that the optimal antithrombotic regime for atrial fibrillation in patients undergoing percutaneous coronary interventions with stenting was undefined. They recommended triple therapy (warfarin, aspirin, clopidogrel) as the most effective regime, but with an increased risk of bleeding. This recommendation may be unreliable, as evidence was limited and from small observational studies, with problems in the review methodology.

Authors' objectives
To assess the evidence for antithrombotic management of people with atrial fibrillation who are undergoing coronary artery stenting.

Searching
MEDLINE database was searched. Bibliographies of identified articles were checked and supplements of major journals checked for abstracts.

Study selection
Studies that assessed the effects of anticoagulation therapy in people receiving oral anticoagulation, who were undergoing percutaneous coronary intervention with stenting, were eligible for inclusion.

In the included studies most participants were on triple therapy (warfarin, aspirin and clopidogrel), others were on dual therapy (aspirin and clopidogrel), or oral anticoagulation with aspirin or oral anticoagulation with clopidogrel. Six studies looked specifically at people receiving triple therapy and the remaining studies were a mix. In some studies comparisons were made between varying treatment regimes. Glycoprotein IIb/IIIa inhibitors were used in between 20% and 71% and heparin was used in some cases.

In two studies, all participants had atrial fibrillation. In the remaining studies, 37% to 80% had atrial fibrillation. Where reported, stenting was undertaken because of ST-elevation myocardial infarction, non-ST-elevation acute coronary syndrome or as elective surgery. Drug eluting stents were used in 2% to 77% of participants (where reported). The mean age of participants ranged from 65 to 76 years.

The primary outcome of interest appeared to be major bleeding. Other outcomes reported were stroke, stent thrombosis, thromboembolic events and myocardial infarction. Time points for outcome evaluation ranged from hospital stay to 21 months and were classified as 30 days, six months and 12 months or over.

The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
The number and percentages of events were extracted. Where necessary study authors were contacted for information.

The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis
Results were presented in tables and discussed in narrative. The authors appeared to have combined results by added...
events for all studies and calculated percentages related to total number of patients.

**Results of the review**

Twelve studies (3,413 participants) were included. Ten were retrospective observational studies and two were post-hoc analyses of registry studies. Study size ranged from 40 to 1,247 participants. Most studies were small, with eight having less than 200 participants.

Triple therapy was associated with major bleeding in 0% to 21% of cases. The incidence of bleeding increased with longer duration of treatment, pooled incidence at 30 days was 4.6% (39 of 852 patients, six studies), pooled incidence at 12 months or longer was 10.3% (64 of 622 patients, five studies). When triple therapy was compared to dual antiplatelet therapy the relative risk of bleeding was five times higher at one, six and nine months (data not presented).

There was insufficient data to assess major bleeding with oral anticoagulation combined with either aspirin or clopidogrel.

Three studies reported on stroke. Triple therapy generally resulted in fewer strokes than dual therapies. In one study, 2.8% of patients on triple therapy had a stroke compared to 8.8% on dual therapy. In a second study, 0.7% of patients had a stroke with triple therapy of warfarin, aspirin and a thienopyridine, compared to 3.4% occurrence of strokes with warfarin and a single antiplatelet.

The numbers of adverse events were small but triple therapy was associated with more favourable results for other outcomes, including stent thrombosis, thromboembolic events and myocardial infarction.

**Authors’ conclusions**

The optimal antithrombotic regime for people with atrial fibrillation undergoing percutaneous coronary intervention with stenting is currently undefined. The limited data suggested that triple therapy appeared to offer best protection against thromboembolic events, but at an increased risk of bleeding complications.

**CRD commentary**

The inclusion criteria were only partly stated, with no details of criteria for study design or for outcomes. Also, some outcomes (e.g. major bleeding) were not clearly defined. Database searching was limited to only one database and no search term or dates were given. Therefore, it is possible that studies were missed, which could have affected the results of the review. Methods of study selection and database extraction were not described, so it was unclear if reviewer error or bias was minimised. The quality of included studies was not assessed. Only limited information was presented about the included studies. The method of pooling data by adding the numbers of events for each study was not the most appropriate method, as it took no account of the differences between studies. Also, the included studies were observational studies and results from these kinds of studies are considered to be of relatively low quality (as compared to randomised studies). These factors make it difficult to assess the reliability of the results. Also, it should be borne in mind that the authors' recommendations are based on very limited evidence.

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

Practice: The authors stated that triple therapy (warfarin, aspirin and clopidogrel) is recommended for those people at intermediate or high risk of thromboembolic events and undergoing percutaneous coronary intervention. The authors gave further recommendations (available in the paper) based on information that was not included in the systematic review.

Research: The authors stated that large scale registry and prospective clinical studies are needed to determine the optimal antithrombotic regime in people with atrial fibrillation undergoing percutaneous coronary intervention with stent. The use of warfarin combined with clopidogrel needs to be assessed.

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