Safety of continuing warfarin therapy during cataract surgery: a systematic review and meta-analysis

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CRD summary
This review concluded that patients who underwent cataract surgery and who received warfarin therapy were at increased risk of small bleeds that were not clinically significant. This was a well-conducted review and the conclusions are likely to be reliable, but it should be noted that they are based on mostly observational evidence.

Authors’ objectives
To determine the efficacy and safety of continuing warfarin treatment before and after cataract surgery.

Searching
MEDLINE, EMBASE and CINAHL (from inception to December 2007 or January 2008), The Cochrane library, BIOSIS Previews and ClinicalTrials.gov were searched. Search terms were reported. There were no language restrictions. Reference lists were searched manually. An expert in the field was contacted to help locate unpublished studies.

Study selection
Primary studies of any design of patients who underwent cataract extraction and who took the anticoagulant warfarin during the perioperative period were eligible for inclusion. Studies had to report the number of bleeding events. Outcomes of interest were bleeding and thromboembolism events. Studies that used other forms of anticoagulation or where warfarin was stopped prior to surgery in all patients were excluded. Surveys were excluded.

The included studies differed in design and included one randomised controlled trial (RCT), one retrospective cohort study, prospective cohort studies and case series. Patient populations had a variety of indications for warfarin including atrial fibrillation, mechanical heart valves or venous thromboembolism. Reported ages (mean or actual) ranged from 66 to 83 years. Length of follow-up ranged from eight minutes to one year. Day of surgery INR (International Normalized Ratio) was between 1.1 and 4.5. Intensity of anticoagulation was between 2.0mg and 3.0mg. The surgical technique for cataract extraction varied with two studies using a clear corneal incision (thought to reduce bleeding risk).

Studies were selected by two reviewers independently. Disagreements were resolved by consensus.

Assessment of study quality
The quality of the cohort studies was assessed using the Newcastle-Ottawa scale to assess representativeness of the cohort and controls, exposure, comparability of groups, outcome assessment and duration and adequacy of follow-up. The RCT was assessed using the Cochrane Collaboration risk of bias tool to assess allocation concealment, blinding, complete outcome data, full reporting and other biases.

Studies were assessed by two reviewers independently. Disagreements were resolved by consensus.

Data extraction
Results for numbers of bleeding events for treatment and control groups were extracted and used to calculate odds ratios (OR) and 95% confidence intervals (CI). Outcomes from case series were expressed as proportions with 95% CI.

Data were extracted by two reviewers independently. Disagreements were resolved by consensus.

Methods of synthesis
Odds ratios were pooled using a random-effects model. Overall proportions of patients with a bleeding event were
transformed using natural logarithms and pooled using a random-effects model for all studies and also for only the case series. Statistical heterogeneity was assessed with the $I^2$ statistic.

**Results of the review**

Eleven studies were included: one RCT (n=84), one retrospective cohort study (n=85), four prospective cohort studies (n=19,530) and six case series (n=approximately 312). The four prospective cohort studies were considered to be good quality (met six or seven out of eight Newcastle-Ottawa scale criteria). The RCT was high quality. Case series were considered poor quality for not having a control group or having flaws in exposure or ascertainment reporting.

Anticoagulation increased the odds of bleeding compared to control (OR 3.26, 95% CI 1.73 to 6.16; five studies). Heterogeneity was low ($I^2=1.1\%$). Over all 11 studies the pooled incidence of bleeding was 0.10 (95% CI 0.05 to 0.19). Heterogeneity was high ($I^2=83.6\%$). Pooled incidence for the six case series was 0.09 (95% CI 0.05 to 0.16) and there was less heterogeneity ($I^2=54.9\%$). Sensitivity analyses (results not shown) indicated that heterogeneity was explained by whether case series were retrospective or prospective as there was no heterogeneity amongst the prospective studies ($I^2=0\%$). Rates of thromboembolism were low (less than 1%), but reporting was inconsistent.

**Authors' conclusions**

Patients who underwent cataract surgery and who received warfarin therapy were at increased risk of bleeding, but the bleeds were not clinically significant. The low quality of the evidence precluded any definitive conclusion about the risk of bleeding for patients who continued warfarin therapy around the time of surgery.

**CRD commentary**

This review was conducted using appropriate methods. The question was clear. There were no language restrictions in the literature search. The authors tried to locate unpublished material. The quality of the evidence was assessed. Study selection, data extraction and quality assessment were performed by two reviewers independently. Methods used in the meta-analysis were appropriate, but there is some doubt as to the validity of pooling the overall proportions with bleeding outcomes due to the high level of heterogeneity and because most of the data came from case series. The authors explored heterogeneity and concluded that it was due to the retrospective studies. On the whole this was a well-conducted review and the conclusions appear reliable, but the fact that they are based on mainly observational evidence needs to be taken into consideration.

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

**Practice:** The authors did not state any recommendations for practice.

**Research:** A large well-designed RCT to evaluate discontinuation of warfarin prior to cataract surgery and report bleeding and thromboembolic events was needed to determine the ideal perioperative strategy.

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