Dental surgery for patients on anticoagulant therapy with warfarin: a systematic review and meta-analysis

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CRD summary
This generally well-conducted review found no apparent increase in risk of bleeding associated with continued regular doses of warfarin compared to discontinued/modified warfarin doses for patients who underwent minor dental procedures. The conclusions appeared to be supported by the data, but poor quality included studies and risk of language bias suggest the findings should be interpreted with caution.

Authors' objectives
To determine the effects of continuing warfarin therapy on the risk of bleeding in patients undergoing elective dental surgery.

Searching
MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched for published and unpublished studies written in English up to June 2008. Further details of the search strategy were published in an appendix. Additional searches were carried out by using reference lists of relevant literature, contacting experts and searching conference abstracts from proceedings of International Association for Dental Research.

Study selection
Randomised controlled trials (RCTs) of patients who received warfarin therapy and underwent an elective dental procedure were eligible if they compared continuance on the usual dose of warfarin with reduction or cessation of usual warfarin dose. Eligible studies had to assess at least one of arterial or venous thromboembolism or postoperative bleeding (major, minor or clinically significant non-major).

All of the included studies assessed patients who underwent dental extractions (single or multiple teeth). Most patients required anticoagulation therapy for prosthetic heart valves (range 45% to 100%); other indications included valvulopathy, deep vein thrombosis and atrial fibrillation. Mean international normalised ratio (INR) across studies of patients who continued warfarin was between 1.8 and 3.4. Warfarin was discontinued two days prior to the procedure in 40% of studies and 20% used a half dose of warfarin for two days prior to the procedure; other studies did not specify details of discontinuation of warfarin although one reported a target INR for control patients. All of the studies used cointerventions that varied between studies and in 60% of studies these differed between control and intervention groups (further details were reported in the review). All except one of the included studies was carried out in a hospital setting. Reported outcomes were non-major and minor bleeding. Where reported, follow-up duration was seven days in all studies.

Two reviewers independently selected studies for inclusion in the review.

Assessment of study quality
Study quality was assessed independently by two reviewers using Jadad criteria of randomisation method, blinding and withdrawals and dropouts. Each study was awarded a total score for overall quality up to a maximum of 5 points. Studies with more than 2 points were considered good quality; those with a score of 2 points or less were described as low quality. Disagreements were resolved by consensus.

Data extraction
Bleeding events were reclassified according to the reviewers’ defined criteria (further details were reported in the review). Standardised effect sizes in the form of relative risks (RRs) with 95% confidence intervals (CIs) were calculated.

Data were extracted independently by three reviewers. Disagreements were resolved through consensus and discussion.
Methods of synthesis
Studies were grouped according to outcome. Pooled relative risks with 95% CIs were calculated using the DerSimonian and Laird random-effects model. Statistical heterogeneity was assessed using $\chi^2$ and $I^2$ statistics.

A sensitivity analysis was performed to assess the effects of study quality. Subgroup analyses were performed to assess effects in patients maintained at higher INRs (mean INR was over three) and studies that used antifibrinolytic agents.

Results of the review
Five trials (n=553) met the inclusion criteria. Sample sizes ranged from 30 to 214. Median quality score was 2 points. Four studies were described as low quality (1 or 2 points). Only one study was described as good quality (3 points).

Patients who continued with usual doses of warfarin therapy in comparison with interrupted warfarin therapy (either partial or complete) showed no significant difference in risk of clinically significant non-major bleeding ($I^2=0\%$, five studies) and minor bleeding ($I^2=0\%$, four studies).

Subgroup analyses reported similar findings. The effects of study quality were not assessed as four out of five studies were of low quality.

Authors’ conclusions
There appeared to be no increased risk of bleeding associated with continuing regular doses of warfarin in comparison with discontinuing or modifying warfarin doses for patients undergoing minor dental procedures.

CRD commentary
The review answered a clearly defined review question. Searches for both unpublished and published studies were carried out. There may have been some risk of language bias as only studies written in English were eligible for inclusion in the review. Attempts were made to reduce risks of reviewer error and bias during study selection, quality assessment and data extraction. Risk of bias within studies was assessed with relevant criteria. All studies except one were described as poor quality, which suggested that findings from these studies may not have been reliable. There were differences between the pooled studies in terms of their clinical characteristics, but there was no evidence of statistical heterogeneity. Clinical differences were particularly evident with respect to interventions and cointerventions. The authors acknowledged that the findings of the review may not be generalisable to private practice or procedures other than dental extractions, given that all but one of the included studies were carried out in a hospital setting and all studies were carried out in patients undergoing extractions. Overall, the conclusions of this generally well-conducted review appeared to be supported by the included data, but the poor quality of the studies and risk of language bias suggest that the findings should be interpreted with caution.

Implications of the review for practice and research
Practice: The authors stated that their findings questioned the current practice of interrupting warfarin therapy prior to dental procedures.

Research: The authors stated that further studies were required to investigate perioperative management of patients who received anticoagulation therapy for dental surgical procedures other than extractions and to determine the upper cut-off point for discontinuation of warfarin and use of bridging therapy in patients with a higher therapeutic INR range. Studies were also required to assess the benefit of antifibrinolytic agents across a range of INR levels.

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