Antithrombotic and fibrinolytic drugs for retinal vein occlusion: a systematic review and a call for action
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CRD summary
This review evaluated the effectiveness of antithrombotic and fibrinolytic drugs for the acute treatment and secondary prevention of retinal vein occlusion and concluded that low-molecular-weight heparin may be effective as acute treatment in some patients. Given the limited evidence presented and inability to judge the relative effectiveness of treatments, this conclusion should be interpreted with caution.

Authors' objectives
To evaluate the effectiveness of antithrombotic and fibrinolytic drugs for the acute treatment and secondary prevention of retinal vein occlusion (RVO).

Searching
MEDLINE and EMBASE were searched without language restrictions for published studies up to January 2009. Search terms were reported. Reference lists of included articles were searched for additional studies. Only English-language studies were included.

Study selection
Randomised controlled trials (RCTs) that evaluated antithrombotic drugs (vitamin K antagonists, heparin, antiplatelet drugs) and fibrinolytic treatments for patients with acute RVO or for secondary prevention of the disease were eligible for inclusion in the review. Included studies had to report outcome data; specific outcomes were not defined.

More than half (60%) of the included patients had central retinal vein occlusions (CRVO); the others had branch retinal vein occlusion (BRVO). Diagnostic methods were reported. Intervention comparisons included: therapeutic doses of low-molecular-weight heparin (LMWH) and low-dose aspirin; ticlopidine and placebo; and intravenous fibrinolytic drugs followed by warfarin or aspirin, compared with haemodilution or no treatment. Time between symptom onset and treatment varied (within seven days to within 30 days). Concomitant treatments were not reported. The outcomes were visual acuity (variably defined), neovascular complications, recurrent events and bleeding complications.

Two reviewers selected studies for inclusion. Disagreements were resolved either by discussion or by involving a third reviewer.

Assessment of study quality
Trial quality assessment was carried out using Jadad criteria of randomisation, blinding and follow-up). A maximum score of 5 points represented high quality, 3 and 4 points were medium quality and fewer than 3 were low quality.

Two reviewers independently carried out the quality assessment.

Data extraction
Data were extracted on incidence rates.

Two reviewers independently carried out the data extraction.

Methods of synthesis
A narrative synthesis was presented.

Results of the review
Six RCTs (n=384) were included in the review. One trial was considered to be high quality, one was medium quality and four were low quality. Sample sizes ranged from 52 to 93. Follow-up ranged from six months to one year.

There was a partial improvement in visual acuity in all studies. The neovascular complication rate ranged from 0% to 39% (four RCTs). Ocular bleeding complications were present in 0% to 20% of patients (six RCTs). Recurrent RVO ranged from 0% to 10% (two RCTs).

No trials evaluated the effects of interventions on secondary prevention.

**Authors' conclusions**
Limited evidence suggested that antithrombotic drugs, particularly LMWH, may be effective in treating the acute phase of RVO in some patients.

**CRD commentary**
The research question was clear and supported by potentially reproducible inclusion criteria for study design, participants and interventions. The search strategy included two relevant databases, but publication and language restrictions meant that relevant studies may have been missed and biases could not be ruled out. The review process was conducted with attempts to minimise error and bias. Some appropriate validity assessment criteria were applied, and the results of this were clearly reported. Allocation concealment was not reported and represents an important potential source of bias. Due clinical variation between studies, the chosen method of synthesis was appropriate. Study characteristics were presented, although there was little description of the patient population. The results did not appear to reflect any comparative data, which precluded judgement about the relative effectiveness of treatments.

The authors’ conclusion appeared overstated as it was based on limited evidence presented from single treatment arms and should be interpreted with caution.

**Implications of the review for practice and research**
**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that future research should consider the importance of time to treatment and stratification of patients according to type of RVO. Multidisciplinary approaches to treatment, including combinations that included newer therapeutic drugs, should be evaluated.

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