Anticoagulation for Cerebral Sinus Thrombosis

Jan Stam, MD; Sebastian de Bruijn, MD; Gabrielle deVeber, MD

Background
Treatment of cerebral sinus thrombosis with anticoagulants has been controversial. Anticoagulants may prevent new venous infarcts, neurologic deterioration, and pulmonary embolism but may also promote hemorrhages.

Objectives
To review the available evidence regarding the effectiveness and safety of anticoagulant therapy in patients with confirmed cerebral sinus thrombosis.

Search Strategy
We searched the Cochrane Stroke Group Trials Register (last searched March 18, 2002). We also searched MEDLINE (1966 to October 2001), EMBASE (1980 to February 2002), and the Cochrane Controlled Trials Register (Cochrane Library, 2002 Issue 1) and contacted authors to identify additional published and unpublished studies.

Selection Criteria
Unconfounded randomized controlled trials in which anticoagulant therapy was compared with placebo or open control in patients with cerebral sinus thrombosis (confirmed by intra-arterial contrast or magnetic resonance angiography).

Data Collection and Analysis
Two reviewers independently extracted outcomes for each of the 2 treatment groups (anticoagulant treatment and control) and analyzed the outcome data for each patient in the treatment group to which the patient was originally allocated (“intention-to-treat” analysis). A weighted estimate of the treatment effects across trials (relative risk, absolute risk reduction) was calculated using the Cochrane statistical software.

Main Results
Two small trials involving 79 patients fulfilled the inclusion criteria. One trial (20 patients) examined the efficacy of intravenous, adjusted-dose, unfractionated heparin. The other trial (59 patients) examined high-dose, body-weight-adjusted, subcutaneous, low-molecular-weight heparin (nadroparin).

Anticoagulant therapy was associated with a pooled relative risk of death of 0.33 (95% CI 0.08 to 1.21) and of death or dependency of 0.46 (95% CI 0.16 to 1.31) (the Figure). No new symptomatic intracerebral hemorrhages were observed. One major gastrointestinal hemorrhage occurred after anticoagulant treatment. Two control patients (placebo) had a diagnosis of probable pulmonary embolism (one fatal).

Two trials were excluded. One study has been published only as an abstract, and another trial did not meet our inclusion criterion of diagnostic confirmation by x-ray or MR angiography. The latter study showed a statistically nonsignificant benefit of heparin compared with placebo.

Implications for Practice
Anticoagulant treatment in patients with cerebral sinus thrombosis appears to be safe and is associated with an apparent reduction in the risk of death or dependency, which did not reach statistical significance. In the absence of more information from randomized trials, clinicians will need to base their treatment decisions on the limited information available.

Implications for Research
Although the estimated pooled risk reductions did not reach statistical significance, patients and doctors may be reluctant to embark on a new trial that includes a placebo group. Reliable data about the occurrence of intracerebral hemorrhages after anticoagulant treatment in consecutive series of patients with CVST are needed to obtain more robust estimations of the risk. Large consecutive cohort studies could also help to identify subgroups of patients with a poor prognosis. In such patients, randomized trials testing more aggressive—and probably more hazardous—therapies such as local (direct) thrombolysis or thrombosuction are justified and needed.

Reviewers’ Conclusions
Based on the limited evidence available, anticoagulant treatment for cerebral sinus thrombosis appeared to be safe and was associated with a potentially important reduction in the
Comparison: overall benefit or harm of heparin
Outcome: death or dependency

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>RR (95%CI Fixed)</th>
<th>Weight %</th>
<th>RR (95%CI Fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1981 Einhaupl</td>
<td>0 / 10</td>
<td>3 / 10</td>
<td></td>
<td>36.5</td>
<td>0.14 [0.01, 2.45]</td>
</tr>
<tr>
<td>1999 CVST Group</td>
<td>4 / 30</td>
<td>6 / 29</td>
<td></td>
<td>63.5</td>
<td>0.64 [0.20, 2.05]</td>
</tr>
<tr>
<td>Total (95%CI)</td>
<td>4 / 40</td>
<td>9 / 39</td>
<td></td>
<td>100.0</td>
<td>0.46 [0.16, 1.31]</td>
</tr>
<tr>
<td>Test for heterogeneity chi-square = 0.97 df = 1 p = 0.32</td>
<td></td>
<td></td>
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<tr>
<td>Test for overall effect z = 1.45 p = 0.15</td>
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</tbody>
</table>

Systematic review of trials comparing therapeutic dose of heparin with placebo for cerebral sinus thrombosis. Results are expressed as relative risks (RR) with 95% CIs. (Figure 01.02.00. Stam J, de Bruijn SFTM, DeVeber G. Anticoagulation for cerebral sinus thrombosis (Cochrane review). In: The Cochrane Library, Issue 4, 2002. Oxford: Update Software. MetaView © Update Software, Oxford.)

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