Anticoagulants for Acute Ischemic Stroke

Peter Sandercock FRCPE; Gord Gubitz, MD; Carl Counsell, MD

Most ischemic strokes are caused by blood clots blocking an artery in the brain. Clot prevention with anticoagulant therapy could have a significant impact on patient survival, disability, and stroke recurrence.

Objective

We sought to assess the effect of anticoagulant therapy compared with control in the early treatment of patients with acute ischemic stroke.

Search Strategy

We searched the Cochrane Stroke Group trials register (last searched 30 October 2003). We selected randomized trials comparing early anticoagulant therapy (started within 2 weeks of stroke onset) with control in patients with acute presumed or confirmed ischemic stroke. Two reviewers independently selected trials for inclusion, assessed trial quality, and extracted the data.

Main Results

Twenty-two trials involving 23,547 patients were included (Figure). The quality of the trials varied considerably. The anticoagulants tested were standard unfractionated heparin, low-molecular-weight heparins, heparinoids, oral anticoagulants, and thrombin inhibitors. Based on 9 trials (22,570 patients), there was no evidence that anticoagulant therapy reduced the odds of death from all causes (odds ratio [OR], 1.05; 95% CI, 0.98 to 1.12) at the end of follow-up. Similarly, based on 6 trials (21,966 patients), there was no evidence that anticoagulants reduced the odds of being dead or dependent at the end of follow-up (OR, 0.99; 95% CI, 0.93 to 1.04). Although anticoagulant therapy was associated with ~9 fewer recurrent ischemic strokes per 1000 patients treated (OR, 0.76; 95% CI, 0.65 to 0.88), it was also associated with a similar-sized 9 per 1000 increase in symptomatic intracranial hemorrhages (OR, 2.52; 95% CI, 1.92 to 3.30). Similarly, anticoagulants avoided ~4 pulmonary emboli per 1000 (OR, 0.60, 95% CI, 0.44 to 0.81), but this benefit was offset by an extra 9 major extracranial hemorrhages per 1000 (OR, 2.99; 95% CI, 2.24 to 3.99). Sensitivity analyses did not identify a particular type of anticoagulant regimen, patient characteristic, or time window associated with net benefit.

Implications for Practice

Evidence from this systematic review indicates that anticoagulants in acute ischemic stroke have no effect in terms of

Systematic review of randomized trials comparing anticoagulants with control in people with acute ischemic stroke. Results are expressed as Peto OR and 95% CI with fixed-effects model. OR < 1 suggests anticoagulants superior to control. Effects on number of patients with poor outcome (dead or dependent in activities of daily living) were at the end of scheduled trial follow-up. (From Sandercock P, Gubitz G, Counsell C. Anticoagulants for acute ischemic stroke (Cochrane Review). In: The Cochrane Library, Issue 3, 2004. Chichester, UK: Update Software. Reproduced with permission from John Wiley & Sons, Ltd.)

Received June 3, 2004; accepted June 8, 2004.

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(Stroke. 2004;35:2916-2917.)

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Stroke is available at http://www.strokeaha.org

DOI: 10.1161/01.STR.0000147725.45220.79

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death or death or dependency after follow-up of at least 1 month. A reduction in recurrent ischemic stroke during the treatment period is exactly offset by an increase in intracranial hemorrhage. There is a dose-dependent increase in both intra- and extracranial hemorrhage, and although low dose regimens decrease deep vein thrombosis (DVT) and pulmonary embolism, the clinical importance of this is unclear, because many DVTs are asymptomatic and pulmonary emboli are rare. The data do not support the routine use of immediate high-dose intravenous or subcutaneous anticoagulants in any form for patients with acute ischemic stroke. Low-dose subcutaneous regimens will prevent DVT but with a small yet definite increased risk of major hemorrhage. It may therefore be advisable to consider safer alternatives in immobile patients (such as aspirin, compression stockings, or early mobilization). The data do not support the use of low-molecular-weight heparins, heparinoids, or thrombin inhibitors in the routine treatment of acute ischemic stroke. The analysis performed did not identify any category of patient where there was clear net benefit. Aspirin is an effective antithrombotic alternative to anticoagulation, which is safe when used in the acute phase of ischemic stroke.

Implications for Research

Further large-scale trials comparing immediate anticoagulation with control in patients with acute ischemic stroke are probably not warranted. This review has not provided clear evidence about the optimum antithrombotic regimen for the prevention of DVT and pulmonary embolism in stroke patients. Aspirin alone, low-dose subcutaneous heparin, the combination of the 2, or the use of compression stockings are all promising possibilities, but a very large scale randomized trial with several tens of thousands of patients would be required to determine which has the most favorable balance of risk and benefit on overall clinical outcome.


Key Words: anticoagulants, cerebrovascular accident, review, academic
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Stroke. 2004;35:2916-2917; originally published online November 4, 2004;
doi: 10.1161/01.STR.0000147725.45220.79
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://stroke.ahajournals.org/content/35/12/2916