

# Review: Anticoagulants are not more effective than antiplatelet agents in acute ischemic stroke

Berge E, Sandercock P. **Anticoagulants versus antiplatelet agents for acute ischaemic stroke.** *Cochrane Database Syst Rev.* 2002;(4):CD003242 (latest version 14 Dec 2002).

## QUESTION

In patients with acute ischemic stroke, what is the comparative effectiveness of anticoagulants (alone or with antiplatelet agents) and antiplatelet agents alone given within 14 days of stroke onset?

## DATA SOURCES

Studies were identified by searching (in April and May 2001) the Cochrane Stroke Group Trials Register, the Cochrane Controlled Trials Register, the trials register of the Anti-thrombotic Therapy Trialists' Collaboration, MEDLINE (1966 to 2000), and EMBASE/Excerpta Medica (1980 to 2000); and by scanning bibliographies of relevant studies.

## STUDY SELECTION

Studies were selected if they were randomized controlled trials comparing anticoagulants with antiplatelet agents, or anticoagulants plus antiplatelet agents with antiplatelet agents alone, given within 14 days of onset of presumed or confirmed acute ischemic stroke. Studies were excluded if treatment allocation was not adequately concealed or if they only assessed patients with transient ischemic attacks.

## DATA EXTRACTION

Data were extracted on study methods and quality, participants, interventions, and outcomes.

## MAIN RESULTS

4 trials (data from 16 558 patients; most had had nonhemorrhagic strokes and were aged > 70 y) were included. Data from 11 721 patients contributed to the comparison of anticoagulants with antiplatelet agents, and data from 9720 patients contributed to the comparison of anticoagulants plus antiplatelet agents with antiplatelet agents alone. All trials included patients within 48 hours of stroke onset. Follow-up was at 10 days in 1 trial, 3 months in 1 trial, and 6 months in 2 trials. The anticoagulants used were unfractionated heparin and low-molecular-weight heparin; aspirin was used as the control in all trials; treatments lasted for 10 to 14 days. Anticoagulants with or without aspirin com-

pared with aspirin alone did not reduce death or dependence at the end of follow-up; however, anticoagulants were associated with a trend toward increased risk for death at the end of follow-up and symptomatic intracranial hemorrhage during treatment (Table).

## CONCLUSION

In patients with acute ischemic stroke, anticoagulants used alone or with antiplatelet agents are not superior to antiplatelet agents used alone.

*Source of funding: Norwegian Research Council.*

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### Anticoagulants (AC) alone or with antiplatelet agents (AP) vs AP alone at end of follow-up (10 d to 6 mo) or during treatment (treatment durations 10 to 14 d)\*

Outcomes	Comparison	Weighted event rates	RRI (95% CI)	NNH
Death or dependence at end of follow-up	AC vs AP	64% vs 62%	3% (0 to 5)	NS
	AC + AP vs AP	62% vs 62%	0% (-3 to 3)	NS
Death at end of follow-up	AC vs AP	22% vs 20%	8% (1 to 16)	NS
	AC + AP vs AP	22% vs 21%	3% (-4 to 12)	NS
Symptomatic intracranial hemorrhage during treatment	AC vs AP	1.6% vs 0.56%	125% (48 to 242)	NS
	AC + AP vs AP	1.5% vs 0.54%	134% (48 to 270)	NS

\*NS = not significant. Other abbreviations defined in Glossary; RRI, NNH, and CI calculated from data in article using a fixed-effects model.

## COMMENTARY

Although most ischemic strokes are the result of clot embolization, the relative value of anticoagulation and antiplatelet therapy in patients with such strokes is still not settled. Berge and Sandercock have done the important task of critically evaluating the existing literature for evidence-based information on the relative value of anticoagulants and antiplatelet agents in treatment of ischemic stroke. They reviewed a plethora of studies that addressed this important subject. However, after applying strict criteria for randomization and concealment of treatment allocation, only 4 trials met the inclusion criteria. Furthermore, almost 90% of the nearly 17 000 patients evaluated came from a single study (1). Therefore, an exhaustive search and analysis in an attempt to create the equivalent of a meta-analysis came down to reanalysis of a single study. The conclusion of the authors was that anticoagulation did not appear to have a significant advantage over aspirin. Berge and Sandercock's analysis also shows that the practicing clinician should take the results of some studies with a grain of salt because many of them have methodological flaws.

Although the analysis by Berge and Sandercock does not include studies on ischemic stroke therapies beyond those using anticoagulation and antiplatelet therapy, the clinician should be aware that statins have been shown to be effective in reducing the risk for recurrent stroke both

in patients with coronary artery disease (2) and in those with aortic arch atherosclerosis (3). Angiotensin-converting enzyme inhibitors have been shown to reduce the risk for recurrent stroke in patients with stroke with or without hypertension (4).

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## References

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2. Plehn JE, Davis BR, Sacks FM, et al. Reduction of stroke incidence after myocardial infarction with pravastatin: the Cholesterol and Recurrent Events (CARE) study. *Circulation.* 1999;99:216-23.
3. Tunick PA, Nayar AC, Goodkin GM, et al. Effect of treatment on the incidence of stroke and other emboli in 519 patients with severe thoracic aortic plaque. *Am J Cardiol.* 2002;90:1320-5.
4. PROGRESS Collaborative Group. Randomised trial of a perindopril-based blood-pressure lowering regimen among 6,105 individuals with previous stroke or transient ischaemic attack. *Lancet.* 2001;358:1033-1041.