

Review: warfarin prevents stroke in non-rheumatic atrial fibrillation but has a higher risk for haemorrhage than other agents

Segal JB, McNamara RL, Miller MR, et al. *Anticoagulants or antiplatelet therapy for non-rheumatic atrial fibrillation and flutter*. *Cochrane Database Syst Rev* 2001;(1):CD001938 (latest version 29 Nov 2000).

QUESTION: In patients with non-rheumatic atrial fibrillation (AF), how effective are anticoagulants and antiplatelet drugs in preventing thromboembolic complications?

Data sources

Studies were identified by searching 3 databases and relevant journals.

Study selection

Studies were selected if they were randomised controlled trials (RCTs) evaluating warfarin, aspirin, combined low dose warfarin and aspirin, low molecular weight heparin, or indobufen for prevention of thromboembolism in AF or atrial flutter and if the outcomes were stroke, major bleeding, or death.

Data extraction

Data were extracted on study quality; patient characteristics and inclusion and exclusion criteria; therapeutic protocol, including intensity of coagulation and percentage of time inside and outside of the target range; and results.

Main results

14 RCTs were included. 6 RCTs compared warfarin with placebo: warfarin reduced the risk for stroke but increased the risk for major haemorrhage; the 23% relative reduction in total mortality was not statistically significant. 4 RCTs compared aspirin with placebo: the modest reduction in stroke (16%) was not significant; no difference was seen for haemorrhage or mortality. 5 RCTs compared warfarin with all antiplatelet drugs: warfarin reduced the risk for stroke and showed no difference for haemorrhage or mortality. 4 RCTs compared warfarin with aspirin: a moderate decrease for stroke was shown with warfarin, and no difference was shown for haemorrhage or mortality. The table gives the results for stroke and haemorrhage. Adjusted dose war-

farin reduced stroke more than low dose warfarin plus aspirin (2 RCTs). No differences were seen in comparisons of warfarin and indobufen (1 RCT) or low molecular weight heparin and placebo (1 RCT).

Conclusions

In patients with non-rheumatic atrial fibrillation, warfarin prevents stroke among those with average or higher risk and is more effective than antiplatelet drugs. The risk for major haemorrhage is increased with warfarin.

COMMENTARY

Despite convincing evidence that warfarin treatment is highly effective in preventing stroke in patients with chronic AF, recent studies indicate that only one half of eligible patients are receiving this treatment.¹ The most commonly cited reasons for warfarin underusage are concerns about bleeding in elderly patients and the feasibility of long term anticoagulation monitoring.²

For clinicians who remain unsure about the risk benefit ratio of warfarin treatment in patients with chronic AF, the meta-analysis by Segal *et al* provides a concise balance sheet of potential benefits and harms associated with warfarin and aspirin treatment. For warfarin treatment, 18 patients need to be treated to prevent 1 additional stroke (RRR 66%), whereas 1 additional major bleed will occur after the treatment of 77 patients. This risk benefit ratio is acceptable because about 70% of cardioembolic strokes are fatal or are associated with major disability.³ About 5% of warfarin associated bleeding episodes are intracranial, and most other bleeds are not associated with long term morbidity.⁴ Aspirin treatment is not associated with an increased risk for major bleeding. It has questionable efficacy, however, in overall stroke prevention (RRR 16%), and its benefit may be limited to the prevention of thrombotic stroke.

Another consideration in deciding about treatment options is a patient's risk profile. Patients with previous stroke, left ventricular dysfunction, age >75 years, and hypertension are at high risk for stroke, whereas those with diabetes, coronary artery disease, and age 65–75 years are at moderate risk, and those <65 years with no risk factors are at low risk. Patients >75 years of age are at the highest risk for bleeding, but will benefit most from treatment with warfarin.

In summary, warfarin should be considered in all patients with chronic AF, and aspirin should be used only in patients with a contraindication to warfarin, or those at low risk of stroke.

James D Douketis, MD
St. Joseph's Hospital, Hamilton, Ontario, Canada

- Smith NL, Psaty BM, Furberg CD, et al. *Arch Intern Med* 1999;159:1574–8.
- Kutner M, Nixon G, Silverstone F. *Arch Intern Med* 1991; 151:1950–3.
- Lin HJ, Wolf PA, Kelley-Hayes M, et al. *Stroke* 1996;27:1760–4.
- Palareti G, Leali N, Coccheri S, et al. *Lancet* 1996;348:423–8.

Source of funding:
Agency for Healthcare
Research and Quality.

For correspondence:
Dr J Segal, Johns
Hopkins School of
Medicine, 720 Rutland
Avenue, Ross Building
#1025, Baltimore, MD
21205, USA.

Anticoagulants or antiplatelets (APs) to prevent stroke in non-rheumatic atrial fibrillation and flutter*

Outcomes†	Comparison	Weighted event rates	RRR (95% CI)	NNT (CI)
Stroke	Warfarin v placebo	2.9% v 8.7%	66% (52 to 76)	18 (14 to 25)
	Aspirin v placebo‡	9.1% v 11.2%	16% (–28 to 45)	Not significant
	Warfarin v APs	3.2% v 5.0%	36% (10 to 54)	56 (33 to 250)
	Warfarin v aspirin	3.6% v 5.4%	33% (3 to 54)	56 (29 to 500)
			RRI (CI)	NNH (CI)
Haemorrhage	Warfarin v placebo	2.2% v 0.9%	139% (27 to 348)	77 (46 to 250)
			RRR (CI)	NNT
	Aspirin v placebo	1.3% v 1.4%	5% (–81 to 51)	Not significant
			RRI (CI)	NNH
	Warfarin v APs	1.5% v 0.8%	83% (–6 to 258)	Not significant
	Warfarin v aspirin	1.6% v 1.0%	56 (–24 to 221)	Not significant

*Abbreviations defined in glossary; RRR, RRI, NNT, NNH, and CI calculated from data in article.

†Duration of follow up not reported.

‡Random effects model was used.