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A. Algra, E.L.L.M. De Schryver, J. van Gijn, L.J. Kappelle and P.J. Koudstaal

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Oral Anticoagulants Versus Antiplatelet Therapy for Preventing Further Vascular Events After Transient Ischemic Attack or Minor Stroke of Presumed Arterial Origin

A. Algra, MD; E.L.L.M. De Schryver, MD; J. van Gijn, MD, FRCP, FRCPE; L.J. Kappelle, MD; P.J. Koudstaal, MD

Background

Patients who are entered in clinical trials after a transient ischemic attack or nondisabling ischemic stroke have an annual risk of important vascular events (death from all vascular causes, nonfatal stroke, or nonfatal myocardial infarction) of between 4% and 11%.[1,2] Aspirin, in a daily dose of 30 mg or more, offers only modest protection after cerebral ischemia: it reduces the incidence of major vascular events by 20% at most.[1–3] Secondary prevention trials after myocardial infarction indicate that treatment with oral anticoagulants is associated with a risk reduction approximately twice that of treatment with antiplatelet therapy.[1,4–7]

Objectives

This review aimed to (1) compare the efficacy of oral anticoagulants and antiplatelet therapy in the secondary prevention of vascular events after cerebral ischemia of presumed arterial origin and (2) compare the safety of oral anticoagulants and antiplatelet therapy in the secondary prevention of vascular events after cerebral ischemia of presumed arterial origin.

Search Strategy

This review draws on the search strategy developed for the Cochrane Stroke Review Group as a whole. Relevant trials were identified in the Specialized Register of Controlled Trials. Authors of published trials were contacted for further information and unpublished data.

Selection Criteria

Randomized trials with concealed treatment allocation on long-term (>6 months) secondary prevention after recent (<6 months) transient ischemic attack or minor ischemic stroke of presumed arterial origin were selected. The oral anticoagulant therapy was to be of specified intensity (by means of the International Normalized Ratio [INR]) with warfarin, phenprocoumon, or acenocoumarol versus a single antiplatelet drug (or combination of antiplatelet agents).

Data Collection and Analysis

Two reviewers selected trials meeting the inclusion criteria and extracted details of randomization methods, blinding of treatments and assessments, whether intention-to-treat analysis is possible from the published data, whether treatment groups are comparable with regard to major prognostic risk factors for outcomes, the number of patients who are excluded or lost to follow-up, definition of outcomes, and entry and exclusion criteria. The method-

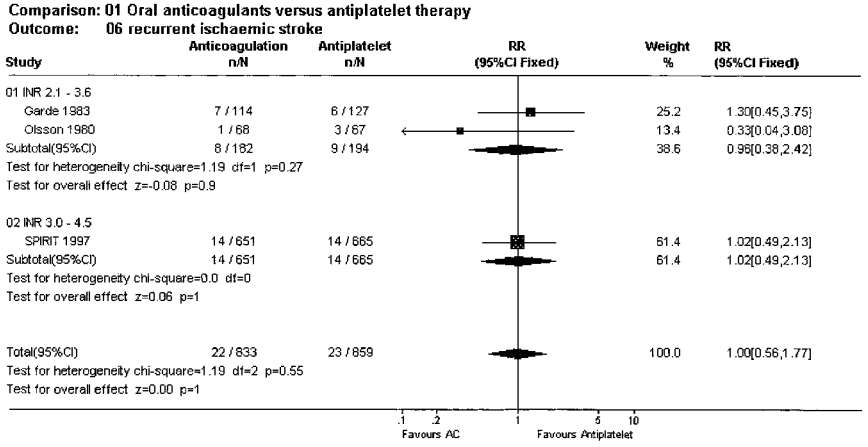

Figure 1. Outcome recurrent ischemic stroke. (Figure 01.06.00. Algra A, De Schryver ELLM, van Gijn J, Kappelle LJ, Koudstaal PJ. Oral anticoagulants versus antiplatelet therapy for preventing further vascular events after transient ischaemic attack or minor stroke of presumed arterial origin [Cochrane Review]. In: *The Cochrane Library*, Issue 3, 2002. Oxford: Update Software. MetaView © Update Software, Oxford.)

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From the Department of Neurology (A.A., E.L.L.M.D.S., J.v.G., L.J.K.) and the Julius Center for Health Sciences and Primary Care (A.A.), University Medical Center Utrecht, the Netherlands; and the Department of Neurology (P.J.K.), Erasmus Medical Center Rotterdam, the Netherlands.

Correspondence to Ale Algra, University Medical Centre Utrecht, Julius Center for Health Sciences and Primary Care, Room D.01.335, PO Box 85500, 3508 GA Utrecht, Netherlands. E-mail A.Algra@neuro.azu.nl

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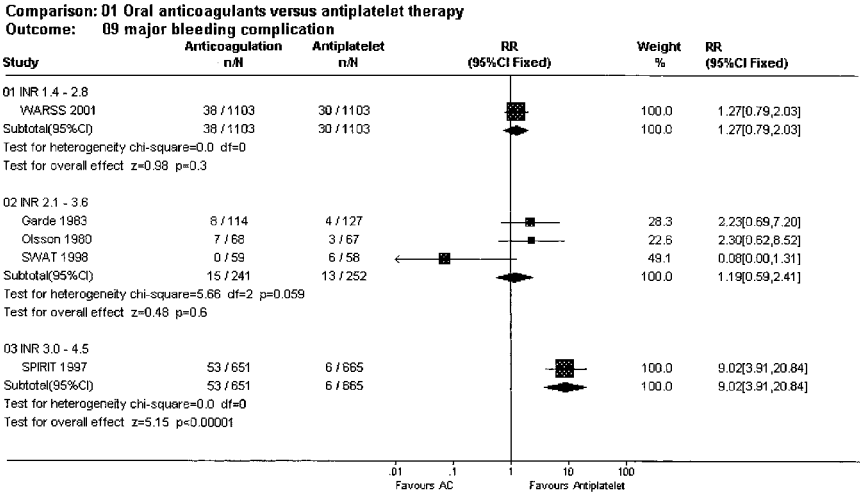

Figure 2. Outcome major bleeding complication. (Figure 01.09.00. Algra A, De Schryver ELLM, van Gijn J, Kappelle LJ, Koudstaal PJ. Oral anticoagulants versus antiplatelet therapy for preventing further vascular events after transient ischaemic attack or minor stroke of presumed arterial origin [Cochrane Review]. In: *The Cochrane Library*, Issue 3, 2002. Oxford: Update Software. MetaView © Update Software, Oxford.)

ological quality of each trial was assessed by the 2 reviewers using these extracted data. In addition, target INR for anticoagulant treatment and dose and type of antiplatelet drug, duration of follow-up, and the numbers of defined outcome events were recorded.

The data were analyzed according to the intention-to-treat principle. Subgroup analyses with treatment INR 1.4 to 2.8 (low intensity), INR 2.1 to 3.6 (medium intensity), and INR 3.0 to 4.5 (high intensity) were performed. Relative and absolute risk reductions were calculated by means of the statistical software provided by the Cochrane Collaboration.

Main Results

Five trials, with a total of 4076 patients, were selected.[8-12]

In the prevention of ischemic stroke after cerebral ischemia of presumed arterial origin, the available data do not allow a robust conclusion on whether anticoagulants (in any intensity) are more efficacious in the prevention of vascular events than antiplatelet therapy (medium-intensity anticoagulation relative risk [RR] 0.96, 95% CI 0.38 to 2.42; high-intensity anticoagulation RR 1.02, 95% CI 0.49 to 2.13) (Figure 1). The (primary) outcome event of WARSS[12] (target INR 1.4 to 2.8) did not contain myocardial infarction of bleeding complications. Recently, the optimal level of anticoagulation for similar patients in an observational study was between INR 2.5 and 3.5.[13]

There is no evidence that treatment with low- or medium-intensity anticoagulation gives a higher bleeding risk than treatment with antiplatelet agents. The RR for major bleeding complications for low-intensity anticoagulation was 1.27 (95% CI 0.79 to 2.03) and for medium-intensity anticoagulation 1.19 (95% CI 0.59 to 2.41). However, it was clear that high-intensity oral anticoagulants with INR 3.0 to 4.5 were not safe, because they yielded a higher risk of major bleeding complications (RR 9.0, 95% CI 3.9 to 21) (Figure 2).

Reviewers' Conclusions

For the secondary prevention of further vascular events after transient ischemic attack or minor stroke of presumed arterial origin, there is insufficient evidence to justify the routine use of medium-intensity oral anticoagulants (INR 2.0 to 3.6); such treatment preferably should be used only as part of a clinical trial. More intense anticoagulation (INR 3.0 to 4.5) is not safe and should not be used in this setting. Low-intensity anticoagulation (INR 1.4 to 2.8) is not likely to be more efficacious than aspirin.

Note: Cochrane Reviews are regularly updated as new information becomes available and in response to comments and criticisms. Readers should consult The Cochrane Library for the latest version of a Cochrane Review. Information on The Cochrane Library can be found at www.update-software.com.

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KEY WORDS: anticoagulants ■ antiplatelet therapy ■ cerebral ischemia ■ randomized controlled trials