Aspirin plus dipyridamole versus aspirin for prevention of vascular events after stroke or TIA: a meta-analysis
Verro P, Gorelick PB, Nguyen D

CRD summary
This review concluded that aspirin with dipyridamole was more effective than aspirin alone for preventing stroke and other vascular events in patients with minor stroke and ischaemic attacks; risk reduction was significant increased for trials primarily using extended-release dipyridamole. The authors’ conclusions reflected the results of the review and are likely to be reliable.

Authors’ objectives
To assess the efficacy of aspirin plus dipyridamole compared with aspirin alone for preventing recurrent cerebral and systemic vascular events in patients with minor stroke and ischaemic attacks.

Searching
MEDLINE was searched from inception to 2006; published or unpublished studies were eligible. Search terms were reported. The most recent review from the Cochrane Database of Systematic Reviews was used to identify eligible trials, as were the reference lists from relevant studies.

Study selection
Randomised controlled trials (RCTs) that compared aspirin plus dipyridamole with aspirin alone in patients with previous non-cardioembolic stroke or transient ischaemic attack were eligible for inclusion. Dipyridamole could be either immediate-release or extended-release, or both formulations. Eligible trials had to report stroke as a primary outcome. Outcomes included stroke prevention, myocardial infarction, vascular death, or the composite endpoint of these outcomes.

In the included trials, the aspirin dose ranged from 50 to 1,300mg; the dipyridamole dose ranged from 150 to 400mg. Most trials used immediate-release dipyridamole; one trial used extended-release dipyridamole and another used both formulations.

The authors did not state how the studies were selected for the review.

Assessment of study quality
Trial quality was assessed according to: blinded concealment of treatment allocation and outcome assessment; assessment of compliance; and completeness of follow-up.

The authors did not state how the quality assessment was undertaken.

Data extraction
Data were extracted to enable the calculation of relative risks (RRs) and 95% confidence intervals (CIs) for the outcomes of interest.

The authors did not state how the data extraction was undertaken.

Methods of synthesis
Relative risks and 95% confidence intervals were pooled in a fixed-effect meta-analysis (Mantel-Haenszel method). Heterogeneity was assessed using the X² test according to the Woolf method.

Subgroup analyses were conducted to explore differential effects of treatment on trials using exclusively immediate-release and predominantly extended-release dipyridamole. High quality trials were used for post hoc analysis.
Results of the review
Six RCTs were included (n=7,648, patients range 36 to 3,299). Four trials were considered high-quality. Four trials had concealed treatment allocation and blinded outcome assessment. One trial did not conceal treatment allocation, but did have blinded outcome assessment. One trial failed both criteria.

Compared with aspirin alone, aspirin plus dipyridamole yielded a significant reduction in the overall risk for stroke (RR 0.77, 95% CI 0.67 to 0.89; six RCTs) and the composite outcome of nonfatal stroke, nonfatal myocardial infarction and vascular death (RR 0.85, 95% CI 0.76 to 0.94; five RCTs). Heterogeneity was absent for these comparisons. Analyses restricted to high quality trials (four RCTs) showed very similar results.

Compared with aspirin alone, trials using predominantly extended-release dipyridamole showed a statistically significant reduction in the overall risk for stroke (RR 0.76, 95% CI 0.65 to 0.89; two RCTs) and the composite outcome (RR 0.82, 95% CI 0.73 to 0.92; two RCTs). Heterogeneity was absent for these comparisons.

For trials using immediate-release dipyridamole, there was no significant reduction in risk for stroke (four RCTs) or the composite outcome (three RCTs).

Authors' conclusions
The combination of aspirin plus dipyridamole was more effective than aspirin alone in preventing stroke and other serious vascular events in patients with minor stroke and transient ischaemic attacks. The risk reduction was greater and statistically significant for trials primarily using extended-release dipyridamole, which may reflect a true pharmacological effect or lack of statistical power in trials using immediate-release dipyridamole.

CRD commentary
The review question and the inclusion criteria were clear. Limited study details were provided. The authors searched a number of relevant databases and additional sources without publication restrictions, but it was unclear whether language restrictions were applied, so language bias may have been introduced. It was unclear whether sufficient attempts have been made to minimise the errors and biases in the review process.

Adequate criteria were used to assess trial quality. Appropriate methods appear to have been used to pool the trials. Reasonable measures were used to assess and explore heterogeneity between trials.

The authors’ conclusions reflected the results of the review and, despite the potential for language bias and reviewer error and bias, these conclusions are likely to be reliable.

Two authors disclosed financial links with various pharmaceutical companies including Boehringer Ingelheim Pharmaceutical (manufacturers of dipyridamole and funders of the review).

Implications of the review for practice and research
The authors did not state any implications for practice or further research.

Funding
Boehringer Ingelheim Pharmaceuticals (manufacturers of dipyridamole).

Bibliographic details

PubMedID
18323511

DOI
Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.