Aspirin for the primary prevention of cardiovascular events: a systematic review and meta-analysis comparing patients with and without diabetes

CRD summary
This review aimed to determine whether the effect of aspirin for prevention of cardiovascular events and mortality differed for patients with and without diabetes. It concluded that available evidence was insufficient to conclusively show a benefit of aspirin therapy in patients with diabetes; the relative benefit may be similar to that in patients without diabetes. These conclusions appear appropriately cautious.

Authors' objectives
To determine whether the effect of aspirin for primary prevention of cardiovascular events and mortality differs for patients with and without diabetes.

Searching
MEDLINE, EMBASE, the Cochrane Library, Web of Science and Scopus were searched for relevant published or unpublished evidence in any language up to November 2008. Search terms were reported. In addition, references of retrieved studies, review articles and guidelines were examined. Authors of eligible studies were also contacted for additional information.

Study selection
Randomised controlled trials (RCTs) that included patients with diabetes without a prior history of myocardial infarction or stroke and assessed the efficacy of aspirin at any dosage were eligible for inclusion in the review. Outcomes of interest were ischaemic stroke, myocardial infarction and all-cause mortality.

Among included RCTs, between 2 and 100% of patients had diabetes. Aspirin doses ranged from 100mg every other day to 650mg daily. Trial duration ranged from 2.3 to 10.1 years.

Two reviewers independently selected studies for inclusion, with any disagreements resolved by a third reviewer.

Assessment of study quality
Two reviewers independently assessed RCTs for quality on the basis of concealment of allocation, blinding, and loss to follow-up.

Data extraction
Rates of ischaemic stroke, myocardial infarction and mortality were extracted for each treatment group. Relative risks (RRs) and related 95% confidence intervals (CIs) were calculated for each of these outcomes. Authors were contacted for additional data where necessary.

Two reviewers extracted the data from included trials.

Methods of synthesis
Relative risks and 95% confidence intervals were pooled using a random-effects model. Firstly, data from participants with and without diabetes were pooled across trials and pooled relative risks calculated. Secondly, the relative risks for patients with and without diabetes within trials were compared using a similar approach. The 95% confidence intervals of these comparisons excluding 1 would provide evidence of an aspirin-diabetes interaction. The degree of inconsistency between pooled trials was estimated using the I² statistic.

In addition, a Bayesian random-effects logistic regression, with diabetes status and aspirin use as the main effect factors, was conducted. Inclusion of 0 within the 95% credible intervals of the regression coefficient of the interaction...
term would indicate no significant aspirin-diabetes interaction.

**Results of the review**

Eight RCTs (n=89,392 participants, range 98 to 39,876) were eligible for inclusion in the review; seven RCTs were included in the meta-analyses. Trials were of generally high methodological quality, with more than half reporting blinding and concealment of allocation. Only one trial stopped early. Most trials had an average length of follow-up of five years or less. Event rates for diabetes patients receiving no treatment were 4% for mortality, 3% for myocardial infarction and 6.6% for stroke.

There was a statistically significant effect of aspirin on mortality versus placebo (RR 0.75, 95% CI 0.60 to 0.93; I²=0%).

There was no statistically significant effect of aspirin on myocardial infarction versus placebo (RR 0.73, 95% CI 0.43 to 1.22; I²=63%).

There was no statistically significant effect of aspirin on ischaemic stroke versus placebo (RR 0.93, 95% CI 0.83 to 1.05; I²=39%).

No analysis provided evidence of a different effect of aspirin in participants with and without diabetes.

**Authors’ conclusions**

Data were insufficient to conclusively show a benefit of aspirin therapy for prevention of cardiovascular events in patients with diabetes. Available data suggested, but did not confirm, the relative benefit was similar to that in patients without diabetes.

**CRD commentary**

The review question was reasonably clearly defined in terms of the participants, interventions, outcomes and study designs of interest. Attempts were made to identify relevant evidence from a range of sources, regardless of language or publication status. Attempts were made to minimise the potential for errors and bias throughout the review process.

The quality of individual trials was assessed. The methods used to synthesise trials and investigate heterogeneity and interactions appeared appropriate, although there appeared to be some inconsistencies in reporting the outcome values. However, these reported differences were small.

Given the limited available evidence (relatively short follow-up and relatively small numbers of events/deaths in participants with diabetes), the authors' cautious conclusions appear appropriate.

**Implications of the review for practice and research**

**Practice:** The authors stated that the decision to use aspirin for preventative treatment in an individual patient should take into account the patient's context and preferences, specifically establishing the risks of coronary artery disease and gastrointestinal and extracranial bleeds.

**Research:** The authors stated that additional evidence from RCTs and individual patient data meta-analyses may be required.

**Funding**

Mayo Clinic Clinician-Investigator Training Programme; Government of Spain, Instituto de Salud Carlos III, Ministerio de Sanidad y Consumo, grant number BA08/90035.

**Bibliographic details**

systematic review and meta-analysis comparing patients with and without diabetes. Diabetes Care 2009; 32(12): 2300-2306

PubMedID
19741185

DOI
10.2337/dc09-1297

Original Paper URL
http://care.diabetesjournals.org/content/32/12/2300.abstract

Indexing Status
Subject indexing assigned by NLM

MeSH
Aspirin /therapeutic use; Cardiovascular Diseases /prevention & control; Diabetic Angiopathies /prevention & control; Female; Fibrinolytic Agents /therapeutic use; Humans; Hypertension /prevention & control; Male; Myocardial Infarction /prevention & control; Observer Variation; Primary Prevention /methods; Randomized Controlled Trials as Topic; Stroke /prevention & control

AccessionNumber
12010000552

Date bibliographic record published
23/06/2010

Date abstract record published
17/11/2010

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.