Aspirin following non-arteritic ischaemic optic neuropathy: a systematic review and meta-analysis

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CRD summary
The review concluded that there was a benefit of aspirin in prevention of second eye NAION. However, the evidence was weak (acknowledged by the authors) and concerns about the quality, quantity and heterogeneity of the evidence used to produce the pooled estimate made its reliability questionable. The authors’ conclusion should be treated with caution.

Authors’ objectives
To determine the efficacy and safety of aspirin in the prevention of second eye non-arteritic anterior ischaemic optic neuropathy (NAION).

Searching
MEDLINE and The Cochrane Library were searched without language restrictions up to December 2006. References of all identified studies were checked.

Study selection
Randomised controlled trials (RCTs) or non-randomised controls trials (with concomitant or historical controls) that compared aspirin with placebo or no treatment in patients with NAION were eligible for inclusion. Relevant study outcomes included incidence of myocardial infarction and cerebrovascular ischaemic accidents following NAION, incidence of second eye NAION and prevalence of patients meeting clinical guidelines for aspirin as primary prevention among patients presenting with NAION.

The setting for all the studies included in the meta-analysis was a tertiary referral center; no further participant or study details were reported.

Two reviewers independently selected studies for inclusion in the review.

Assessment of study quality
The quality of RCTs was assessed according to the criteria: allocation sequence generation; allocation concealment; blinding; intention-to-treat analysis; and number of patients excluded from outcome assessment. For non-randomised studies, the authors distinguished between prospective studies with concomitant controls and other designs, recorded the number of patients unavailable for follow-up and recorded the confounding variables corrected for.

The authors did not state how many reviewers performed the quality assessment.

Data extraction
Incidence of myocardial infarction, cerebrovascular accidents and second eye NAION following NAION were extracted in order to calculate relative risk (RR).

Two reviewers independently extracted data from the included studies; in cases of disagreements a third reviewer was consulted.

Methods of synthesis
Summary relative risks and 95% confidence intervals (CIs) were estimated using a random-effects model for risk of second eye NAION. The number needed to treat (NNT) was calculated and compared with the reported incidence of...
severe haemorrhagic aspirin complications. Statistical heterogeneity was assessed using the $X^2$ test and the $I^2$ statistic.

**Results of the review**

Four studies (n=944) were included in the meta-analysis: three controlled studies and one prospective cohort study. Length of follow-up ranged from two to five years. Loss to follow-up ranged from 7% to 43%.

Pooled results found no statistically significant difference between groups for risk of second eye NAION (RR 0.62, 95% CI: 0.36, 1.07, $I^2$=66.3%; four studies, n=142). Assuming the risk for second eye NAION in untreated patients during two years was 20%, the NNT with aspirin to prevent one occurrence of second eye NAION was approximately 12. Three studies found an increase in the incidence of cerebrovascular events following NAION (3% to 7%).

**Authors' conclusions**

The results suggested a benefit of aspirin in prevention of second eye NAION, but the evidence was weak.

**CRD commentary**

The review addressed a focused question and inclusion criteria were clearly defined. Only two databases were searched, so relevant studies may have been missed. No specific attempts were made to locate unpublished studies, which raised the possibility of publication bias. Appropriate steps were taken to minimise error and bias for study selection and quality assessment; it was unclear whether similar steps were taken for data extraction. Study quality was assessed with appropriate criteria, but reporting of the results was incomplete. There was a lack of reporting of patient and study characteristics. It was unclear whether studies adjusted for different confounders and whether adjusted estimates were used in the summary. The primary objective in one of the four included studies was to compare visual outcome following optic nerve sheath fenestration surgery versus observation in NAION. Evidence of significant statistical and clinical heterogeneity may suggest that the pooling of these studies was not appropriate. The authors highlighted several limitations of the included studies and indicated caution when interpreting the results.

The authors' conclusion of a suggested benefit of aspirin in prevention of second eye NAION seemed optimistic and concerns about the quality, quantity and heterogeneity of the evidence used to produce the pooled estimate should be born in mind.

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

**Practice:** The authors stated that patients who had experienced or were at high risk of cardiovascular or cerebrovascular events and who were not already treated with aspirin should be offered aspirin regardless of NAION. In patients with NAION and at low risk for cardiovascular events, use of aspirin should be explored carefully.

**Research:** The authors considered that an RCT of the required size of patients with NAION randomised to aspirin or control would not be feasible, but further focused and larger observational studies would be useful. Differentiation of the effect between people with risk factors for cardiovascular events and those without was needed. It would be useful if aspirin studies for the prevention of other cardiovascular disorders were to collect data on NAION.

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