Aspirin and cataract

The lively debate about the protective effect of aspirin taking on cataract formation continues. In this issue Hankey et al looked at the association and concluded that 'results do not support the hypothesis that 300–1200 mg daily aspirin, taken for a few years is an effective cataract prophylactic'.

However, the authors freely admit the limitations of a study which only looked for cataracts among survivors of the trial at a single point in time, not to mention the fact that the study was primarily designed to test the effect of aspirin on transient ischaemic attacks. Thus the sample size was not geared to test the effect on cataract and may have substantially reduced the power of detecting any effect of aspirin on the lens. The numbers of patients actually having surgery was four and three in the control and aspirin groups respectively and such small numbers are insufficient for reliable statistical tests. The small sample size is reflected in the wide confidence intervals.

While there are a number of case control studies showing that aspirin or aspirin-like substances protect against cataract, some case control and cohort studies claimed not to have shown any such effect. What is the reader to believe?

A problem with case control studies is the ever present possibility that some variables are not allowed for in matching, and the finding of an association is not proof of a causal relationship. Rather, the finding of an association provides a lead for cohort studies, clinical trials, and studies on mechanisms of action. Causation of cataract is multifactorial and it would be surprising if the ingestion of a single substance could protect against all types of cataract. It is, therefore, not surprising that a beneficial effect is not readily apparent in some of the studies.

So far, no work has disproved the association and several of the studies which claim not to show a protective effect, if anything, lend support to it. For example, West et al in their article disclaiming the association, actually found a reduced prevalence of cataract in subjects who had used any aspirin at all (p<0.03) though no dose-response relationship. There are two large randomised controlled trials whose results have been published, but there are methodological flaws with respect to cataract which have been pointed out by Harding.

In the UK trial on physicians there was no placebo group, and aspirin-like analgesics were not denied the controls, many of whom later used aspirin for various reasons. In the Physician Health Study (PHS) involving 22,071 subjects, while the groups were well matched the study was stopped too soon in respect of aspirin taking, when it demonstrated a striking protective effect on non-fatal myocardial infarction but before a significant divergence in the rate of cataract formation in the groups could be demonstrated.

Nevertheless, in the PHS study, the aspirin-taking group did have fewer cataract operations. A further problem with this study is that 'control' subjects had a trial of aspirin or aspirin-like non-steroidal anti-inflammatory agents before commencement of the study in order to minimise non-compliance. In view of the findings of some case control studies that the taking of any aspirin could have conferred some protection, such a preliminary step could have produced a confounding effect.

The exact mechanism of action in preventing cataract is not known, but a plausible theory is the acetylation of lens proteins by aspirin which may protect against glycation and carbamylation. This is presumably the explanation given by protagonists that aspirin taking in the past could confer protection.

Whatever the mechanism the protective effect has yet to be established. Meanwhile, cataract is the commonest cause of blindness in the world and, though operable, treatment is not accessible to the majority of the blind in the developing world. In developed countries cataract is a major drain on resources and poses a problem which the health service is failing to solve. As an age-related problem it can be expected to worsen with an increasingly aged population. One estimate suggested that if cataract could be delayed by 10 years the number of cataract operations needed would be decreased by 40%. Therefore, any hopeful preventive measure deserves to be studied. To date, no study has been reported that was specifically designed to test the effect of aspirin on cataract.

In view of the increasing magnitude of the problem to which no solution is in sight, aspirin still deserves a serious look.

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