Aspirin and asthma: barking up the right tree?

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According to World Health Organization estimates, 300 million people worldwide suffer from asthma. It is the most common chronic condition in childhood and continues to impose a huge burden of morbidity and mortality in adulthood; over 250 000 people are thought to have died from asthma in 2005. In the UK 5.2 million people are currently receiving treatment for asthma.

There has been an apparent increase in incidence over recent years, at least in children and adolescents. Data in adults are more sparse but suggest that incidence increases slightly with age, albeit to a level much lower than that in children. The aetiology of asthma at all ages is still not fully understood although environmental allergens, immunological and genetic factors are all known to contribute. In this issue of Thorax Kurth et al report interesting post hoc data from the Women’s Health Study which suggest that assignment of 100 mg aspirin on alternate days reduces the relative risk of newly reported diagnosis of asthma in otherwise healthy adult women (see page 514).

The first descriptions of aspirin-like medication come from the time of Hippocrates when the bark of the white willow was used as an antipyretic agent. In the 1700s its use is again described to treat “ague” (fever). The active compound was extracted and purified during the 1800s. Most physicians associate aspirin with its ability to precipitate or worsen asthma symptoms. Aspirin-sensitive asthma is in fact a distinct clinical syndrome. Bayer released aspirin onto the market in 1899 as an analgesic and antipyretic agent. It became clear soon after this that aspirin ingestion could lead to severe asthma attacks. The clinical triad of aspirin sensitivity, asthma and nasal polyps was first described by Widal et al in 1922. This was further characterised by Samter and Beers in 1968, leading to the diagnostic label of “Samter’s triad”. Typically, these patients develop symptoms 2–5 h after ingestion of aspirin, characterised by bronchospasm, profuse rhinorrhea, conjunctival injection, periorbital oedema and generalised flushing. Studies estimate the prevalence of aspirin sensitivity among individuals with asthma at 5–20%. These patients usually develop perennial rhinitis in their third decade followed by asthma and aspirin sensitivity a few years later.

The mechanism of these effects is thought to involve disordered arachidonic acid metabolism. Evidence suggests that a reduction in cyclo-oxidase-1 derived prostaglandin E2 production and increased levels of leukotrienes are both important.
Two recent large studies have suggested that aspirin use can reduce the risk of adult-onset asthma. Other studies have shown that some individuals with asthma improve after challenge with aspirin or non-steroidal anti-inflammatory drugs (NSAIDs). The Women’s Health Study was designed to determine the effect of aspirin and vitamin E on cardiovascular risk. Kurth and colleagues have performed post hoc analysis on the data to assess the effects of aspirin on new diagnoses of asthma. The women taking part were all over 45 years of age and mainly Caucasian, with no history of major previous illnesses. A total of 39,876 women entered the study; previous aspirin or NSAID use was not documented but was assumed to be equal in both groups due to the sample size. Women reporting a diagnosis of asthma before the study were excluded, leaving a total of 37,080. Mean follow-up was for 8.9 years during which 196 women reported a new diagnosis of asthma, a cumulative incidence of 5.3%. Women who received alternate day aspirin had a 10% reduction in the relative risk for a new asthma diagnosis. This effect was not modified by age, smoking status, exercise, postmenopausal hormone use and randomised vitamin E intake. The effect of aspirin was lost in women with a body mass index of >30.

Limited evidence exists that aspirin can alter Th1 and Th2 lymphocyte function away from the imbalance thought to exist in asthma. Aspirin also induces the production of non-cyclooxygenase-derived arachidonic acid metabolites that have been shown to reduce airway hyper-responsiveness. The authors speculate that such effects may underlie the observed reduction in asthma risk.

The study has a number of limitations acknowledged by the authors. The Women’s Health Study was not designed to investigate the hypothesis tested here, its primary purpose being the study of cardiovascular risk. The diagnosis of asthma was not based on any accepted diagnostic test but relied on self-reporting. In this age group this is likely to lead to other conditions such as chronic obstructive pulmonary disease or heart disease being mislabelled as asthma. As previously discussed, the women involved in the study were all over 45 and mainly Caucasian, making generalisation to other ethnic and age groups difficult. Prior aspirin and NSAID use was not assessed in each group, but those randomised were asked to forgo these drugs for the duration of the study. However, the original Women’s Health Study states that, despite this, an unquantified number of women started taking NSAIDs during the trial. Clearly, this may be an important confounding factor.

Of potentially greater concern is the observation that women randomised to take aspirin had a significantly increased risk of gastrointestinal bleeding requiring blood transfusion (relative risk 1.40; 95% confidence interval 1.07 to 1.83). It is debatable whether such a risk is acceptable in order to achieve the reduction in asthma risk.

Despite these limitations, the observations made by Kurth and others seem tenable. It is clear that further studies are needed specifically to test the hypothesis that aspirin can reduce the risk of developing adult-onset asthma.

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REFERENCES


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