

## **ASPIRIN, COGNITIVE DECLINE AND DEMENTIA**

### *Key points*

- Observational data suggest that low-dose aspirin may be associated with a reduced risk of cognitive decline and dementia
- The mechanism for such an effect in patients with Alzheimer's disease is uncertain
- Low-dose aspirin reduces the risk of stroke and this probably reduces the risk of cognitive decline secondarily
- Prospective randomised trials are needed to confirm whether aspirin can prevent cognitive decline

Failing mental ability is amongst the most feared consequences of ageing and dementing illnesses are of growing individual, clinical and public health concern. Cerebrovascular disease is well recognised as a major risk factor for cognitive impairment and vascular lesions may also contribute to the clinical manifestation of Alzheimer's disease, probably due chiefly to summation of subclinical vascular and Alzheimer lesions. The Antiplatelet Trialists' Collaboration shows that long-term anti-platelet treatment given to people after TIA/mild ischaemic stroke reduces proportional risk of non-fatal stroke by one-third and fatal stroke by one fifth. It follows that low dose aspirin has an important role to play in preventing progression of cerebrovascular pathology and this is likely to help to preserve cognitive function.

Retrospective case-note analysis of patients with vascular dementia has shown a trend towards increased life expectancy and time to institutionalisation in those regularly taking low dose aspirin. In the only published RCT of aspirin in vascular dementia claimed highly significant improvements in cerebral perfusion, cognitive performance, quality of life and independence in aspirin-treated patients compared to untreated controls over 3 years of follow up. Unfortunately the methodology of this trial was seriously flawed and so a recent Cochrane Review concludes that there is still no specific evidence that aspirin is effective in treating people with a diagnosis of vascular dementia. Nevertheless, over 80% of UK and Canadian specialists consider aspirin should be prescribed to patients with cognitive impairment and vascular risk factors. It must be of some concern that cohort studies have shown that dementia is a significant independent determinant of non-treatment with aspirin when otherwise indicated after a first ischaemic stroke or myocardial infarction.

Other evidence suggesting a protective effect of aspirin against Alzheimer's disease comes from observational studies reporting an inverse relationship between risk of developing Alzheimer's disease and use of NSAIDs, particularly when taken long term. This is in line with post-mortem studies of brain tissue pointing to an inflammatory process associated with the extracellular amyloid plaques characteristic of Alzheimer's pathology. Thus use of NSAIDs, such as aspirin, may attenuate pro-inflammatory prostaglandin synthesis and so reduce risk of Alzheimer's disease. Alternatively, they could act independently of changes in cyclo-oxygenase activity by influencing processing of beta amyloid-42 peptide, the principal component of the amyloid plaques. Recent studies lend support to this hypothesis, showing that aspirin at clinically relevant low doses inhibits the polymerisation and aggregation of amyloid into the neurotoxic, fibrillar form. The need for a large prospective trial of aspirin as a simple intervention against cognitive decline is compelling.

**Tony Bayer (Department of Geriatric Medicine, University of Wales College of Medicine, Cardiff)**

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**References for further reading on this subject are as follows:-**

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