

# Newsletter



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## **Lower Alzheimer's risk with NSAIDs not due to anti-amyloid action**

NSAIDs are equally effective in reducing the risk of Alzheimer's disease (AD), regardless of their effects on a brain protein linked with the disease, a new study has shown.<sup>1</sup> This is the second recent study to show that the protective effect of NSAIDs is probably unrelated to this effect.<sup>2</sup>

AD is associated with deposition in the brain of a protein, amyloid beta peptide. Some NSAIDs, including ibuprofen, have been shown to inhibit this process and are known as Selective Amyloid-Lowering Agents (SALAs). If this property is clinically meaningful, SALAs may be more effective in reducing the risk of AD than non-SALA alternatives.

The latest study pooled the results of six earlier prospective studies to form a group of 13,499 people who were initially free of dementia. Of these, 820 developed AD over a period of 5 - 15 years. Comparing those who did and did not develop AD, the use of any NSAID was associated with a 23 per cent lower risk of developing AD; ibuprofen accounted for more than half of all NSAID use. When the NSAIDs were divided into SALAs and non-SALAs, the difference between them was not statistically significant. This study also showed that paracetamol was not associated with a lower risk of AD.

These findings are consistent with the earlier study, which retrospectively compared SALAs and non-SALAs prescribed for 49,349 people who

developed AD and 196,850 who did not. Although there were no differences in risk reduction between the two types of NSAID, the use of any NSAID for more than 5 years was associated with a 24 per cent reduced risk of AD. For ibuprofen, the risk was reduced by 44 per cent.

Together with previously published studies, the balance of data now shows there is no difference between SALA and non-SALA NSAIDs in their protective effect against AD. This suggests that the mechanism of action does not involve lowering amyloid beta peptide. Further prospective studies are needed to establish the balance of risks and benefits associated with NSAIDs taken to reduce the risk of AD.

### References

1. Szekely CA, Green RC, Breitner JC et al. No advantage of A $\beta$ <sub>42</sub>-lowering NSAIDs for prevention of Alzheimer dementia in six pooled cohort studies. *Neurology* 2008;70:2291-8
2. Vlad SC, Miller DR, Kowall NW, Felson DT. Protective effects of NSAIDs on the development of Alzheimer's disease. *Neurology* 2008;70:1672-7

## **Topical ibuprofen advisable for knee pain**

Research in UK general practice has shown that older patients with knee pain should normally be advised to use topical rather than oral ibuprofen. But for those who prefer oral treatment or have pain elsewhere, oral administration remains a reasonable option.<sup>1</sup>

Until now, it has not been certain whether oral or topical treatment was better. The study, part of the prestigious NHS research programme, was carried out to clarify how GPs should advise their patients to treat knee pain. The GP could either prescribe treatment or advise the patient to buy the medicine over the counter.

There were two parts. In a randomised controlled trial, 282 people were assigned treatment with oral ibuprofen up to 1200 mg/day or topical ibuprofen at a dose of 1.5 g of gel or cream three times a day. In the second part (a patient preference study), patients chose which form of treatment they wanted - oral or topical.

After one and two years' treatment, there was no difference between oral and topical ibuprofen in reducing pain, stiffness or physical function or overall effects in either part of the study. In the randomised trial, there were slightly more adverse events affecting the respiratory system and kidney function with oral administration but this was not observed in the patient preference study.

One interesting finding was that people who knew little about their knee pain and how their treatment worked were more likely to put up with symptoms. The authors suggest they could therefore be at greater risk of side effects.

Overall, the authors concluded that oral administration of ibuprofen is associated with more minor side effects than topical application, so older people with knee pain should generally be advised to try this first. But the differences between the treatments is not great, so oral administration is reasonable for patients who prefer it - provided they are warned of possible side effects.

#### Reference

1. Underwood M, Ashby D, Carnes D et al. Topical or oral ibuprofen for chronic knee pain in older people. The TOIB study. Health Technology Assessment 2008;12:No. 22

## **Treating acute headache in children**

There is a lack of evidence on which to base the treatment of acute headache in children, according to specialists in the US and Canada, but ibuprofen has a primary role.

Little is known about how best to manage headache in children presenting at a hospital emergency department, say investigators in Washington.<sup>1</sup> Most published studies involve children with migraine and have evaluated the triptans, while none has trialled treatments for tension headache. Most authors endorse an initial trial of ibuprofen for children over 12 years of age followed by intranasal sumatriptan for persistent migraine symptoms. When nausea or vomiting are prominent, antiemetics offer a further option.

Montreal investigators reviewed randomised clinical trials of potential emergency treatments for acute migraine but found only one carried out in a hospital emergency department in children whose pain persisted after initial therapy.<sup>2</sup> This showed that prochlorperazine was more effective than the NSAID at relieving pain after one hour. Other trials have evaluated initial treatments in outpatient settings (representing a patient population with acute but not refractory pain). These studies demonstrated the efficacy of ibuprofen and paracetamol but cast doubt on the value of oral sumatriptan or dihydroergotamine; evidence for other triptans was inconclusive.

#### References

1. Walker DM, Teach SJ. Emergency department treatment of primary headaches in children and adolescents. *Curr Opin Pediatr* 2008;20:248-54

2. Bailey B, McManus BC. Treatment of children with migraine in the emergency department: a qualitative systematic review. *Pediatr Emerg Care* 2008;24:321-30

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