

Newsletter



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NSAIDs and blood pressure

Short-term use of NSAIDs has no significant effect on blood pressure in healthy people, say specialists at London's National Heart and Lung Institute (*J Hypertens* 2006;24:1457-69).

Their analysis of published evidence found that healthy people with normal blood pressure who take an NSAID for up to 2 weeks do not experience a significant increase in blood pressure. People who have hypertension are more likely to have an increase in blood pressure but its magnitude is unpredictable and depends on age, blood pressure, antihypertensive treatment (possibly least impact with ACE inhibitors and some calcium channel blockers) and the type of NSAID. The size of any effect is similar with NSAIDs and paracetamol and slightly smaller with low-dose aspirin.

The new analysis confirms the finding of a 1993 meta-analysis that NSAIDs have markedly different effects on blood pressure (*Arch Intern Med* 1993;153:477-84). That review concluded that the average effects of short-term use of ibuprofen were negligible.

The Story of Ibuprofen

A new PowerPoint presentation telling the story of ibuprofen is now available

as a free download from the IIF website at www.ibuprofen-foundation.com. The presentation includes 54 slides detailing the development of ibuprofen and its clinical uses, and illustrations of ibuprofen products and manufacturing facilities.

'No significant risk of serious cardiac events' with ibuprofen

A new study has concluded that ibuprofen is not associated with an increased risk of serious cardiac events (*eular2006SCIE-abstract*).

The findings come from a nested case control study of the Kaiser Health Plan in California, previously used to determine the risks of COX-2 selective NSAIDs (see *Lancet* 2005;365:475-81). Comparison of NSAID use by 8,143 patients with acute myocardial infarction or sudden cardiac death with that in over 32,000 matched controls showed that ibuprofen was not associated with a statistically significant increased risk (odds ratio, OR, 1.078; CI_{95%} 0.973- 1.195). There were similar findings for diclofenac, piroxicam, etodolac, sulindac and nabumetone. However, both naproxen (OR 1.143, CI_{95%} 1.002 - 1.303) and indomethacin (OR 1.270, CI_{95%} 1.037 - 1.556) were associated with slightly increased risks. The risk with

indomethacin approaches that associated with rofecoxib, the authors note.

Dose-response for ibuprofen analgesia

It's official: higher doses of OTC analgesics are significantly more effective than lower doses, according to a systematic review of randomised controlled trials by Oxford pain specialists (*Br J Clin Pharmacol* 2006;July 21: Epub ahead of print).

Their analysis of data pooled from fifty trials showed that 400 mg of ibuprofen provides superior analgesia to 200 mg. The number of people who would need to be treated with the higher dose for one person to obtain additional benefit (the number needed to treat, or NNT) was 10. Similar differences were found for aspirin (1000/1200 mg superior to 500/600 mg; NNT 16) and paracetamol (1000 mg superior to 500 mg; NNT 9).

Concerns about alternating antipyretics in febrile children

In February, Israeli investigators published a trial showing that a 4-hourly alternating regimen of ibuprofen and paracetamol was superior to either agent alone in reducing fever in infants and children (*Arch Pediatr Adolesc Med* 2006;160:197-202). Now, concerns have been raised about the safety and evidence base underlying this strategy.

An editorial in the *British Medical Journal* (2006;333:4-5) reviewed several studies of the alternating regimen. The authors found that the participants were probably more ill than children at home, that fever was measured inconsistently, and that the findings of the Israeli study were

compromised by methodological problems. There is insufficient evidence to support an alternating regimen, they concluded, and a lack of data on its safety.

Correspondents to the *Archives of Pediatric and Adolescent Medicine* (2006;160:757) raise additional concerns about safety and add that parents could be confused by the relatively complex dose instruction. There is also a risk that parents anxieties about controlling fever would be fuelled, resulting in unnecessary hospital visits.

IV ibuprofen for preterm newborns

A systematic review of trials of intravenous ibuprofen and indomethacin for patent ductus arteriosus (PDA) in premature infants has concluded that both have a role (*Semin Perinatol* 2006;30:114-20).

The two drugs were similarly effective in a direct comparative trial but indomethacin was associated with abnormal renal function and decreased mesenteric and cerebral blood flow. However, ibuprofen did not reduce the risk of intraventricular haemorrhage. This led the authors to suggest that indomethacin may be preferred on the first day of life, when there is a risk of intraventricular haemorrhage; thereafter, ibuprofen is probably the drug of choice for PDA closure due to its better adverse event profile.

Ibuprofen in a dressing for ulcer pain

A new wound dressing containing ibuprofen could reduce pain and improve quality of life in elderly patients with chronic leg ulcers, say Danish researchers (*Wound repair Regen* 2006;14:233-9).

Biatain-Ibu is a foam wound dressing that releases ibuprofen into the wound and surrounding skin; the dose released from the dressing depends on the amount of exudate absorbed into the dressing.

[http://www.biatain-ibu.coloplast.com/ECompany/BiatainIbu/homepage.nsf/\(VIEWDOCSBYID\)/80267A8038E4FF01C12571310063456B](http://www.biatain-ibu.coloplast.com/ECompany/BiatainIbu/homepage.nsf/(VIEWDOCSBYID)/80267A8038E4FF01C12571310063456B).

Plasma levels of ibuprofen are undetectable during use. In this study, mean pain intensity score was reduced from 7 at baseline to 2.5 with the dressing and quality of life scores were improved.

Ibuprofen as effective as triptan for childhood migraine

A comparison of ibuprofen with zolmitriptan in the treatment of migraine in children has concluded that they relieve pain equally well (*Neurology 2006;67: June 14th, Epub ahead of print*).

In this crossover study, 32 children reporting a mean duration of migraine of 4 years and a mean of 2.6 attacks per month treated their next three attacks with single doses of placebo, ibuprofen 300 or 400 mg (depending on age) and zolmitriptan 2.5 mg. Pain relief at 2 hours was reported by 69% of children with ibuprofen and 62% with zolmitriptan compared with 28% with placebo ($p < 0.01$ for drugs vs. placebo). Significantly more children were pain-free at 2 (ibuprofen 48%, zolmitriptan 45%) and 4 hours (79% and 66% respectively) with either drug than placebo (7% at both times).

Headache recurrence rates were not significantly different but zolmitriptan was associated with less use of rescue medication (7% vs. 28% with placebo and 17% with ibuprofen). Both ibuprofen and zolmitriptan reduced migraine-associated symptoms such

as nausea and photophobia/phonophobia.

Zolmitriptan, but not ibuprofen, was associated with significantly more adverse events than placebo.

Ibuprofen inhibits cancer cells independent of COX inhibition

Epidemiological studies have shown that use of ibuprofen is associated with a lower risk of certain cancers, notably colon and breast cancer. This has been assumed to be due to inhibition of the enzyme cyclo-oxygenase (COX), the same mechanism that underlies its anti-inflammatory effects, but researchers from Germany have suggested this may not be so (*Eur J Pharmacol 2006;540:24-33*).

They compared with activity of the S- and R- enantiomers of ibuprofen in two cultures of human colon cancer cells - one expressing both COX-1 and COX-2, the other expressing only COX-1. Even though S-ibuprofen is a more potent inhibitor of COX-1 and COX-2 than R-ibuprofen, the enantiomers induced programmed cell death (apoptosis) and blocked cell replication in both cell lines to a similar extent. The authors conclude that ibuprofen may inhibit cancer cells by a mechanism other than its main anti-inflammatory actions.

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