

**APRIL 2004**

## **Getting the dose right in cystic fibrosis**

Ibuprofen is used in high doses to reduce airways inflammation in children with cystic fibrosis. Long-term treatment has been shown to slow the rate of deterioration in lung function and is associated with improved nutritional status. However, ibuprofen appears to have a dual effect: at a concentration of 50 – 100 mg/L, it inhibits the activity of pro-inflammatory neutrophils, but at lower concentrations there is some evidence that inflammatory mediators are increased.

It is therefore essential to use the correct dose of ibuprofen but this is complicated by the fact that its pharmacokinetics are profoundly altered in children with cystic fibrosis – bioavailability is lower and volume of distribution and clearance are increased.

A recent study involving 59 children aged 2 – 18 years (*Arch Dis Child* 2003;88:1128-30) identified four factors that contributed to inter-individual variation in blood levels: the dose form (whether ibuprofen was present as a free acid or the lysine salt), dose, body weight and fasting status. Weighing up the evidence, US investigators have concluded that therapeutic drug monitoring of ibuprofen therapy is essential for children with cystic fibrosis (*Clin Pharmacokinet* 2004;43:145-56). This must take into account the contrasting absorption profiles associated with different formulations.

## **Ibuprofen protects lipoproteins against oxidation**

The oxidation of lipoproteins is believed to be one mechanism by which LDL-cholesterol becomes atherogenic. Ibuprofen has long been known to inhibit this process (*Life Sci* 1999;65:2289-303) and now, a Chinese team has used nuclear magnetic resonance spectroscopy to study more closely the interaction between ibuprofen and lipoprotein particles in human plasma (*Anal Biochem* 2004;324:292-7).

They found that ibuprofen interacts with phospholipids in the lipoprotein particle (to be precise, at the  $N^+(\text{CH}_3)_3$  functional group of phosphatidylcholine and sphingomyelin, and on olefinic chains and ethyl and methyl groups of the unsaturated lipid component). Whether this is a direct interaction or due to a structural change in the lipoprotein remains unclear, but the result seems to protect plasma lipids against oxidation and confirms that ibuprofen may have anti-atherosclerotic properties.

## **Ibuprofen gives longer lasting relief in fever**

Ibuprofen gives a longer lasting relief of antipyretic action in children with fever but paracetamol has a slightly faster onset, according to a systematic review from the United States (*Pharmacotherapy* 2004;24:280-4).

The review included 22 trials of ibuprofen or paracetamol in children with fever published between 1966 and 2000. Overall, the drugs were equally well tolerated. Paracetamol produced a greater reduction in body temperature 30 minutes after administration, but ibuprofen was more effective at 4 hours and the initial fall in temperature was more sustained.

A second review of antipyretic efficacy in children, this time of publications published between 1966 and 2003 (*Ann Pharmacother* 2004;38:146-50), has also concluded that ibuprofen is superior. It is significantly more effective at reducing fever than paracetamol 6 hours after a single dose (though not after a longer period). Studies of multiple doses have not reported any difference between the two.

### **Ibuprofen vs. paracetamol for typhoid fever**

Ibuprofen has proved its worth as adjunctive treatment in children with typhoid fever, according to a team of tropical disease specialists in London, Oxford and Vietnam (*Ped Inf Dis J* 2004;23:226-30).

Eighty children with uncomplicated fever were randomised to treatment with ibuprofen syrup 10 mg/kg or paracetamol syrup 12 mg/kg every 6 hours, until 36 hours after their fever had subsided. In children treated with ibuprofen, the median time to fever clearance was substantially and significantly lower than with paracetamol (68 vs. 105 hours), though the range of clearance times was large in both cases (4 – 260 hours with ibuprofen and 12 to 404 hours with paracetamol). There was a similar difference in the area under the temperature-time curve  $>37^{\circ}\text{C}$  (74 vs. 127).

*Salmonella typhi* was isolated from 90 percent of children. The differences between ibuprofen and paracetamol were found to occur largely in 24 children infected with a strain resistant to nalidixic acid, who responded more slowly to antibiotic therapy and had a more prolonged fever. Both antipyretics were well tolerated.

### **IIF re-launches website**

The International Ibuprofen Foundation (IIF) re-launches its website at [www.ibuprofen-foundation.com](http://www.ibuprofen-foundation.com)

The site has been enhanced to make it more visually attractive and consumer-friendly while continuing to retain the high degree of professional content. It has been carefully structured into easily identifiable segments from the Home Page to provide a valuable information resource. The site will appeal to a broad range of visitors, including consumers, healthcare professionals and members of the medical press.

The IIF site will be frequently updated with news releases and newsletters which visitors can receive automatically with simple online registration.

The IIF was founded in January 2002 to mark the 40<sup>th</sup> anniversary of the ibuprofen patent which was the revolutionary result of a team of British scientists. In celebration, the IIF held an international scientific meeting at the Royal College of Physicians in London on 15/16 April 2002. 'Highlights' of the conference and the full Proceedings can be obtained on the IIF website.

Further information from:-

**Secretariat**  
**International Ibuprofen Foundation**  
**PO Box 2566, Marlborough, SN8 4YY, UK**  
**Tel: +44(0)1672 810836**  
**Fax: +44(0)1672 810865**  
**Email: [ibuprofen@healthcom.eu.com](mailto:ibuprofen@healthcom.eu.com)**  
**Website: [www.ibuprofen-foundation.com](http://www.ibuprofen-foundation.com)**