Figure 3 Percentage of children showing a temperature reduction of 1°C or more at three hours by dose of ibuprofen.

ing fever control than 10 mg/kg paracetamol.⁸ However, doses of 15 mg/kg paracetamol are commonly prescribed.

Although 39 children warranted 'rescue' treatment, only five of these children had received an initial 5 mg/kg dose of ibuprofen. The 'rescue' medication was given if the child's axillary temperature remained above 37.2°C three hours after the initial randomised dose and the apparent 'failure' of the 5 mg/kg dose in these five children must be viewed against this very strict temperature criterion and in comparison with other antipyretic measures. The mean baseline axillary temperature was 39°C in the 5 mg/kg ibuprofen group of our study. In an earlier study in which children had a mean baseline oral temperature of 39°C, the mean oral temperature three hours later remained at 38.7°C if only nursing measures were used and was 37.8°C if 10 mg/kg paracetamol had been given.⁸

Finally, the 5 mg/kg ibuprofen dose did not compare unfavourably in our study with the weaker doses in acceptability or in the nature of adverse events.

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Commentary

NEW DRUG FOR OLD?

Fever is universal. We all experience it from time to time and the average child in Britain is given an antipyretic drug on four or five days a year.¹ Since the demise of aspirin for childhood fever in 1986, paracetamol has had the field to itself. Fever in itself is unlikely to be harmful. As a response to infection it almost never rises above 41°C and, provided dehydration is avoided and heat loss is not prevented by overheating or overclothing, fever of that degree is not damaging.² Even in those prone to febrile convulsions, treatment of fever does not seem to prevent attacks.³ The reasons for giving an antipyretic drug are to relieve discomfort and to relieve the anxiety felt particularly by parents (and by medical and nursing attendants). Do we need a new drug for this purpose and what risk are we prepared to take to develop one?

Paracetamol was first used in 1893 and has been in regular use since 1949.⁴ It has so far not been associated with serious toxicity in therapeutic dosage and, despite its ready availability, overdosage has not been a serious problem in children.⁵ It is effective.⁶⁻⁸

What properties should a drug have in order for it to replace paracetamol as an antipyretic for children? Laying aside considerations of presentation and expense, I suggest the following: (i) it should be demonstrably more effective in relieving discomfort and (ii) it should be free of serious toxicity when given to very large numbers (millions) of children. Therein lies the rub. Does a possibly slightly greater temperature reduction with ibuprofen translate into significantly greater comfort for children in practice? There seems to be little evidence on that point. The second of these conditions is, of course, impossible to satisfy without taking the risk and whether the risk is worthwhile depends on the seriousness of the condition to be treated and the effectiveness of present treatment. If aspirin were a certain cure for leukaemia, for instance, its association with Reye's syndrome would be disregarded in that context because the benefit would far exceed the risk. The risk-benefit equation is very different for childhood fever.

So far there is no known serious toxicity for ibuprofen but it has not until very recently been used in very large numbers of children. It has been used in the treatment of juvenile chronic arthritis for 11 years but only recently been used as an antipyretic.⁹ Aspirin was in use for over 80 years before its use in children was discontinued. Drug surveillance is now much improved but to recommend any drug for use in a condition that affects virtually all children several times a year is to suggest an experiment. There are many other non-steroidal anti-inflammatory drugs, the manufacturers of at least one of which have to my knowledge seriously considered promoting its use for childhood fever but have so far not done so, so the

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number of experiments can be expected to proliferate. Such experiments should be driven by need. Do we need them?

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Reply to the commentary by the authors

We are not proponents of any particular drug for children. We are, however, proponents of choice in prescribing for children and this choice should be well informed. The purpose of our study was to determine the minimum effective dose of ibuprofen for childhood fever, and the safety of this drug in this context, rather than to compare it directly with paracetamol, which others have done. Whether ibuprofen should have been granted a product licence as a childhood antipyretic is a decision for the Medicines Control Agency, which enforces the Medicines Act 1968.

The commentary states that paracetamol overdosage has not been a serious problem in children. However, in the reference quoted it is

stated that 'since the withdrawal of paediatric aspirin formulations, the incidence of accidental paracetamol poisoning in children appears to be increasing'.¹ Although hepatotoxicity and death are rare in children under the age of 5 years,² this is probably because children ingest smaller doses and present earlier for treatment than adults. If an entire bottle of paediatric ibuprofen suspension were ingested by a child aged 1 to 2 years, serious toxicity would be unlikely.¹

The consideration that an antipyretic drug should relieve discomfort is an important one. Analgesia for children has perhaps not always been given the attention that it deserves. Ibuprofen has been used as an analgesic and anti-inflammatory drug in childhood arthritis for some time³ and at much larger doses than in our study. Although fever may be seen by doctors as a trivial and common feature of childhood illness, the discomfort which accompanies febrile illnesses is very real to that child. It has been estimated that over 240 million doses of ibuprofen have been given to children. To try to improve the relief of pain is not to experiment, provided we adhere to the principle of *primum non nocere*. It is surely better that drugs used for children are subjected to the same scrutiny as those introduced for adults, rather than these drugs being absorbed into the paediatric formulary on an *ad hoc* basis, as has been the case with many other childhood treatments over the last decades. Perhaps if aspirin had been subjected to the same scrutiny, and the same surveillance after it was marketed,⁴ the association with Reye's syndrome would have been detected before 80 years had elapsed?

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