Review of the analgesic efficacy of ibuprofen

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SUMMARY There is a clear relationship between single doses of ibuprofen over the range 50–400 mg and the peak analgesic effect and the duration of analgesia. The smallest clinically useful dose of ibuprofen is 200 mg. Ibuprofen 400 mg has been shown to be as effective as aspirin 600 or 900 mg/day in models of moderate pain but superior to aspirin or paracetamol in more sensitive models such as dental pain. The duration of action of ibuprofen 400 mg is at least 6 hours compared with 4–6 hours for ibuprofen 200 mg or paracetamol. In patients undergoing oral surgery, ibuprofen 200 mg was broadly comparable with naproxen 220 mg and ibuprofen 400 mg comparable with ketoprofen 25 mg. The combination of ibuprofen and hydrocodone is more effective than either drug alone in patients undergoing abdominal and gynaecological surgery. The absorption of ibuprofen acid is influenced by formulation, and certain salts of ibuprofen (lysine, arginine, potassium) and solubilised formulations have an enhanced onset of activity. These differences are clinically important, offering a shorter time to onset of relief of tension headache compared with paracetamol.

The analgesic efficacy of ibuprofen has been evaluated in several clinical models of acute pain. These have described the characteristics of its dose–response curve and, in particular, the minimal effective dose and the ceiling or plateau of its analgesic activity. Comparative studies with aspirin and paracetamol have evaluated the peak and total analgesic effects, the duration of analgesia and the speed of onset of clinically meaningful analgesia. Other studies have compared ibuprofen with other non-steroidal anti-inflammatory drugs (NSAIDs) and opioids, and evaluated the efficacy of special formulations of ibuprofen.

Models of pain
For many years, no non-opioid analgesic was shown to be more effective than aspirin 650–1000 mg or paracetamol 1000 mg and the peak analgesic effect could only be increased by the addition of an opioid such as codeine. Early studies suggested that ibuprofen was no different. However, these studies utilised pain models, such as mild to moderate pain associated with episiotomy, that were relatively insensitive. The advent of the oral surgery impaction model, which is associated with moderate to severe pain, proved much more discriminating.

Characteristics of analgesia with ibuprofen
There is a clear relationship between single doses of ibuprofen over the range 50–400 mg and the peak analgesic effect and the duration of analgesia in the oral surgery model (Figure 1).1 In this study, maximum analgesia occurred 2–3 hours after each dose (except for 50 mg) and effective analgesia was sustained for at least 6 hours (the end of the monitored period). Higher single doses were not associated with significantly greater analgesia in this model.2 Ibuprofen 400 mg has also been shown to be superior to a 200 mg dose in patients with migraine headache.3

Comparisons with aspirin and paracetamol
In patients with moderate pain associated with episiotomy, there was little difference in efficacy between single doses of aspirin 900 mg and ibuprofen 300 mg or 900 mg though all were superior to placebo.4
However, in the same model but in patients with severe pain, ibuprofen 400 mg was significantly superior to aspirin 600 mg. This difference is borne out in patients undergoing oral surgery, in whom aspirin 325 mg and 650 mg were less effective than ibuprofen 200 mg and 400 mg (Figure 2). Ibuprofen 200 mg and aspirin 650 mg were broadly comparable in analgesic effect, though peak analgesia occurred earlier with aspirin (2 versus 3 hours).

In comparisons with paracetamol in the oral surgery model, ibuprofen 200 mg was equivalent to paracetamol 1000 mg but ibuprofen 400 mg was significantly more effective (Figure 3). The duration of action of ibuprofen 400 mg was at least 6 hours compared with 4–6 hours for ibuprofen 200 mg or paracetamol. These studies further indicate that the smallest clinically useful dose of ibuprofen is 200 mg.

Comparative studies have demonstrated that ibuprofen 400 mg is superior to paracetamol 1000 mg in relieving other types of pain, including tension headache and sore throat. In patients with sports soft tissue injuries, ibuprofen 1200 mg/day more rapidly reduced pain than aspirin 3 g/day.
Comparisons with NSAIDs and other analgesics

In patients undergoing oral surgery, ibuprofen 200 mg was broadly comparable with naproxen 220 mg, though the latter was longer acting;\textsuperscript{12} and ibuprofen 400 mg was comparable with ketoprofen 25 mg (but less effective than ketoprofen 100 mg, an unlicensed dose).\textsuperscript{13}

The value of combining two analgesics with complementary mechanisms of action is demonstrated by a comparison of ibuprofen and hydrocodone, given separately and in combination, in patients undergoing abdominal and gynaecological surgery. Hydrocodone 15 mg was little better than placebo whereas ibuprofen 400 mg was substantially more effective; however, the combination of the two drugs was more effective than either alone in both peak analgesic effect and duration of action.\textsuperscript{14} For this reason, the combination of aspirin 650 mg with codeine in doses of 30–60 mg is a popular choice with prescribers. The peak analgesic effect of the combination is greater than either of the component drugs; however, ibuprofen 400 mg is at least as effective as the combination (Figure 4) and probably

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**Figure 3. Comparative analgesic efficacy of ibuprofen 400 mg and paracetamol 1000 mg in the oral surgery model.\textsuperscript{8} Reproduced with permission from Sage Publications, Inc (J Clin Pharmacol 1989; 29: 1026–1030)**

**Figure 4. Comparison of ibuprofen and aspirin-opioid combinations in the oral surgery model. (Partial data from reference 15. Reproduced with permission from Pharmacotherapy)**
Effects of formulation on the analgesic activity of ibuprofen

The absorption of ibuprofen acid is influenced by formulation, and certain salts of ibuprofen (lysine, arginine, potassium), and solubilised formulations have an enhanced onset of activity. In the oral surgery model, for example, ibuprofen lysine 400 mg produces faster onset and higher peak analgesia than a conventional tablet of ibuprofen acid 400 mg. In the same model, solubilised ibuprofen 400 mg had more rapid onset than paracetamol 1000 mg and had a longer duration of action than either paracetamol 1000 mg or ketoprofen 25 mg. These differences are clinically important: in patients with tension headache, the median time to clinically meaningful relief of pain was shorter after solubilised ibuprofen 400 mg than after paracetamol 1000 mg (Figure 5).

Summary

After more than a quarter of a century of patient use, ibuprofen has withstood the test of time and has become the standard reference in controlled clinical trials of newer NSAID analgesics. Ibuprofen 400 mg is clearly more effective and longer acting than aspirin or paracetamol, and special formulations provide a more rapid onset of analgesia. Ibuprofen 400 mg compares favourably with opioid combination products, and no other NSAID, at approved analgesic doses, is more effective or faster acting.

References

8. Cooper SA, Schachtel BP, Goldman E et al. Ibuprofen and acetaminophen in the relief of...


