

# Relative efficacy of oral analgesics after third molar extraction – a 2011 update

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## IN BRIEF

- Summarises the known evidence on efficacy of oral analgesics in dental pain.
- Describes shorter term pain relief and time needed before remedication.
- Provides an evidential context for making decisions about individual patients, or practice guidelines.

This article provides a summary of the efficacy, and relative efficacy, of 38 different drugs or drug combinations tested in standard postoperative pain trials. It will help clinicians and patients make informed choices about analgesia based on pain relief, duration of action, and adverse events, which can then be put into context for the individual patient, depending on local availability. This article highlights the fact that no single drug is effective in all patients – even the best drugs fail to provide good levels of pain relief in at least 30%. These patients should try a different analgesic.

In 2004 the *British Dental Journal* carried a review examining analgesic efficacy measured after third molar extractions,<sup>1</sup> predominantly derived from Cochrane reviews of single dose analgesics in established moderate or severe pain. In the intervening years the reviews on which it was based have been extended to other analgesics, and updated to include relevant additional clinical trials performed in the past decade.

The culmination of this work has been the publication by the Cochrane Collaboration of an overview of these updated systematic reviews.<sup>2</sup> The overview included 35 separate Cochrane Reviews with 38 analyses of single dose oral analgesics tested in acute postoperative pain models, with results from about 45,000 participants studied in approximately 350 individual studies. About 29,000 patients contributed data to trials in dental pain.

Each individual review reported results for dental studies where data were available, overwhelmingly in the third molar extraction pain model. Because all of the reviews used identical methods, outcomes,

**Table 1 Efficacy results in dental pain studies for a range of commonly used analgesics**

Drug and dose (mg)	Number of:		Percent with at least 50% maximum pain relief		NNT	Median time to remedication (hr)
	Trials	Patients	Active	Placebo		
Aspirin 600/650 mg	45	3581	36	14	4.5 (4.0 to 5.2)	3.0
Aspirin 1,000 mg	4	436	35	11	4.2 (3.2 to 6.0)	no data
Celecoxib 400 mg	4	620	34	3	2.5 (2.2 to 2.9)	8.4
Diclofenac 50 mg (Na and K)	9	1119	56	19	2.7 (2.4 to 3.1)	4.3
Diclofenac 50 mg K	5	622	65	16	2.1 (1.9 to 2.4)	no data
Etoricoxib 120 mg	4	500	71	9	1.6 (1.5 to 1.8)	>24
Ibuprofen 400 mg	49	5428	55	12	2.3 (2.2 to 2.4)	5.6
Ibuprofen 400 mg soluble	9	959	66	10	1.8 (1.7 to 2.0)	no data
Ibuprofen 200 mg + paracetamol 500 mg	2	280	74	10	1.6 (1.4 to 1.8)	>8
Naproxen 500/550 mg	5	402	61	7	1.8 (1.6 to 2.1)	8.9
Paracetamol 1,000 mg	19	2157	41	10	3.2 (2.9 to 3.6)	3.9

Note that data for remedication time were not generally available for dental studies separately, and the values reported apply to all postoperative conditions, though predominantly third molar extraction

and reporting, and were all of high methodological quality, the relative efficacy of different analgesics is justifiable when established against the common comparator of placebo.<sup>3</sup> Moreover, the methods have been extensively examined and validated using individual patient data analyses.<sup>4,5</sup>

Several approaches can be used to present results. The percentage of patients who benefit with treatment is one approach; obviously the higher the number

the better. Another way is to look at the number needed to treat (NNT) for one patient to benefit; this is the *treatment-specific* effect, and can be expressed as  $100\% / (\text{active}\% - \text{placebo}\%)$ . The ideal NNT is 1, where everyone gets better with treatment and no one does with placebo; lower numbers are better. In dental trials where about 10% of patients benefit with placebo, the best possible NNT is  $100\% / (100\% - 10\%) = 1.1$ .

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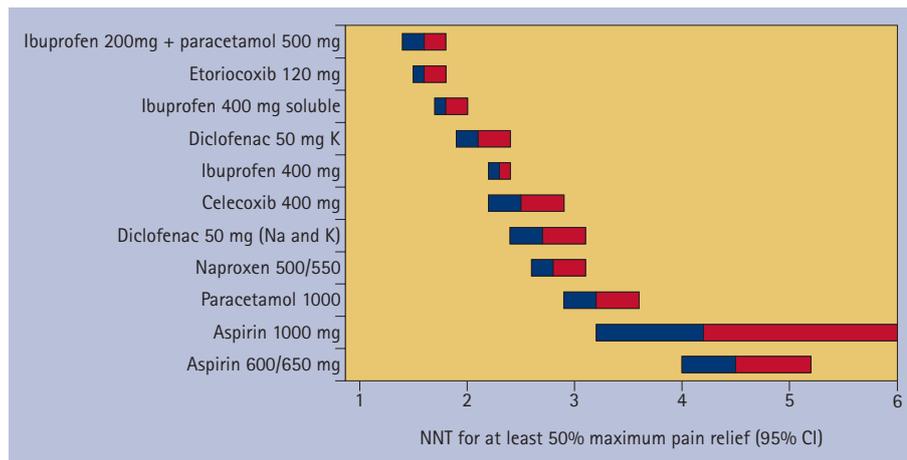


Fig. 1 NNTs in dental pain studies for a range of commonly used analgesics

This brief report describes the main results of interest to dentists, using results from the Cochrane overview and from a recent analysis of a combination of ibuprofen and paracetamol.<sup>5</sup>

## RESULTS

Table 1 reports data for aspirin, celecoxib, diclofenac, etoricoxib, ibuprofen, ibuprofen plus paracetamol, naproxen, and paracetamol. Widely differing amounts of information were available for individual drugs, from as few as 402 patients for naproxen 500/550 mg, and as many as 5,428 for ibuprofen 400 mg.

One outcome reported is the percentage of patients with initially moderate pain (30–60 mm on a 100 mm VAS) or severe pain (more than 60 mm) who obtained at least 50% of the maximum possible pain relief over a 4–6 hour period after taking the tablets. This is a high test of efficacy, achieved by only about 10% of patients who received no active treatment (placebo), but achieved by 34–74% of those who did get the active drug. Ibuprofen 200 mg plus paracetamol 500 mg, and etoricoxib 120 mg, achieved

response rates above 70%; paracetamol 1,000 mg achieved only a 41% response rate.

Several products had an NNT of about 2 or below: the combination of ibuprofen 200 mg plus paracetamol 500 mg, etoricoxib 120 mg, ibuprofen 400 mg in a soluble form, naproxen 500/550 mg, and 50 mg of the potassium salt of diclofenac (the sodium salt being much less effective in this assay; Fig. 1).

A new outcome that some will consider relevant is the time required for half the patients to need more analgesia, the time to remedication. Longer duration is another indicator of greater effect, and for a number of analgesics median remedication times are beyond eight hours.

## DISCUSSION

The 2004 review included evidence for rofecoxib and valdecoxib, neither of which is available today. New relevant information includes data on the ibuprofen plus paracetamol combination, different ibuprofen and diclofenac formulations, and etoricoxib, all of which are among the most efficacious analgesics after third

molar surgery. Greater efficacy and longer duration of action tended to go together.

For one analgesic relevant to dentistry, the evidence is largely silent. For dihydrocodeine 30 mg (still commonly used by dentists) only 136 patients were found in trials in dental pain, with only 24% obtaining at least 50% maximum pain relief, compared with 7% with placebo. The resultant NNT was 6, far worse than available for drugs in Table 1, and far worse than ibuprofen 400 mg in the only direct comparison.<sup>6</sup> The Cochrane overview concluded that the results for dihydrocodeine were not robust because of the smallness of the data set available, and that unpublished results from just 46 patients in zero effect trials would be needed to make any result clinically irrelevant.

## CONCLUSION

The amount of evidence available on single dose studies of analgesics in dental pain is large and readily available. These results are tools to help formulate policy and prescribing for individuals and populations.

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