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Ibuprofen and/or paracetamol (acetaminophen) for pain relief after surgical removal of lower wisdom teeth (Review) Copyright © 2013 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd. WILEY

## [Intervention Review]

# Ibuprofen and/or paracetamol (acetaminophen) for pain relief after surgical removal of lower wisdom teeth

Edmund Bailey<sup>1</sup>, Helen V Worthington<sup>2</sup>, Arjen van Wijk<sup>3</sup>, Julian M Yates<sup>1</sup>, Paul Coulthard<sup>1</sup>, Zahid Afzal<sup>4</sup>

<sup>1</sup>Department of Oral and Maxillofacial Surgery, School of Dentistry, The University of Manchester, Manchester, UK. <sup>2</sup>Cochrane Oral Health Group, School of Dentistry, The University of Manchester, Manchester, UK. <sup>3</sup>Social Dentistry and Behavioural Sciences, Academic Centre for Dentistry Amsterdam (ACTA), Amsterdam, Netherlands. <sup>4</sup>Oral and Maxillofacial Surgery, City Hospital, Birmingham, UK

**Contact address:** Edmund Bailey, Department of Oral and Maxillofacial Surgery, School of Dentistry, The University of Manchester, Coupland III Building, Oxford Road, Manchester, M13 9PL, UK. edmund.bailey@manchester.ac.uk.

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## ABSTRACT

## Background

Both paracetamol and ibuprofen are commonly used analgesics for the relief of pain following the surgical removal of lower wisdom teeth (third molars). In 2010, a novel analgesic (marketed as Nuromol) containing both paracetamol and ibuprofen in the same tablet was launched in the United Kingdom, this drug has shown promising results to date and we have chosen to also compare the combined drug with the single drugs using this model. In this review we investigated the optimal doses of both paracetamol and ibuprofen via comparison of both and via comparison with the novel combined drug. We have taken into account the side effect profile of the study drugs. This review will help oral surgeons to decide on which analgesic to prescribe following wisdom tooth removal.

## Objectives

To compare the beneficial and harmful effects of paracetamol, ibuprofen and the novel combination of both in a single tablet for pain relief following the surgical removal of lower wisdom teeth, at different doses and administered postoperatively.

## Search methods

We searched the Cochrane Oral Health Group'sTrials Register (to 20 May 2013); the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2013, Issue 4); MEDLINE via OVID (1946 to 20 May 2013); EMBASE via OVID (1980 to 20 May 2013) and the *meta*Register of Controlled Trials (to 20 May 2013). We checked the bibliographies of relevant clinical trials and review articles for further studies. We wrote to authors of the identified randomised controlled trials (RCTs), and searched personal references in an attempt to identify unpublished or ongoing RCTs. No language restriction was applied to the searches of the electronic databases.

#### **Selection criteria**

Only randomised controlled double-blinded clinical trials were included. Cross-over studies were included provided there was a wash out period of at least 14 days. There had to be a direct comparison in the trial of two or more of the trial drugs at any dosage. All trials used the third molar pain model.

#### Data collection and analysis

All trials identified were scanned independently and in duplicate by two review authors, any disagreements were resolved by discussion, or if necessary a third review author was consulted. The proportion of patients with at least 50% pain relief (based on total pain relief (TOTPAR) and summed pain intensity difference (SPID) data) was calculated for all three drugs at both two and six hours postdosing and

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meta-analysed for comparison. The proportion of participants using rescue medication over both six and eight hours was also collated and compared. The number of patients experiencing adverse events or the total number of adverse events reported or both were analysed for comparison.

## **Main results**

Seven studies were included, they were all parallel-group studies, two studies were assessed as at low risk of bias and three at high risk of bias; two were considered to have unclear bias in their methodology. A total of 2241 participants were enrolled in these trials.

Ibuprofen was found to be a superior analgesic to paracetamol at several doses with high quality evidence suggesting that ibuprofen 400 mg is superior to 1000 mg paracetamol based on pain relief (estimated from TOTPAR data) and the use of rescue medication meta-analyses. The risk ratio for at least 50% pain relief (based on TOTPAR) at six hours was 1.47 (95% confidence interval (CI) 1.28 to 1.69; five trials) favouring 400 mg ibuprofen over 1000 mg paracetamol, and the risk ratio for not using rescue medication (also favouring ibuprofen) was 1.50 (95% CI 1.25 to 1.79; four trials).

The combined drug showed promising results, with a risk ratio for at least 50% of the maximum pain relief over six hours of 1.77 (95% CI 1.32 to 2.39) (paracetamol 1000 mg and ibuprofen 400 mg) (one trial; moderate quality evidence), and risk ratio not using rescue medication 1.60 (95% CI 1.36 to 1.88) (two trials; moderate quality evidence).

The information available regarding adverse events from the studies (including nausea, vomiting, headaches and dizziness) indicated that they were comparable between the treatment groups. However, we could not formally analyse the data as it was not possible to work out how many adverse events there were in total.

## **Authors' conclusions**

There is high quality evidence that ibuprofen is superior to paracetamol at doses of 200 mg to 512 mg and 600 mg to 1000 mg respectively based on pain relief and use of rescue medication data collected at six hours postoperatively. The majority of this evidence (five out of six trials) compared ibuprofen 400 mg with paracetamol 1000 mg, these are the most frequently prescribed doses in clinical practice. The novel combination drug is showing encouraging results based on the outcomes from two trials when compared to the single drugs.

# PLAIN LANGUAGE SUMMARY

## Ibuprofen versus paracetamol (acetaminophen) for pain relief after surgical removal of lower wisdom teeth

#### **Review question**

This review, carried out by the Cochrane Oral Health Group, seeks to compare the effectiveness of two commonly used painkillers, paracetamol and ibuprofen and the combination of both in a single tablet in the relief of pain following surgical removal of lower wisdom teeth.

## Background

Worldwide the number of surgical operations to remove wisdom teeth is immense, in England alone approximately 63,000 are removed in National Health Service (NHS) hospitals each year. Many patients need time off work and their quality of life is significantly affected. However, despite these consequences, people are often most concerned about pain following the operation which can be severe. It is suggested that the most intense pain is felt three to five hours after surgery. The pain experienced after oral surgery is widely used as a model to measure the effectiveness of painkillers in general.

Both paracetamol and ibuprofen are commonly used for the relief of pain following the surgical removal of lower wisdom teeth. In 2010, a new painkiller (marketed as Nuromol) containing paracetamol and ibuprofen in the same tablet was licensed for use in the United Kingdom.

All the drugs studied in this review had minimal side effects noted when used correctly for short-term pain relief.

## Study characteristics

The evidence on which this review is based was current as of 20 May 2013. Seven studies with a total of 2241 participants all involving a direct comparison of ibuprofen to paracetamol or the combination of both were included in this review. All participants had surgery to remove a lower wisdom tooth or teeth that required bone removal or at least caused moderate to severe pain. Painkillers were taken after surgery and different doses of the drugs were compared.

The majority of the studies took place in the USA with one in Puerto Rico. Four of the trials took place in clinical research facilities, two in university dental hospitals and one in a private oral surgery clinic. The age of participants differed slightly between studies but was broadly similar, ranging from 15 to 65 years old. All studies included male and female participants.

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All the studies included in this review looked only at pain relief and intensity information after a single dose of the painkiller after surgery. It is known that pain does continue after this and the drugs evaluated in this review are normally taken every six to eight hours (maximum of four times per day).

## **Key results**

Ibuprofen is more effective than paracetamol at all doses studied in this review. On limited evidence, the combination of ibuprofen and paracetamol appeared to be no more effective than the single drugs when measured two hours after surgery. However, again on limited evidence, it was found to be more effective than the drugs taken singly when measured at six hours after surgery. Participants taking the combined drug also had a smaller chance of requiring rescue medication.

The information available regarding adverse events from the studies (including nausea, vomiting, headaches and dizziness) indicated that they were comparable between the treatment groups. However, review authors could not formally analyse the data as it was not possible to work out how many adverse events there were in total.

## **Quality of the evidence**

All of the results (outcomes) comparing ibuprofen to paracetamol are of high quality. This means that further research is very unlikely to change our confidence in the estimates of the effect.

When comparing combined versus single drugs, the body of evidence for the proportion of patients with > 50% maximum pain relief (TOTPAR) over two and six hours, was assessed as of moderate quality due to imprecise estimates based on single studies. This means that further research is likely to have an important impact on our confidence in the estimate of the effect. The body of evidence for the use of rescue medication was assessed as being of high quality.