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The effect of Ibuprofen (Brufen®) following the removal of impacted third molar teeth

Garwood, A.J., Lownie, J.F., Cleaton-Jones, P.E. and Butz, S.J.

Division of Maxillo-facial and Oral Surgery, University of the Witwatersrand, and MRC/University of the Witwatersrand Dental Research Institute, Johannesburg

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SUMMARY

Pain, swelling and trismus are common features after the surgical removal of impacted third molar teeth. The purpose of this study was to compare the efficacy and side effects of ibuprofen (Brufen®), a non-steroidal anti-inflammatory agent, with that of a control analgesic in a double blind clinical trial following the removal of impacted third molar teeth. The operative procedure was carried out on 100 patients by one surgeon using a standardised surgical technique while the survey was carried out by an independent observer. The results showed that ibuprofen compared favourably with the control analgesic, both of which produced acceptable analgesia, although ibuprofen appeared superior in the postoperative ambulatory phase in that dizziness and drowsiness were significantly less with the drug than with the control analgesic.

OPSOMMING

Pyn, swelsel en trismus kom dikwels voor ná die chirurgiese verwydering van geïmpakteerde derde molare. Die doel van hierdie ondersoek was om die doeltreffendheid en newe-effekte van ibuprofen (Brufen®), 'n nie-steroïed anti-inflammatoriese middel, te vergelyk met dié van 'n kontrole-pyndoder, in 'n dubbel-blinde toets na die chirurgiese verwydering van bogenoemde tande. Die operatiewe prosedure is op 100 pasiente deur een chirurg onderneem, 'n gestandaardiseerde chirurgiese tegniek is gebruik en die ondersoek is deur 'n onafhanklike waarnemer gedoen. Die resultate het getoon dat ibuprofen goed vergelyk met die kontrole pyndoder. Albei het aanvaarbare analgesie veroorsaak, alhoewel ibuprofen skyn beter te wees in die naoperatiewe lopende fase. Duiseligheid en lomerigheid het betekenisvol minder voorgekom by gebruik van die middel as wat die geval was by die kontrole middel.

INTRODUCTION

Oral surgery, and particularly the surgical removal of impacted third molar teeth, is generally accompanied by pain and discomfort as a result of postoperative swelling and trismus. For these symptoms, the maxillofacial and oral surgeon frequently prescribes an analgesic or analgesic combination (Forbes et al, 1981).

In recent times, the non-steroidal anti-inflammatory agents have received much attention as short-term analgesics after surgery. The majority of these drugs have anti-inflammatory analgesic and antipyretic properties and many have been considered particularly good in reducing pain in the postoperative phase, probably by reducing inflammation and by inhibiting the chemicals of the inflammatory process, mainly prostaglandins. It is also postulated that by reducing the inflammatory process, improved tissue viability can be maintained in inflamed tissues (Laurence, 1978).

The analgesic effect of indomethacin following third molar tooth removal has been studied by Petersen (1975), while Breytenbach (1978) compared the effect of oxyphenbutazone, chymoral and an unspecified placebo. In all cases the anti-inflammatory agents significantly improved pain, and Breytenbach noted superior intermaxillary opening. With regard to ibuprofen, Lokken *et al* (1975) studied the efficacy of the drug in 24 healthy patients who had two separate operations for the removal an impacted third molar tooth from either left or right side of the lower jaw. These patients were given ibuprofen (400 mg three times daily) or an unspecified placebo for 5 days, commencing the day prior to surgery, the order of the drugs being reversed at the second operation, carried out approximately 26 days later. These authors noted that the ibuprofen significantly reduced pain on the day of operation, and also reduced trismus. The patients expressed their preference for ibuprofen in the postoperative phase, and swelling was also somewhat reduced postoperatively, although not immediately after surgery.

The drug was well tolerated and subjective assessments indicated that neither wound healing nor bleeding during or after the operation was affected by the drug.

Cooper, Needle and Kruger (1977) attempted to evaluate the efficacy of ibuprofen for the relief of dental pain. They compared the efficacy of aspirin, ibuprofen and placebo after the removal of third molar teeth. A minimum of 37 patients in each of five treatment groups were assessed for pain relief after the surgical removal of impacted third molar teeth under local

anaesthesia. Usually a mandibular tooth, or the mandibular and maxillary teeth on one side were removed at one visit. The results of this study showed that ibuprofen 400 mg was the most effective drug, followed by ibuprofen 200 mg, aspirin 325 mg and lastly the unspecified placebo. There was no significant difference in the side effects of these drugs.

Dionne and Cooper (1978) undertook a study to assess whether ibuprofen administered preoperatively would have any effect on postoperative pain and swelling. Seventy-three patients were used in their analysis of postoperative pain following removal of impacted third molar teeth. Ibuprofen 400 mg, aspirin 650 mg and an unspecified placebo were the drugs used in this study and one of the drugs was given to a specific patient 30 minutes preoperatively. The patients were then given the same drug postoperatively when the pain became moderate to severe. It was noted that patients who received Ibuprofen preoperatively had a significantly delayed onset and decreased severity of postoperative pain. The incidence of side effects was negligible. In all the reported studies, the efficacy of ibuprofen following oral surgery has been compared to aspirin, a drug not commonly used for the above procedures. Trials relating the efficacy of ibuprofen to a more potent and commonly used analgesic combination, for example, Syndol, a combination of paracetamol, codeine phosphate and doxylamine succinate, have not been undertaken.

The aims of the present study were:

1. to undertake a double blind clinical trial to assess the analgesic effects of ibuprofen compared with a standard analgesic compound; and
2. to note any adverse effects resulting from the use of the drug.

MATERIALS AND METHODS

The sample comprised 100 patients who were to undergo surgery for the removal of impacted third molar teeth in a Johannesburg maxillofacial and oral surgery practice. The methods and reasons for the clinical trial were explained to them and informed consent was obtained in all cases.

This survey took the form of a double blind clinical trial using Syndol®* as control. This analgesic was chosen as it has been found to provide complete or satisfactory analgesic response in 80 per cent or more of patients who had undergone surgical removal of impacted third molar teeth (Reitzik and Lownie, 1976). Both the ibuprofen and the Syndol were packed in unlabelled plastic containers marked only with the batch number (1 or 2) and the instructions to the patient on how the drug should be taken.

Pregnant patients, or patients with a previous history of gastrointestinal tract ulceration were excluded from the survey. No distinction was made with regard to the sex of the patient. All the patients selected for this study were to have a minimum of two wisdom teeth removed, these being either mesioangular, distoangular or horizontal impactions, requiring raising a mucoperiosteal flap and removing sufficient bone to expose the amelocemental junction of the impacted tooth. Patients requiring forceps extraction of wisdom teeth without bone removal were not included in the series.

All procedures were carried out under general anaesthesia with naso endotracheal intubation following premedication with atropine, 0,6 mg and Omnopon® (papaveretum) 10 mg by intramuscular injection.

A standardized surgical technique was used by one surgeon who performed all the operations. To minimize bias in the study this was not the same person responsible for the survey.

Immediately on return to the ward, that is, about 20 minutes after completion of the operation, all patients were given 10 mg of Omnopon (papaveretum) by intramuscular injection. Any patients complaining of nausea were given 50 mg of Valoid® (cyclizine hydrochloride), also by intramuscular injection. All patients were placed on routine antibiotics postoperatively. In all cases the ibuprofen and Syndol were only administered to the patient on discharge approximately 12 h postoperatively.

The ibuprofen and the control analgesic were then given to each patient taking part in the trial. The patients were instructed to take the tablets according to the instructions. The dosage of ibuprofen was 400 mg (1 tablet) 8 hourly and the dosage of Syndol, 2 tablets 8 hourly. The name of the analgesic compound was not stated on the containers.

At the same time, on discharge, the patients were given a questionnaire and were asked to note their observations on the specific analgesic they were taking. At the end of the survey 52 patients had filled in a questionnaire regarding ibuprofen and 48 patients had completed a similar form for Syndol. The answers on the questionnaires were then transferred to punch cards for analysis.

The data were analyzed using an IBM 370/148 computer and the Statistical Package for the Social Sciences (Nie *et al*, 1975). The statistical test used as the Chi-square test without Yates' correction and the critical level of statistical significance chosen was $p < 0,05$.

RESULTS

The age of the patients in this study ranged from 15 to 69 years and comprised 64 females and 36 males. Twenty-seven patients had four widom teeth removed, 8 patients had three wisdom teeth removed and 3 patients had two wisdom teeth removed.

Nine patients (17,3 per cent) taking ibuprofen had to take more tablets than prescribed. Of the other 43 patients (82,7 per cent) using ibuprofen, the drug was taken as prescribed or less than prescribed. All the patients to whom Syndol was given took either the prescribed or less than the prescribed dose. The time of onset of pain is shown in Table I. Both groups of patients had very similar times of onset of analgesia except 4 patients (7,7 per cent) in the ibuprofen group who did not experience analgesia at all. Ninety-seven

*Mer National, Johannesburg

Table I: Frequency distribution of time of onset of analgesia by type of analgesic given.

Onset time after taking analgesic compound (in minutes)	Syndol n	Syndol %	Ibuprofen n	Ibuprofen %
0-15	25	52,1	22	42,4
15-30	20	41,7	21	40,4
More than 30	3	6,3	5	9,6
No analgesia	0	0,0	4	7,7
Total	48	100,1	52	100

Chi square = 4,56 d.o.f. = 3 p = 0,21

per cent of patients taking Syndol and 82,7 per cent of the patients taking ibuprofen experienced adequate analgesia within 30 min of taking the drug.

The proportion of pain relief related to the type of analgesic taken is shown in Table II. It is interesting to note that patients to whom Syndol had been given were grouped mainly in the 2 — 4 h period whereas the patients taking ibuprofen tended to be more spread out in the 4 h period of analgesia. Fifteen per cent of patients taking ibuprofen still had adequate analgesia after 4 h, whereas only 6,3 per cent of patients on Syndol had similar results. The differences were not, however, statistically significant.

Table II: Frequency distribution of duration of pain relief by type of analgesic given.

Duration (hours)	Syndol n	Syndol %	Ibuprofen n	Ibuprofen %
Less than 2	6	12,5	12	23,1
2 - 3	15	31,3	7	13,5
3 - 4	24	50,0	25	48,1
More than 4	3	6,3	8	15,4

Chi square = 7,1 d.o.f. = 3 p = 0,07

The depth of analgesia related to the type of analgesic given showed no significant difference between the two types of analgesics. The length of time it was necessary for patients to take analgesics postoperatively is shown in Table III. In both groups, no patient took analgesics for less than two days. The majority of patients required analgesics for 3 to 5 days. The group of patients taking ibuprofen had to take this drug for a slightly longer period of time than the Syndol group. This difference was significant at the $p < 0,05$ level.

Tabel III: Frequency distribution of the length of time the analgesics were taken by the type of analgesic taken

Length of time (days)	Syndol n	Syndol %	Ibuprofen n	Ibuprofen %
2	10	20,8	6	11,5
3	13	27,1	4	7,7
4	13	27,1	23	44,2
More than 4	12	25,0	19	36,5
Total	48	100	52	99,9

Chi square = 10,60 d.o.f. = 3 p = 0,03

Each group of patients was assessed as to improvement in jaw function on each type of analgesic. The results showed that there was a remarkable similarity between the two groups in relation to jaw movement which seems to suggest that it is the pain that is mainly responsible for lack of jaw movement postoperatively.

When considering the general side effects in both groups of patients, there was very little difference in adverse effects between the two groups. When considering specific side effects, however, the difference between the two groups was significant. In the group taking ibuprofen, the side effects were mainly gastrointestinal in nature with 9,6 per cent of the patients complaining of nausea and 21,2 per cent of the patients complaining of constipation. In all cases these effects were mild and transient.

In the group taking Syndol, 33,3 per cent of the patients complained of drowsiness and dizziness and some of the patients felt that these were severe enough to prevent them from driving a motor vehicle. This is a significantly larger group of patients complaining of this side effect than in the series of Reitzik and Lownie (1976).

The pain rating for each analgesic related to the type of analgesic given is shown in Table IV. All patients taking part in this study were asked to assess the average amount of pain experienced over the first 5 postoperative days and to relay this to a scale of 0 to 10 with 0 being no pain at all and 10 being unbearable pain. Both groups of patients gave a fairly similar pain rating with the patients on ibuprofen indicating that they had slightly more pain than the patients on Syndol. The mean pain rating in patients on Syndol was 3,6 and in the patients on ibuprofen the rating was 4,3. These figures, however, are not significantly different statistically.

Table IV: Frequency distribution of the pain rating by the type of analgesic given.

Pain rating given	Syndol n	Syndol %	Ibuprofen n	Ibuprofen %
0	3	6,3	3	5,8
1	10	20,8	6	11,5
2	2	4,2	2	3,8
3	7	14,6	5	9,6
4	12	25,0	14	26,9
5	3	6,3	9	17,3
6	3	6,3	1	1,9
7	5	10,4	4	7,7
8	3	6,3	7	13,5
9	0	0,0	1	1,9
Total	48	100,2	52	100,00

Mean = 3,6 (sd = 2,3) Mean = 4,3 (sd = 2,4)

Chi square = 8,05 d.o.f. = 9 p = 0,53

DISCUSSION

In most respects, both analgesics have proved to be adequate in that over 80 per cent of patients experienced moderate to total analgesia within 30 minutes of taking the particular drug they were prescribed. The majority of patients also had adequate analgesia for the

desired length of time. As none of the analgesic compounds used in this study was administered to the patient prior to discharge from hospital, approximately 12 h postoperatively, the intramuscular effect of omnopon postoperatively could not have any effect on the drugs assessed in this trial.

A small group of patients (17,3 per cent) taking the ibuprofen were forced to increase the prescribed dose to obtain adequate analgesia over the 5-day period. As ibuprofen has a very short half-life in man (Adams *et al,* 1976). There is a high excretion rate of the drug, and it may be worth considering a regime of prescribing the drug on a 6-hourly and not an 8-hourly basis. Levernieux (1975) has also shown that a daily dosage of 180 mg is not only effective in the treatment of acute rheumatoid conditions, but is also well tolerated. In his series of 100 patients treated with this dose, only 11 patients were withdrawn because of side effects. Seven developed gastric pain, two developed urticaria, one developed a rubella-type rash and one developed facial oedema. No serious side effects were considered. One may therefore also postulate increasing the dosage in the immediate postoperative state.

In the present study there were 4 patients who experienced no analgesia with ibuprofen and some patients had to take it for a longer period of time than Syndol. From this one could postulate that there appears to be a higher degree of patient specificity with ibuprofen compared to Syndol. Moreover, it must be stressed that ibuprofen is an anti-inflammatory drug and Syndol is an analgesic compound. As the majority of patients experienced improved function with both analgesics, it seems possible to postulate that the impotance of jaw function is not the direct result of the anti-inflammatory component of ibuprofen, but rather its analgesic effect.

The adverse effects resulting from ibuprofen were mainly gastrointestinal in nature, these being mild and transient. The side effects from Syndol were mainly that the patients were drowsy or dizzy. This is not an important problem, and may in fact be advantageous in the immediate postoperative phase, but is not desirable in the ambulant patient. These findings related to ibuprofen are similar to those of Cooper *et al,* 1977.

CONCLUSION

In conclusion therefore, the ibuprofen appears to be an adequate analgesic for mild to moderate postoperative oral surgical trauma, with minimal side effects. The drug appears particularly useful in the ambulant patient, where sedation is not required.

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