Effectiveness of Preoperative Analgesics on Postoperative Dental Pain: A Study

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Patients undergoing extractions of third molar teeth under general anesthesia were given a placebo, diclofenac (a nonsteroidal anti-inflammatory drug) 100 mg, or methadone (an opiate) 10 mg 60 to 90 min prior to surgery, and their pain scores and postoperative medication requirements were measured for 3 days. All patients received local anesthetic blocks and analgesic drugs during the perioperative period. There were no significant differences between the three groups in the pain scores and medication requirements during the period of study. It was concluded that preoperative use of nonsteroidal anti-inflammatory drugs and opiates may not offer a preemptive analgesic effect in patients who have had adequate analgesia during the surgery. Continued use of analgesic drugs during the postoperative period is perhaps more useful for this purpose. There appears to be a higher incidence of vomiting following opiates (methadone), precluding its clinical use in day-care patients.

Key Words: Postoperative dental pain; Preemptive analgesia; Diclofenac; Methadone.

Postoperative pain following surgical procedures has attracted considerable interest in the last few years.[1,2] Much excitement has been generated by the concept of "preemptive analgesia,"[3] or the concept that the degree and intensity of post-injury pain can be reduced by the use of local anesthesia injections or analgesic drugs (nonsteroidal anti-inflammatory drugs [NSAIDs] or opiates) during the pre-injury period. Many publications have recently appeared on this topic advocating the preoperative use of local anesthetics, opioids, or NSAIDs.[4-6] A number of publications, however, appeared in the dental literature well before the current world-wide interest shown in this topic.[7,8] Some recent studies also suggest that there is perhaps no great clinical evidence for preemptive analgesia, as has been generally claimed.[9-12] The present study was designed to assess whether preoperative analgesic medications have a beneficial effect in alleviating the postoperative pain following third molar surgery.

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METHODS

Permission of the Area Health Board Ethics Committee was obtained for the trial. American Society of Anesthesiologists classification I-II patients undergoing surgical removal of similarly impacted third molar teeth (upper and lower, bilateral) under general anesthesia were invited to take part in the trial and their informed consent obtained. Those with a history of intolerance to NSAIDs or opiates and those with history of asthma were excluded from the trial. The details of the trial were explained in the preoperative period.

In the pre-anesthetic period, the patients were asked to complete a visual analogue scale (VAS) for continuous pain as well as pain when opening the mouth. They were randomly allocated to receive one of the following pre-anesthetic medications 60 to 90 min before surgery: placebo, diclofenac 100 mg, or methadone 10 mg. The drugs were placed in previously coded bottles by the pharmacy department of the hospital and the code was available in a sealed envelope if required in an emergency. The different drugs were dispensed in ge-

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latinous capsules of the same color to prevent recognition by the administrator or the patient.

General anesthesia was induced with propofol (Diprivan) 2 to 3 mg/kg, atracurium besylate 0.5 mg/kg, and alfentanil 10 μg/kg. Following the introduction of a nasotracheal tube, anesthesia was maintained with oxygen, nitrous oxide and isoflurane, and controlled ventilation. Soon after the induction of anesthesia, each patient received the long-acting NSAID tenoxicam 20 mg intravenously, dexamethasone 8 mg, and penicillin 1 mega unit. A local anesthetic block was performed using 8 to 10 ml of lidocaine 2% with 1/100,000 epinephrine solution. The block consisted of inferior dental, lingual, and buccal blocks for the mandibular teeth and buccal infiltration for the maxillary teeth. The surgery proceeded after 5 min. The degree of surgical difficulty was assessed by the operator based on the amount of bone removal and need for tooth sectioning, and a score of 1 to 3 was assigned to each tooth.[12]

The patient was transferred to the recovery room at the end of the operation and carefully observed for pain and other problems. The operation's protocol required exclusion of patients with complaints of severe pain immediately on recovery from the operation, but none did so. If they had severe and prolonged nausea and vomiting, metoclopramide 10 mg was administered intravenously as an antiemetic. At the end of 1 hr, the VAS for pain was repeated, and each patient received oral paracetamol (acetaminophen) 1 g with codeine 16 mg. They were discharged when ready after further completing the VAS for pain. During the postoperative period, they received daily doses of tenoxicam 20 mg in addition to a mixture of paracetamol 1 g with codeine 30 mg, 6 hourly, if required. Patients were requested to complete the VAS for pain for the next 2 days at predetermined times, four times daily. They were also instructed to record all medications they consumed. Possible side effects like nausea and vomiting, gastrointestinal upset, sleepiness, and tiredness were recorded at appropriate intervals.

The data collected were analyzed at the end of the study period. Patients who received a placebo were labeled as Group 1; those receiving diclofenac were labeled as Group 2; and Group 3 consisted of those who received methadone. The pain scores were analyzed using the mean scores as well as by a method measuring the area under the curve. The statistical methods used were unpaired Student's *t*-test and a chi-square test with contingency correction.

RESULTS

The demographic details are given in Table 1. There were 40 patients in the trial (placebo $n = 12$; diclofenac $n = 15$; methadone $n = 13$). There were no differences between the three groups in the distribution of males and females, age, weight, duration of anesthesia, duration of operation, or degree of surgical difficulty.

Table 1. Demographic Details for Groups 1 through 3[a]

	Placebo Group (Group 1)	*Diclofenac Group (Group 2)*	*Methadone Group (Group 3)*
Male : Female	4 : 8	7 : 8	8 : 5
Number	12	15	13
Age (yr)	21.0 (19.7–22.3)[b]	23.0 (20.5–25.5)	22.4 (20.3–24.4)
Weight (kg)	65.8 (58.7–72.9)	70.1 (64.2–75.9)	71.2 (66.7–75.6)
Duration of anesthesia (min)	67.9 (55.2–80.6)	59.6 (50.5–68.7)	63.7 (57.8–69.5)
Duration of operation (min)	45.8 (34.4–57.2)	38.7 (30.2–47.3)	43.8 (37.6–50.1)
Difficulty of operation	7.5 (6.3–8.7)	6.9 (5.9–7.8)	7.2 (6.6–7.8)

[a] No significant differences were seen between the groups.
[b] Mean and 95% confidence intervals are shown in parentheses.

The mean pain scores during the trial period showed no significant difference between continuous pain and pain on opening the mouth at any of the recording times for the three groups. Hence, the pain data was combined and further analyzed. The mean pain scores and 95% confidence intervals are given in Figure 1. There was a significant difference ($P < 0.05$) between the preoperative pain scores and pain scores at all other times, which was seen in all three groups. There was no significant difference between the three groups at any time during the study. Although the methadone group (Group 3) appears to have lower mean pain scores, the effect was not statistically significant ($P > 0.05$). The statistical analysis of the area under the curve showed the same results. The small number of cases in the trial gives only a power of 55% for the results.

Figure 2 shows the mean medication requirements during the postoperative period. No significant differences existed between the three groups in the medication intake at any recording time. Within each group, the only significant difference was the increased requirement seen on the morning of the first postoperative day ($P < 0.05$).

During the study period some side effects and complications were recorded; the results are given in Table 2. There were no differences between the three groups in the incidence of abdominal discomfort, tiredness, or sleepiness. The overall incidence of complaint of nausea was slightly higher with the methadone group, but was not statistically significant. The incidence of vomiting and the use of the antiemetic metoclopramide in the

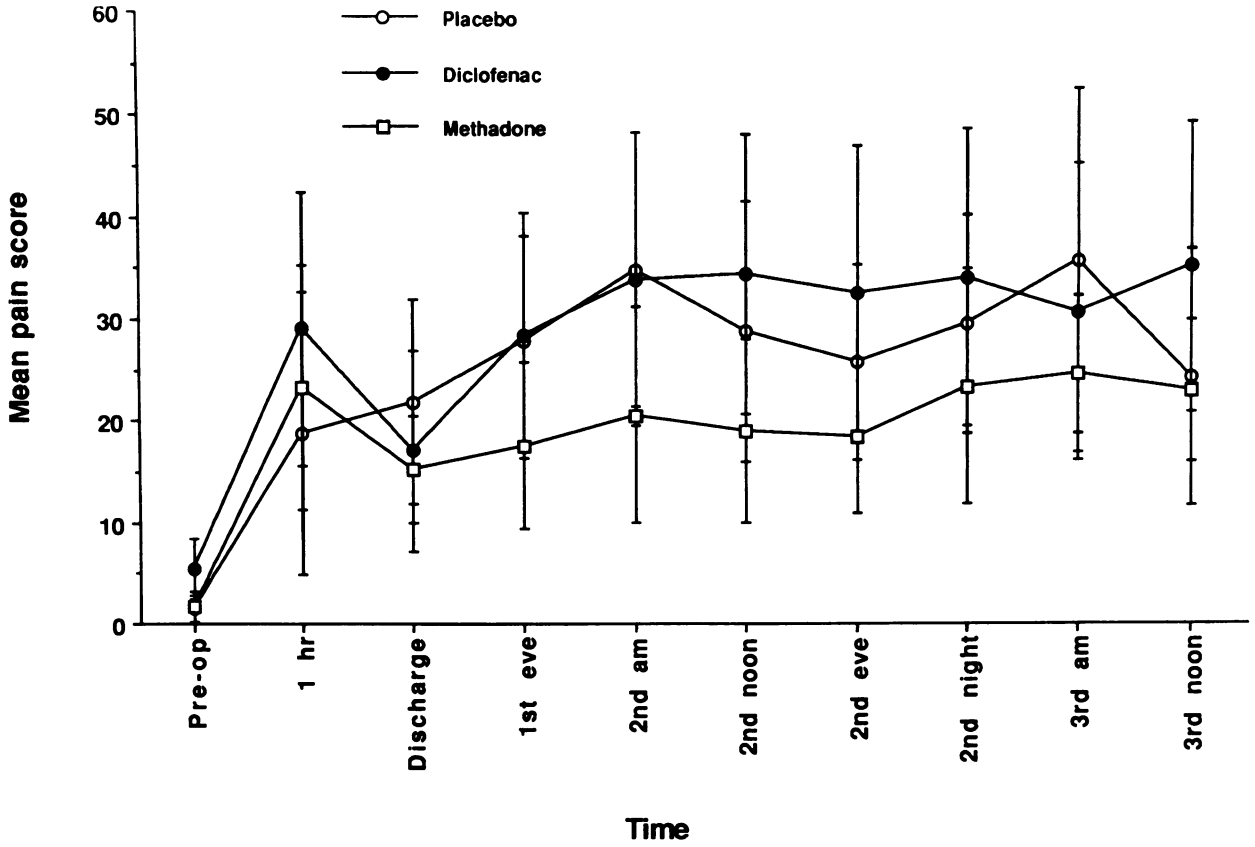

Figure 1. The mean pain scores, with 95% confidence intervals, in the three groups during the period of study. Patients recorded the pain scores at prescribed times. Pre-op, pre-operative period; 1 hr, one hour after operation; Discharge, Upon discharge from hospital.

postoperative period were significantly higher in the methadone group ($P < 0.05$).

DISCUSSION

This study was designed to test the currently popular belief that preoperative measures are helpful in the prevention or modification of postoperative pain,[3-6] even for days.[13] The use of local anesthesia and opiates has been suggested for this purpose,[14] and NSAIDs have been used before surgery.[8] This benefit of preemptive analgesia is not accepted by all because of lack of clear evidence from clinical studies.[9-12]

The three groups in the study were comparable (Table 1). Follow-up data for up to 2 postoperative days suggest that there is no difference in the pain experience (mean pain scores) between the three different groups. This is in contrast to the generally held belief that both opiates[14] and NSAIDs,[8] as well as local anesthetic blocks,[4] administered in the preoperative period may be useful in postoperative pain control. In the current study, all patients received adequate local anesthetic blocks before the surgery began, so any beneficial effects of the preoperative medications may have occurred during the period of the local anesthetic block. It may be that the effect of preoperative analgesics only extends to the pharmacological duration of action of the drug. Hence, the argument that preoperative analgesics may be useful to alleviate postoperative pain is called into question. There is a suggestion of lower mean pain scores in those receiving methadone, although no statistical differences were noted. The present study has its limitations, including a low power (55%); a larger number of patients may have shown a difference or confirmed that there was no type II error. Hence, we are unable confidently to rule out that the use of methadone may not result in a lower pain level in patients than either placebo or diclofenac, as has been suggested for opiates.[5,15]

The patients received similar doses of analgesics during the perioperative period. At the start of the surgery, all patients received a long-acting NSAID, tenoxicam 20 mg intravenously, as well as dexamethasone 8 mg for its anti-inflammatory effects and usefulness in reducing swelling and pain.[16] A dose of paracetamol with codeine

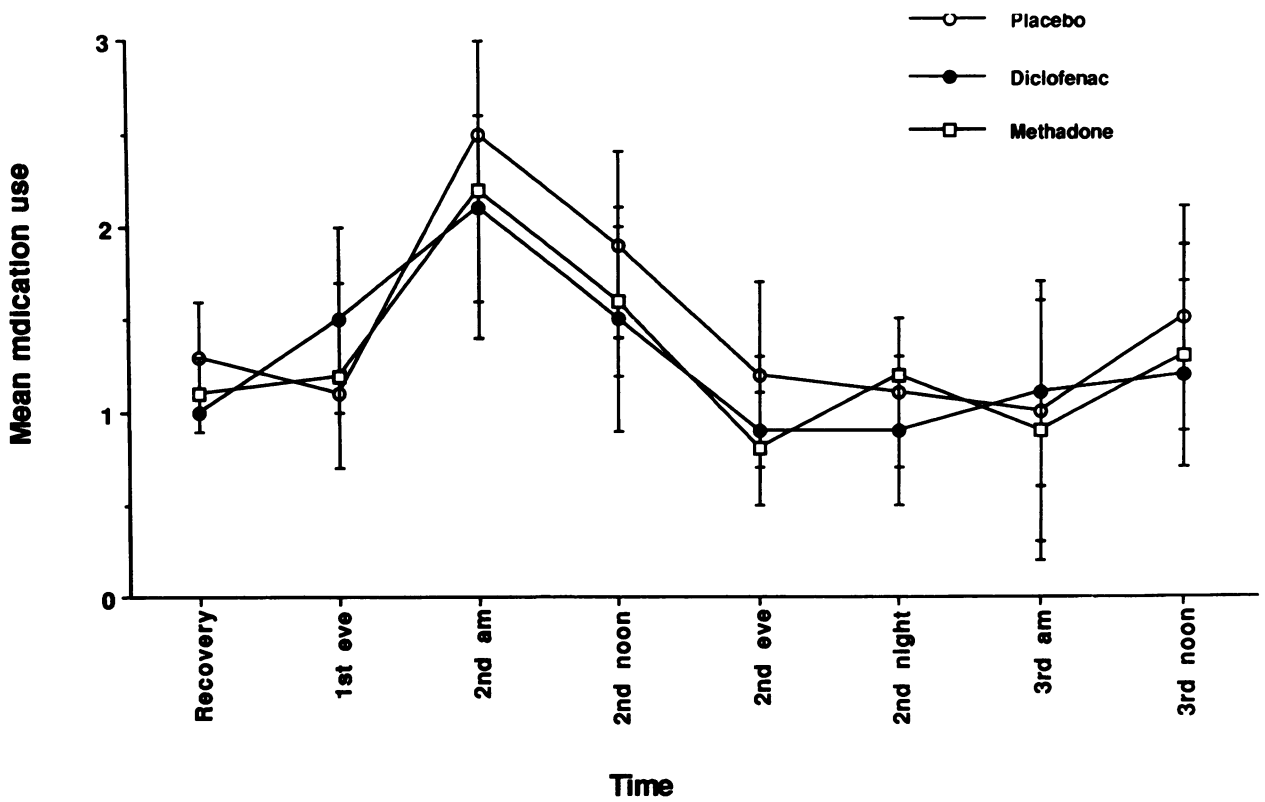

Figure 2. The mean medication intake, with 95% confidence intervals, in the three groups during the period of study. The medication intake recorded is for the period preceding each of the time intervals shown.

at 1 hr after surgery, as well as a daily dose of tenoxicam, were given to all. The only variability was the top-up doses in the intervening period, with paracetamol–codeine elixir on an as-required basis. Hence, the postoperative medication requirement could be compared between the three groups. No differences were found between the three groups in this respect. There was an increase in the requirement for medication on the morning of the first postoperative day; this was not an unexpected finding because patients require an increased amount of analgesics in the first 24 to 48 hours after third molar surgery.[12] The lack of any significant differences for the three groups in the medication requirements reinforces the other finding of this study: the lack of any differences in the mean pain scores.

Table 2. Incidences of Reported Problems in the Three Groups for the Duration of the Study

Group	Number	Nausea	Vomiting	Antiemetic Required	Stomach Upset	Sleepy	Tired
Placebo	12	2	0	0	1	9	6
Diclofenac	15	4	1	1	3	7	11
Methadone	13	7	4*	4*	1	10	10

* $P < 0.05$ (significant difference).

In the present study, we were unable to show any beneficial effects for preoperative use of NSAIDs and methadone over placebo. Use of local anesthetic in all cases could have prevented any distinction in the pain perception in the few hours following the surgery. The results of this study support the view that preoperative use of both NSAIDs and opiates alone may not give long-lasting pain relief, as has been previously suggested.[8,15] In some recent publications, it has been suggested that attention needs to be paid to continually preempting central sensitization of the spinal cord during the postoperative period.[9,15,17] The peripheral mechanisms of pain are also brought into play during this period,[18] and thus NSAIDs may be useful at this stage. These views differ from the earlier view that prolonged postoperative pain relief could be obtained by as little as a single local anesthetic block.[13] Hence, continuous attempts may be required to deal with the pain during the postoperative period. It does not appear from the current study that one single dose of either an NSAID or an opiate is effective in preventing pain by reducing pain scores or medication requirements in the postoperative period when adequate intraoperative local anesthetic blocks and systemic analgesics are given.

Table 2 shows some of the side effects noted in this study. The incidence of sleepiness and tiredness were

similar in all three groups. In addition, the incidence of abdominal discomfort, a problem commonly associated with NSAIDs, did not differ among the three groups. However, differences were seen in the incidence of vomiting and the use of antiemetic; these were significantly more common when the patients had methadone in the preoperative period. It is well known that opiates cause a higher incidence of nausea and vomiting, particularly in the ambulant patient.[19] The long duration of action of methadone may have led to this problem. There was an increase in the incidence of nausea with methadone, but the numbers were not large enough to be statistically significant.

It may be concluded that preoperative use of both NSAIDs and opiates may not be very useful for the purpose of reducing postoperative pain in patients who have had adequate nerve blocks and intraoperative analgesics. Continued use of analgesics during the postoperative period is perhaps more useful for this purpose. There appears to be a higher incidence of nausea and vomiting following opiates (methadone), and hence they may not be of clinical use in day-care patients.

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REFERENCES

1. Woolfe CJ: Recent advances in the pathophysiology of acute pain. Br J Anaesth 1989;63:139–146.

2. Cousins MJ: Acute pain and the injury response: immediate and prolonged effects. Reg Anaesth 1989;14:162–178.

3. Katz J, Kavanagh BP, Sandler AN, Nierenberg H, Boylan JF, Friedlander M, Shaw BF: Pre-emptive analgesia: clinical evidence of neuroplasticity contributing to post operative pain. Anesthesiology 1992;77:439–446.

4. Ejlersen E, Anderson HB, Eliasen K, Mogensen T: A comparison between pre incisional and post incisional lidocaine infiltration and post operative pain. Anesth Analg 1992;74: 495–498.

5. Richmond CE, Bromley LM, Woolf CJ: Preoperative morphine pre-empts post operative pain. Lancet 1993;342: 73–75.

6. McQuay HJ: Pre-emptive analgesia. Br J Anaesth 1992;69:1–3. [Editorial]

7. Hill CM, Carroll MJ, Giles AD, Pickvance N: Ibuprofen given pre- and post-operatively for the relief of pain. Int J Oral Maxillofac Surg 1987;16:420–424.

8. Jackson DL, Moore PA, Hargreaves KM: Preoperative non-steroidal anti-inflammatory medication for the prevention of post operative dental pain. J Am Dent Assoc 1989;119: 641–647.

9. Dahl JB, Kehlet H: The value of pre-emptive analgesia in the treatment of post operative pain. Br J Anaesth 1993;70:434–439.

10. Dahl JB, Hansen BL, Hjortso NC, Erichsen CJ, Moiniche S, Kehlet H: Influence of timing on the effect of continuous extradural analgesia with bupivacaine and morphine after major abdominal surgery. Br J Anaesth 1992;69:4–8.

11. Dierking GW, Dahl JB, Kanstrup J, Kahl A, Kehlet H: Effect of pre-vs post-operative inguinal field block on post operative pain after herniorrhaphy. Br J Anaesth 1992;68:344–348.

12. Zacharias M, Thyne GM, Luyk NH: Local anaesthesia during surgery: when is the best time to give it? Anesth Pain Control Dent 1993;2:9–12.

13. Tverskoy M, Cazacov C, Ayache M, Bradley EL, Kissin I: Post-operative pain after inguinal herniorrhaphy with different types of anesthesia. Anesth Analg 1990;70:29–35.

14. McQuay HJ, Carroll D, Moore RA: Post operative orthopaedic pain—the effect of opiate premedication and local anaesthetic blocks. Pain 1988;33:291–295.

15. Richmond CE, Bromley LM, Woolf CJ: Preoperative morphine pre-empts post operative pain. Lancet 1993;342: 73–75.

16. ElHag M, Coghlan K, Christmas P, Harris M: The anti-inflammatory effects of dexamethasone and therapeutic ultrasound in oral surgery. Br J Oral Maxillofac Surg 1985;23:17–23.

17. Katz J: Preop analgesia for postop pain. Lancet 1993;342:65–66. [Commentary]

18. Dahl JB, Kehlet H: Non-steroidal anti-inflammatory drugs: rationale for use in severe post operative pain. Br J Anaesth 1991;66:703–712.

19. Dob DP, Whitwam JG: Pharmacology and day-care anaesthesia. In: Whitwam JG, ed: Day Care Anaesthesia. Oxford, Blackwell, 1994:20–57.