EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 6
Issue: 12
348-350
Year: 2019

INTRAVENOUS DICLOFENAC USED FOR POSTOPERATIVE PAIN PREVENTION IN PATIENT OF THIRD MOLAR EXTRACTION. A RESEARCH ANALYSIS

Dr. Konark[1] and Dr. Anju Singh[2]*

[1]B.D.S(HONS), M.D.S, Senior Lecturer, Department of Conservative Dentistry and Endodontics, Patna Dental College and Hospital.
[2]B.D.S, M.D.S, Assistant Professor, Department of Dentistry, Nalanda Medical College and Hospital.

***Corresponding Author: Dr. Anju Singh**
B.D.S, M.D.S, Assistant Professor, Department of Dentistry, Nalanda Medical College and Hospital.

Article Received on 05/09/2019 **Article Revised on 25/09/2019** **Article Accepted on 15/10/2019**

ABSTRACT
Aims and Objective- To assess the analgesic efficacy and tolerance of a single preoperative intravenous infusion of 100 mg of diclofenac in patients undergoing removal of the third molar. **Material and method**- 100 patients undergoing a standard removal of an impacted lower third molar were given a single dose of 100 mg sodium diclofenac or saline (placebo) intravenously before operation, on a double-blind basis. Pain was measured postoperatively by means of a visual analogue scale hourly for the first 8 h and during the first and second days after operation. **Result**-Administration of diclofenac resulted in greater pain relief than administration of placebo for the first 3 h after surgery, where after the treatments did not differ. The results suggest that intravenous preoperative diclofenac may be useful in some clinical situations but generally it probably offers little benefit over the corresponding oral treatment.

KEYWORDS: Third molar, pain, placebo, diclofenac.

INTRODUCTION
Increasing knowledge of the mechanisms of pain and inflammation have resulted in effective new means of controlling postoperative pain. Following the discovery of the roles of inflammation and increased prostaglandin synthesis in the local pain process,[1] nonsteroidal anti-inflammatory analgesics (NSAIDs) have increasingly been used to treat postoperative pain. In third molar surgery, in particular the analgesic efficacy of opioids seems low.' Use of NSAlDs has, therefore, become a routine. The nonsteroidal anti-inflammatory analgesic diclofenac is an inhibitor of cyclo-oxygenase,[2] the key enzyme involved in the metabolism of arachidonic acid into various prostaglandin mediators of inflammation and pain.[3] Diclofenac has significant anti-inflammatory and analgesic activities. When administered preoperatively, diclofenac gave better pain relief than preoperative administration of placebo or postoperative administration of diclofcnac,[4] indicating that early inhibition of the inflammation resulting from operative trauma provides best pain relief. Intravenous preoperative drug administration is the simplest way to ensure optimum plasma drug levels at the time of surgical intervention. Because of extensive first-pass metabolism, an intravenous infusion of 100 mg of diclofenac corresponds roughly to the recommended daily oral dose of 150 mg,' i.e. tolerance is likely to be better after intravenous than after oral administration of diclofenac. However, the possibility of irritation at the site of injection must be borne in mind.

The aim of this trial was to assess the analgesic efficacy and tolerance of a single preoperative intravenous infusion of 100 mg of diclofenac in patients undergoing removal of the third molar, which was used as a fairly standardized mode for acute surgical pain.

MATERIAL AND METHOD
Fifty patients undergoing a removal of a single impacted lower third molar, (classes A II (= l), B I (= 2) and B II (=3) according to Pell and Gregory's classification of impacted third molars), which involved bone removal, were studied.[5] This classification is based on the relation of the third molar to the ramus of mandible (I to III) and the relative depth of the tooth in bone (A to C). The difficulty of tooth removal increases from class I to III and A to C respectively. The details of this classification arc published by Pell *et al.* in 1933 and 1942.[5,6] Radiographic recordings were made under standardized conditions using an orthopantomographic technique. Patients characteristics are shown in Table 1 and 2.

Table 1: Patient detail.

	Group A	Group B
Women	30	32
Men	18	20
Total	48	52

Table 2: Characteristic of patient impaction and duration of surgery.

	Group A	Group B
Age(mean)	24	25
Degree of impaction	2.1	2.41
Duration of operation in minute	17	18

The groups were homogeneous as regards age, degree of tooth impaction and duration of operation. Exclusion criteria included allergy to diclofenac, peptic ulcer, asthma and pregnancy. The protocol for the study had been approved by the local ethical committee, and was in accordance with the 1977 Declaration of Helsinki. Informed written consent was obtained from all patients. The trial was double blind and randomized. The trial medications were infused intravenously for 15 min before surgery. Group A patients received 100 mg of diclofenac, group B patients saline. The diclofenac was diluted with saline to 100 ml. This volume of saline was also administered as placebo. All operations were carried out by the same surgeon. Lignocaine (20 mg/ml) containing 12.5 mg/ml of epinephrine was used for local anaesthesia. All patients received an oral antibiotic postoperatively, either phenoxymethyl penicillin 660 mg or erythromytin acistrate 400 mg: three times daily, for 1 week. During the study patients were allowed to take 50 mg codeine phosphate 30 mg, caffeine 100 mg for pain relief as needed. Patients recorded pain by means of a visual analogue scale (0 mm = no pain, 100 mm = intolerablepain) hourly for 8 h after operation. On the first and second days after operation, pain was recorded in the morning and evening. Ability to eat and problems in mouth opening were recorded on the first and second mornings after operation. Mouth opening was measured as interincisal distance. Side effects were also recorded.

A prior estimate of the required sample size was done. the data in Figure 1 were analysed with three way repeated measures analysis of variance ANOVA, the within subject factor being time (l-5 h) and between subject factors treatment and degree of impaction. For pairwise comparisons between the groups the least significant difference test was used. For analysis of all the other data two way ANOVA for repeated measures was used and differences between two means were analysed with Student's t-test for dependent or independent observations (CSS statistical software). Correlations between degree of the tooth impaction, duration of operation and sum of the pain score over the first 8 h after operation were analysed using Spearman's rank correlation. Results are shown as means f standard errors of means.

RESULTS

Preoperative intravenous administration of diclofenac gave greater pain relief" than placebo for the first 3 h after operation. Thereafter the pain relief was similar to that given by placebo.

The degree of tooth impaction did not correlate significantly with duration of operation or the sum of the pain scores over the first 8 h. The correlation coefficients were 0.03 and 0.07, respectively. In accordance to the linear correlation analysis 3-way ANOVA showed that the degree of impaction did not significantly affect the extent or course of development of pain. There was no significant difference in mean pain intensities during the first and second days after operation between groups A and B. In both groups, pain intensity increased slightly towards nightfall on the first day after operation but there was no such increase during the second day. Patients' ability to cat was moderately impaired in both groups during the first day after operation but only slightly impaired on the second day after surgery. No differences were observed between the groups during the first and second days after operation with respect to patients' abilities to open their mouths. There was significant impairment of mouth opening in both groups during the first and second days after operation as compared to the preoperative situation. The need for additional analgesic medication during the first 5 h after operation was lower in the diclofenac group than in the placebo group. During the rest of the day of operation and on postoperative days 1 and 2 there were no significant differences between the groups. The number of side effects recorded was low in both groups. One patient in the diclofenac group and one patient in the placebo group reported a burning sensation in the vein during infusion of the trial medication before operation. This side effect disappeared after saline infusion in the patient who had been given diclofenac: and spontaneously in the patient given saline. No other side effects were reported by the patients during the study.

DISCUSSION

As needed dosing of analgesics is the conventional method of treating postoperative pain. If NSAIDs were used as analgesics, preoperatively, maximum inhibition of the synthesis of arachidonic acid-derived mediators of pain and inflammation at the time of surgical trauma should theoretically be achieved. In oral and maxillofacial surgery, at least. preoperative administration of NSAIDs appear more effective in relation to analgesia than postoperative administration of NSAIDs.[4]

We are aware of only a few reports dealing with intravenous administration of NSAlDs for postoperative pain prevention in outpatient surgery.[7] Possible advantages of intravenous administration of NSAlDs are, firstly: the ability to use lower dosages in the case of drugs undergoing extensive first-pass metabolism, such as diclofenac and, secondly, higher peak plasma levels of

the drug when inflammatory processes are surgically induced and, thirdly, minimization of gastrointestinal side effects. Problems of irritation at infusion sites can be minimized if the concentration of the drug, e.g. diclofenac, in saline is not too great and the infusion rate is not too fast. In the study described here, 100 mg of diclofenac were infused preoperatively. The dose used was half the recommended daily oral dose. Such pre oprative treatment proved superior to administration of placebo. Wuolijoki et al have reported similar. Postoperative prevention of pain by a preoperative intravenous infusion of diclofenac lasted 5 h. This finding is in accordance with kinetic data showing that diclofenac levels reach baseline values 5.5 h after a single intravenous administration." The need for additional analgesic medication during the first 5 h after operation was less than in the placebo group and was similar to that in placebo group subsequently. These findings are in agreement with the observations of Valanne et al.' Because, obviously. of the mechanical strain at the operation site during the active daytime hours, there was also a slight increase in pain intensity towards night, as we had also found before.'" Although the intravenously administered analgesic proved to be superior over placebo the comparison with the results from previous studies suggest that after intravenous NSAID the extent and duration of analgesia are not improved when compared with the corresponding oral treatment. Furthermore, quite satisfactory results are obtained when oral NSAID treatment is combined with a long-acting local anaesthetic.[8] One reported side effect of diclofenac infusion is local venous irritation. Careful infusion technique, choice of an appropriate infusion time (15 min) and dilution of the compound in 100 ml of saline led to such irritation being reported by only one of the 24 patients. Placebo injection of saline was followed by local irritation in one out of 26 patients. Modern postoperative pain treatment should involve appropriate timing of therapy in relation to surgical trauma: as a few recent studies have stressed.[9] The advantages of intravenous administration of NSAIDs appear to be few while being more laborious than oral or intramuscular administration in outpatient surgery. Although not proven to be superior in terms of analgesic efficacy intravenous administration is indicated at least in outpatient surgery under general anaesthesia and when the patient is unable to eat. Preoperative intravenous infusion of diclofenac results in adequate pain prevention only in the immediate postoperative period. Discomfort during the first and second days after operation may require NSAID therapy adjusted to patient needs. Our conclusion is that limited duration of action and higher cost of the treatment are the facts that favour the administration of peroral NSAID preparations routinely instead of intravenous route.[10]

REFERENCES

1. Seymour RA. Walton JG. Pain control after third molar surgery. Int J Oral Surg, 1984; 13: 457 485.
2. Todd PA, Sorkin EM. Diclofenac Sodium. A reappraisal of its pharmacodynamic and pharmacokinetic properties. And therapeutic cfhcacy. Drug, 1988; 35: 244-285.
3. Insel PA. Analgesic-antipyrctics and anti-inflammatory agents: drugs employed in the treatment of rheumatoid arthritis and gout In: Goodman Gihnan et a/. cd, Goodman and Gilman's The pharmacological basis of therapeutics. 8th ed. New York: Pergamon Press. Macmillan Publishing Co. Inc., 1990: 638-644.
4. Wuolijoki E, Oikarincn VJ, Ylipaavalniemi P, er al. ElTective postoperative pain control by preoperative injection of diclofenac. Eur J Clin Pharmacol, 1987; 32: 249 252.
5. Pcll GJ, Gregory GT. Impacted mandibular third molars: classification and modified technique for removal. Dent Digest, 1933; 39: 330.-338.
6. Pell GJ, Gregory CT'. Report on a ten-year study of a tooth division technique for the removal of impacted teeth. Am J Orthod, 1942; 28: 660 666.
7. Valanne J. Korttila K. Ylikorkala 0. Intravenous diclofenac sodium decreases prostaglandin synthesis and postoperative symptoms after gcncral anaesthesia in outpatients undergoing dental surgery. Acta Anaesthcsiol Stand, 1987; 31: 722-727.
8. Fisher SE, Frame JW, Rout PJG: er al. Factors alIecting the onset and severity of pain followinS the surgical removal of unilateral impacted mandibular third molar teeth. Br Dent J, 198s; 1 I: 351-354.
9. Willis IV. Kendall MJ. Flinn KM, er *al*. The pharmacokinetics of diclofenac sodium following intravenous and oral administration. Eur J Clin Pharmacol, 1979; 16: 4055410.
10. Hyrkls T, Ylipaavalnicmi P, Oikarinen VJ? er al. Postoperative pain prevention by single dose formulation of diclofcnac producing a steady plasma concentration. J Oral Maxillofac Surg, 1992; 50: 124-127.