Effect of Ketorolac on Postoperative Pain Relief in Dental Extraction cases - a comparative study with Pethidine

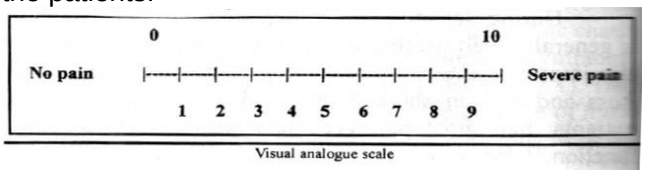
S. M. Abbas (Department of Anaesthesiology, Aga Khan University Hospital, Karachi.)
R. S. Kamal (Department of Anaesthesiology, Aga Khan University Hospital, Karachi.)
G. Afshan (Department of Anaesthesiology, Aga Khan University Hospital, Karachi.)

Introduction

Pain is the most common complaint of the human beings. Dental pain specifically third molar extraction is said to be the one of the most acute post-surgical painful conditions.1 Third molar dental extraction model has been used previously by many researchers during last two decades1-6 to see the efficacy of postoperative analgesics. Despite a massive expansion and diversification in clinical practice over recent years, the surgical removal of impacted third molar teeth continues to be the most common procedure performed by oral and maxillofacial surgeons.7 This study was designed to compare the analgesic efficacy of ketorolac with pethidine for postoperative pain relief as well as their side effects in patients undergoing surgical extraction of third molar teeth..

Methods

After approval from human subjects protection committee of the hospital and patient\'s consent, 60 patients were included in this study. They received either pethidine or ketorolac. Only ASA I, II and III patients of 14 to 50 years of age for two or more third molars extraction with at least one mandibular molar, were included in this study. Patients with a history of acid peptic disease, asthma, haemorrhagic diathesis, renal impairment, known hypersensitivity to NSAIDs, concurrent treatment with NSAIDs or lithium salts, and nursing mothers were excluded. Drugs were prepared by an anaesthetist, not related to the study, in 10 ml syringe, containing either ketorolac 30 mg or pethidine 0.8 mg/kg, diluted to 10 ml, labeled A and B. Primary investigator remained blinded to the contents of the syringes. The way the Visual Analogue Scale would be used, was explained to the patients.



Visual analogue scale

Midazolam 7.5 mg was given as premedication one hour before surgery. In the operating room ECG, NIBP (Non invasive blood pressure), pulse oximetry, and capnography were used for every patient. At the time of induction, study drug was given I/V in 30 seconds. Induction was done with Propofol in a dose of 2 to 3 mg/kg. To facilitate intubation Atracurium was used. Anaesthesia was maintained with incremental doses of Atracurium and Isoflurane with 60:40 N2O and O2. Each patient received local anaesthesia with 2% Lignocain with 1 ml 1:200.000 Adrenaline at the root of each tooth to be extracted. At the end of the surgery patients were reversed with Neostigmine and Atropine. In the recovery room they were asked about pain intensity according to Visual Analogue Scale at immediate, half, one, two, three and four hours. Pethidine 10 mg i/v in titrated doses was given as rescue analgesia at a pain score of 5 or >5. Adverse events specifically nausea, vomiting, drowsiness (defined as increased sleepiness) and excessive bleeding (defined as soakage of 4×4 gauze which needs to be changed within half an hour) were recorded.

Statistical Analysis

Comparison of the need for rescue analgesia was done through Odds ratio by applying 2x2 table, whereas side effects were analyzed by applying Chi square test. P value <0.05 was taken as significant

Results

There was no significant difference in the demographic data of both groups (Table).

Table. Demographic data.

	Pethidine	Ketorolac
Age (years) Mean +SD	26.73+5.6	26.56+6.1
Sex M:F	14:16	11:19

Need for rescue analgesia rather than the mean pain score was used for statistical analysis of two

treatment groups, which at immediate, half hour, one, two, three and four hours after arrival in recovery room, showed no significant difference at any time interval (Figures 1 and 2).

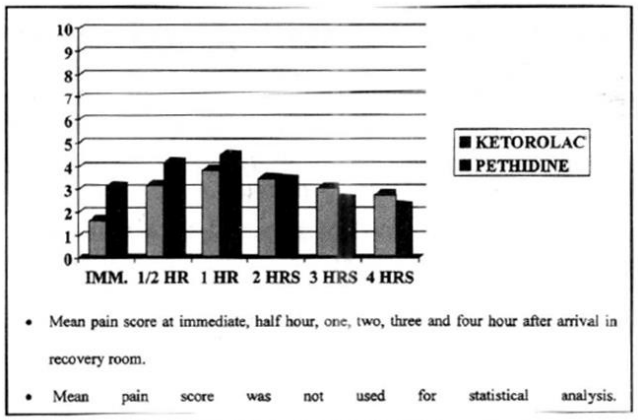


Figure 1. Mean pain score.

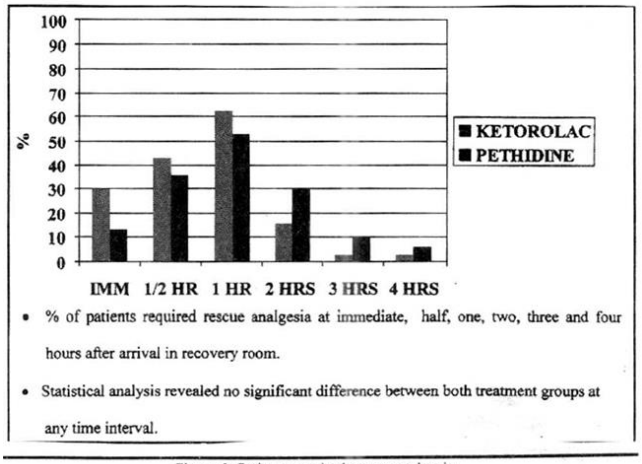


Figure 2. Patients required rescue analgesia.

Statistical analysis of the side effects revealed that only nausea and excessive drowsiness was significantly higher in pethidine group as compared to ketorolac (Figure 3).

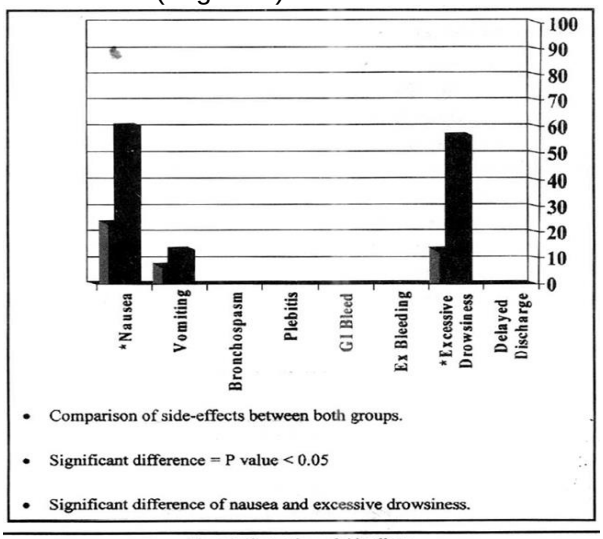


Figure 3. Comparison of side effects.

The rest of the side effects i.e. bronchospasm, phlebitis, GI bleed, and excessive bleeding from surgical site among both groups were statistically insignificant. No patient in either group had delay in discharge from phase II recovery room, at the end of fourth hour.

Discussion

Postoperative pain control is one of the most important aspects of management of surgical patients. Various drugs, which are used to control the postoperative pain, are mainly categorized in two groups. i.e., Non-steroidal anti-inflammatory drugs and opioids. Different pain models have been used to evaluate the efficacy of different members of these two groups.

Surgical removal of impacted third molar is the most common outpatient procedure in oral surgery. Normally, it is followed by an inflammatory reaction characterized by pain, swelling and trismus.1 The management of this postoperative pain has been extensively studied with several non-steroidal anti-inflammatory drugs and narcotics.2 The dental impaction pain model has become one of the primary models used in developing analgesic drugs; it provides a readily available healthy population and a relatively uniform surgical procedure confined to one area of the body.3 No single analgesic regimen has so far been developed to provide sufficient pain relief without any side effect. To avoid the dose related side effects of narcotics, use of NSAIDS has become popular for mild to moderate postoperative pain. Ketorolac is also a non-steroidal anti-inflammatory drug, which has been compared and found effective with pethidine 50-100 mg, Morphine 6-12 mg and Pentazocin 30mg.4 Ketorolac has been proved to be more potent than several other NSAIDs studied under similar experimental conditions. In a study, the efficacy and safety of NSAIDs analgesic in the treatment of acute postoperative dental pain have revealed that ketorolac has a greater global efficacy than ketoprofen or placebo.3

In another study of third molar extraction, Fricke et al5 found 30 mg of ketorolac significantly better than 50 and 100 mg pethidine. In his study all patients received sedation regimen consisting of 25-75 mg of pethidine. Therefore the study drugs were given 3 hours postoperatively. But in our study, study drug was given at induction and pain score was evaluated immediately after arriving in recovery room upto 4 hrs. Since ketorolac has a longer half-life than pethidine the difference between two drugs is supposed to be greater at longer time intervals. Peak pain intensity in our study was at one hour.

In a recent study, of postoperative dental pain, Olmedo et al3 found no difference in pain intensity between the drug and the placebo groups at 8, 24 and 48 hours interval. In a recent study Watton et al6 reported mean time at which 50% of the population needed rescue analgesia in control group was 2.95 hrs but he did not mention the intraoperative analgesia, which could have been the reason of this long interval. Narcotics are notorious in causing nausea, vomiting and drowsiness which may lead to unplanned admissions in an ambulatory surgery. In a recent study, even the shorter acting Fentanyl produced undesirable dose related effects on recovery period. 7

If we compare the frequency of nausea, vomiting and drowsiness from Fricke's study5 it is different. Most probable explanation of this difference is the immediate postoperative period during which we evaluated both drugs. In this period, frequency of vomiting and nausea may be high due to the anaesthetic drugs.

Nonsteroidal anti-inflammatory drugs (NSAID) have become popular for pain relief after different major and minor surgical procedures.8-11 NSAIDs reduce the biosynthesis of prostaglandins by inhibition of the enzyme cyclo-oxygenase (COX). 12 Ketorolac is a member of the pyrrolopyrrole group of nonsteroidal anti-inflammantory drugs. This prostaglandin synthesis inhibitor has been developed for its analgesic properties and it is marketed by Syntex Laboratories. 12 Ketorolac exhibits analgesic activity mediated by peripheral effects. At analgesic doses it has minimal anti-inflammatory and antipyretic activity.10,13 It is also a potent platelet aggregation inhibitor.9 Ketorolac is not an anaesthetic agent and possesses no sedative or anxiolytic properties.13 It is concluded that Ketorolac is a useful alternative to opioid and to other non-steroidal analgesics in ameliorating moderate to severe post surgical pain .

References

1.Berg TI, Egil O. Predictor evaluation of postoperative morbidity after surgical removal of mandibular third molar. Acta Odontol Scand. 1994;52:162-9.

2.Antila H, Lehtinen R, Heinoro I, et al. Successful pain management by Finnish oral surgeons: a clinical follow up study. Oral Surg Oral Med Oral Pathol 1992;74:19-23.

3.Olmedo MV, Galvez R, Vallecillo M. Double-blind parallel comparison of doses of ketorolac, ketoprofen and placebo administered orally to patients with postoperative dental pain. Pain 2000;90:135-41.

4.Stanski DR, Cherry C, Bradley R. Efficacy and safety of single doses of intramuscular ketorolac tromethamine compared with meperidine for postoperative pain. Pharmacotherapy 1990;10:40-4.

5.Fricke JR, Angeloccietal D. Comparison of the efficacy and safety of Ketorolac and Meperidine in the relief of dental pain. J Clin Pharmacol 1992;32:376-84.

6.Walton GM, Rood JP, Snowdon AT, et al. Ketorolac and diclofenac for postoperative pain relief following oral surgery. Br J Oral Maxillofac Surg 1993;31:158-60.

7.Pavlin DJ, Chen C, Penaloza DA,et al. Pain as a factor complicating recovery and discharge after ambulatory surgery. Anesth Analg 2002;95:627-34 .

8.Laitinen J, Nuutinen LS. Intravenous diclofenac coupled with PCA fentanyl for pain relief after total hip replacement. Anesthesiology 1992; 76:194-8.

9.Kostamovaara PA, Laitinen J, Nuutinen LS, et al. Intravenous Ketoprofen for pain relief after total hip or knee replacement. Acta Anaesthesiol Scand 1996;40: 697-703.

10.Kinsella J, Moffat AC, Patrick JA, et al. Ketorolac trometamol for postoperative analgesia after orthopaedic surgery. Br J Anaesth 1992; 69:19-22.

11.Kostamovaara PA, Hendolin H, Kokki H, et al. Ketorolac, diclofenac and ketoprofen are equally efficacious for pain relief after total hip replacement surgery. Br J Anaesth 1998; 81: 369-72.

12.Current Product-Information Booklet, regarding Ketorolac, its pharmacokineties and pharmacodynamics, January 2001, by Roche pharmaceuticals.

13.Buckley MMT, Brogden RN. Ketorolac: a review of its pharmacodynamic and pharmacokinetic properties, and therapeutic potential. Drugs 1990; 39:86-109.

Abstract

Objective:

To compare the analgesic efficacy and side effects of ketorolac with pethidine in a day care procedure.

Study Design:

Single dose, double blind, case matched study.

Methods:

Sixty patients were divided into group A and group B, who received either ketorolac 30 mg or Pethidine 0.8 mg/kg (both I/V) respectively at the time of induction of general anaesthesia. Patients were assessed in recovery room for pain according to visual analogue scale and any side effects. Amount

of rescue analgesia required by both groups were also recorded. Odds Ratio and and Chi Square test were used for statistical analysis.

Results:

Statistical analysis showed no significant differences between these two drugs at any time interval, however a significantly decreased incidence of nausea and drowsiness was found in ketorolac group.

Conclusion:

Ketorolac 30 mg intravenously provides similar analgesic effects as Pethidine with much less incidence of nausea and drowsiness (JPMA 54:319;2004).