

Evaluation of Efficiency of Various Analgesics on Post Extraction Pain- A Clinical Study

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Abstract

Background: The extraction of the mandibular third molars is one of the most commonly performed dentoalveolar procedures in oral and maxillofacial surgery and it is often associated with varying degree of postoperative discomfort. Pain, swelling and trismus are the most common postoperative complaints. These discomforts greatly influence the quality of life of the patients in the days after the dental procedure. **Objective:** The study was conducted to evaluate the efficiency of various analgesics namely paracetamol, ketorolac, ibuprofen, tramadol and diclofenac in one, three and five days of the postoperative administration of the analgesics. **Methodology:** In the present study, twenty five systemically healthy male subjects were included who were undergoing non-surgical extraction of mandibular third molar due to grossly decayed tooth. The subjects were divided into five groups with five subjects in each group according to the analgesic they had received postoperatively; namely paracetamol, ketorolac, ibuprofen, tramadol and diclofenac. Pain was assessed by using a Visual Analog Scale (VAS) respectively on one, three and five days of administration of analgesics postoperatively. A data was collected on the respective days. The recorded data was tabulated and analyzed accordingly. As the data for this study were collected at different time points, analysis for the longitudinal study was done. **Result:** The outcome of the present study revealed that the efficiency of all the analgesics was almost similar with a sound management of acute postoperative pain. According to results, ketorolac has shown a relatively better effect on the pain control after one day of administration of the drug. After three days of administration of the drugs, the efficacy of all the analgesics except that of paracetamol was almost similar and the efficiency of all the analgesics was equal after the five days as all them could control the pain successfully and there was no pain experienced by any the patients after five days of the dental procedure. Moreover, the non- NSAID i.e., tramadol also had shown similar efficiency as that of NSAIDs. Thereby, in the present study, the analgesics have shown almost equal efficacy at different time points. **Conclusion:** This study has demonstrated that there was no significant difference in the efficiency of all the analgesics included in the present study and they were able to alleviate the postoperative pain evaluated at different point of time.

Keywords: Analgesia, dental pain, nonsteroidal anti-inflammatory drugs, opioid analgesics, third molar.

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INTRODUCTION

According to the International Association for the Study of Pain (IASP), the pain can be described as “an unpleasant sensory or emotional experience associated with actual or potential tissue damage, or described in terms of such damage” [1, 2]. The pain control, especially controlling the postoperative pain holds great importance in the management of the

patient. Certainly, the postoperative pain is an inevitable outcome of any surgical procedure and the most studied is the pain related to oral surgery. The most common complaint which is encountered by the clinician is the pain for which the patient seeks solution and report to the health care giver. Among the most acute postoperative painful conditions, specifically the dental pain after the third molar extraction is said to be

one of the most painful [3]. The extractions of third molars encompasses a large number of cases in the contemporary oral surgical practice and it requires much surgical skill as well as the planning during both preoperative diagnosis of the case and postoperative management of the patient [4]. The pain experienced following the surgery of third molar done under the local anesthesia has been shown to be of short duration and commonly reaches to its maximum intensity in the initial postoperative period and therefore, in most of the cases, the patients require some form of the analgesic to manage the painful situation [5]. In general, it is found and accepted that the pain following the third molar surgery reaches moderate-to-severe intensity within first five hours after the surgery. However, there are studies that shows that the postoperative pain reaches to its peak intensity during the first eight hours after the surgery [6]. Apart from analgesics, opiates are also the standard of management of the moderate-to-severe postoperative pain. Most of the opioids used in the clinical practice produce analgesia by activating the opioid receptors on neurons of the pain transmission pathway. The pain of dental extraction especially third molar extraction is mostly moderate to severe pain, which is customarily treated with the nonsteroidal anti-inflammatory drugs (NSAIDs) for 2–3 days [7-9]. The advantage of NSAIDs is that they act as analgesic as well as anti-inflammatory and therefore they are the rational choice alleviating pain associated with inflammation [10, 11]. At the same instant, the NSAIDs are also liable to cause the gastrointestinal adverse effects such as gastritis and peptic ulcer and thereby should be used cautiously. Opioid pain medication like tramadol is also used to treat moderate to moderately severe pain. Analgesics such as tramadol, which are non-NSAIDs, can be given to such patients having postoperative pain. The excellent clinical model for acute pain is the dental extraction, especially the third molar extraction pain because the pain can be debilitating. The wisdom tooth surgery has been commonly used in the studies in order to investigate the efficacy of single analgesic or combination of analgesics [12-15]. This study was designed to compare the analgesic efficacy of paracetamol, ketorolac, ibuprofen, tramadol and diclofenac for relieving the postoperative pain in the patients undergoing third molar extraction.

MATERIALS AND METHODS

This is a prospective randomized study where twenty five systemically healthy male subjects who required non-surgical extraction of mandibular third molar due to grossly decayed tooth were included. All the subjects who were included in the study were given information regarding the procedure. The patients were randomly divided into five groups according to the received analgesics postoperatively namely paracetamol (500mg TID), ketorolac (10mg BD), ibuprofen (400MG BD), tramadol (100mg TID) and diclofenac (50mg BD). The ideal dosage was given as per pharmacopoeia.

Inclusion criteria- age group 20–30 years, subjects who were willing to participate. Exclusion criteria- Medically compromised subjects, female subjects, subjects who were not willing to participate and the subjects allergic to the drugs. The efficiency of the analgesics had been evaluated by using 10-cm visual analog scale (VAS) were zero means no pain and 10 unbearable pain after 1, 3 and 5 day of extraction respectively.

The data was recorded on respective days and was tabulated for further evaluation and statistical analysis was done accordingly.

RESULTS

Twenty five male subjects participated in the study that were divided in the five groups (5 subjects in each group) in respect to the analgesic they received postoperatively namely paracetamol, ketorolac, ibuprofen, tramadol and diclofenac. After one day, the efficiency was more of ketorolac as compared to other (Figure-1). After three days (Figure-2), the efficiency of almost all the analgesics were same except the paracetamol, in which mild pain experienced was more as compared to the other analgesics and after five days (Figure 3), all analgesics had almost same efficiency and pain was completely alleviated.

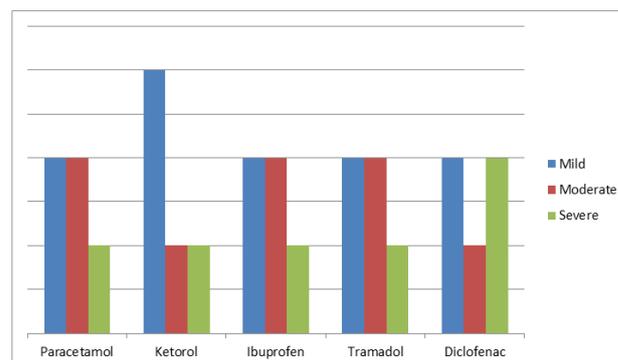


Fig-1: Efficiency of respective analgesic after one day of administration of analgesics

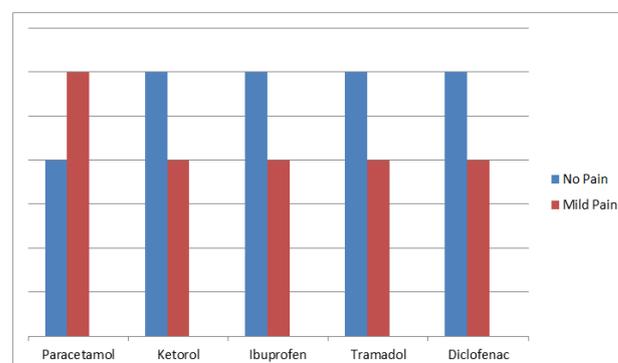


Fig-2: Efficiency of respective analgesic after three days of administration of analgesics

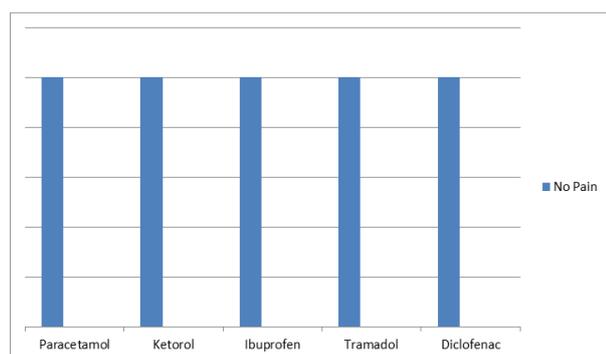


Fig-3: Efficiency of respective analgesic after five days of administration of analgesics

DISCUSSION

Controlling the postoperative pain is one of the most crucial aspects of the management of surgical patients. There are various drugs which are used to alleviate the postoperative pain. These are mainly categorized into two groups, i.e., nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids [16]. Third molar extraction is the most common outpatient procedure in the department of oral surgery. Normally, the extraction is followed by an inflammatory reaction which is characterized by pain, swelling, and trismus [17]. This postoperative pain management has been studied extensively with various NSAIDs [18]. Multiple studies have been done on single as well as combination therapy of several analgesics given postoperatively. Patients often experience severe pain after the removal of the third molar. Nonsteroidal anti-inflammatory drugs (NSAIDs) have gained popularity for relieving pain after various kinds of major as well as minor surgical procedures. The mechanism of action of NSAIDs is by decreasing the biosynthesis of prostaglandins (inflammatory mediator) by inhibition of the enzyme cyclooxygenase (COX). Prostaglandins, prostacyclin (PGI₂), and thromboxane A₂ (TXA₂) are produced from the arachidonic acid by the enzymes cyclooxygenase (COX) which exists in two isoforms, namely a constitutive (COX-1) and an inducible (COX-2). COX-1 carried out “housekeeping” functions and is present in most of the cells of the body, whereas COX-2 is not normally present in the body but is induced by certain cytokines, serum factors and other signal molecules at the site of inflammation [19-23]. The opioid analgesics act as agonists at the opioid receptors in the central nervous system, although some opioids have both agonist as well as antagonist effects. In comparison to pure agonists, agonist-antagonist drugs have less potential for drug abuse in the patients with a known history of abuse/addiction, and studies have shown that they may not induce a withdrawal syndrome in patients already physically dependent on opioids, though caution is advised in this setting. However, the agonist-antagonist medications have a ceiling effect for analgesia or pain. In general, the acute pain is best treated with the short-acting pure agonist drugs, while the chronic pain is best treated with the longer-acting

pure agonist drugs. The adverse effects related to the opioids are sedation, nausea, vomiting, constipation and pruritus. It is possible that it can cause the respiratory depression but it is rare when opioids are administered in appropriate doses [24]. According to a study, the efficiency and the safety of NSAIDs analgesic in the management of the acute postoperative dental pain have revealed that ketorolac has a greater global efficacy. Another study on the third molar extraction by Fricke *et al.*, [25] found that 30 mg of ketorolac was significantly better than the 50 and 100 mg pethidine. In the present study the efficiency of ketorolac after one day of postoperative administration was highest as compared to other analgesics. Ketorolac exhibits the analgesic activity mediated by the peripheral effects. At the analgesic doses, it has minimal anti-inflammatory action and antipyretic activities. It is also a potent inhibitor of platelet aggregation. Ketorolac does not possess anxiolytic or sedative properties and is also not an anesthetic agent. It is stated that ketorolac can be used alternatively to opioid and also to other nonsteroidal analgesics in relieving moderate to severe postoperative pain. In the present study, the postoperative pain was evaluated by the Visual Analog Scale (VAS). VAS is a 10cm long line representing the continuum of the pain experienced by the patient. The two terminal ends have the marking as no pain on the edge of zero cm and the worst possible pain on the edge of 10cm. The participants are oriented in order to mark their pain intensity experienced on a point of this line and the scores may vary from zero to 10. Scores are obtained by measuring, in centimeters; the distance between the edges anchored by the words no pain and the point marked by the participant. The advantage of the scale is that it is easy to apply. Pain evaluation including that of the postoperative pain by VAS is well accepted. The present study has used VAS without any pre-existing marks to prevent any type of bias when the patients marked the experienced intensity of pain. NSAIDs are known to cause gastrointestinal side effects like gastric irritation which may lead to ulceration. They also have an antiplatelet effect which can inhibit the platelet aggregation and can cause bleeding disorders. Despite of the presence of inflammatory component, one of the drugs used in this study was a non-NSAID (tramadol), so that the comparison of the efficiency of the ideal dosages of different analgesics can be determined. The present study attempted to evaluate the efficiency of the analgesics after non-surgical extraction of third molar. The postoperative pain was assessed after 1, 3 and 5 days of administration of the analgesics. The study has shown that the efficacy after one day of administration of various groups of analgesics, ketorolac was the most efficient in postoperative pain (Figure 1), while the efficiency of paracetamol, ibuprofen and tramadol was also similar and that of diclofenac was least. After three days of administration of analgesics, the efficiency to control pain is almost similar for ketorolac, ibuprofen, tramadol and diclofenac while that of paracetamol was

least. After five days of administration of analgesics, the efficiency of all the analgesics was same as they all were able to completely control the postoperative pain. According to these results of the present study, we can infer that there is no significant difference in the efficacy of the analgesics administered postoperatively. All the analgesics have shown almost equal efficacy at different time points.

CONCLUSION

This analysis of randomized clinical trial has presented the efficacy of the various analgesics for acute post-operative dental pain control. We have identified that all the analgesics were of almost similar efficacy and moreover, the overall reduction of pain in all the groups of subjects has no significant difference. Although, it was noted that ketorolac is more effective for immediate pain reduction than other analgesics when evaluated after one day of administration of analgesics.

This study also demonstrated that postoperative administration of tramadol is equally effective as traditional NSAIDs in relieving pain in the after the mandibular third molar extraction, and therefore, it can be tried in patients who are intolerant to NSAIDs. The present findings showed that there is no statistically significant difference between the five treatment groups. Hence, the clinician can use any of the given analgesic agents for the management of mild, moderate or severe postoperative dental pain. However, a firm conclusion regarding the time of intervention (i.e., pre and postextraction) for optimal pain control is still a point that needs clarification and further analysis is required.

REFERENCE

- de Santé, H. A. (2005). Prévention et traitement de la douleur postopératoire en chirurgie buccale. *Recommandations pour la pratique clinique*.
- Merksey, H. N. B. (1994). Pain terms: A current list with definitions and notes on usage. In: Merksey, H. N. B, Ed. IASP Task Force on Taxonomy, Seattle: IASP Press.
- Abbas, S. M., Kamal, R. S., & Afshan, G. (2004). Effect of Ketorolac on Postoperative Pain Relief in Dental Extraction cases-a comparative study with Pethidine. *Journal-Pakistan Medical ASSOCIATION*, 54(6), 319-321.
- Susarla, S. M., & Dodson, T. B. (2004). Risk factors for third molar extraction difficulty. *Journal of oral and maxillofacial surgery*, 62(11), 1363-1371.
- Comfort, M. B., Tse, A. S. K., Tsang, A. C. C., & McGrath, C. (2002). A study of the comparative efficacy of three common analgesics in the control of pain after third molar surgery under local anaesthesia. *Australian dental journal*, 47(4), 327-330.
- Khiavi, R. K., Pourallahverdi, M., Pourallahverdi, A., Khiavi, S. G., Oskoue, S. G., & Mokhtari, H. (2010). Pain control following impacted third molar surgery with bupivacaine irrigation of tooth socket: a prospective study. *Journal of dental research, dental clinics, dental prospects*, 4(4), 105-109.
- Alling, C. C., & Alling, R. D. (1993). Indications for management of impacted teeth. In: Alling, C. C., Helfrick, J. F., & Alling, R. D., editors. *Impacted teeth*. Philadelphia: W. B. Saunders; 46-49.
- Howard, B. G., & Akil, H. (2006). Opioid Analgesics. In: Brunton, L. L., Lazo, J. S., Parker, K. L., editors. *Goodman and Gilman's: The Pharmacological Basis of Therapeutics*. 11th ed. New York: Mc Graw Hill; 547-90.
- Dale, M. M., Rang, H. P., Ritter, J. M., & Flower, R. J. (2006). Analgesic drugs. Rang and Dale's *Pharmacology*, 6th ed. Philadelphia: Churchill Livingstone; 588-609.
- Alpaslan, C., Alpaslan, G., & Uğar, D. (1997). Postoperative pain control by single doses of piroxicam administered sublingually and aspirin. *Journal of Marmara University Dental Faculty*, 2(4), 658-664.
- Bloomfield, S. S., Barden, T. P., & Mitchell, J. (1976). Aspirin and codeine in two postpartum pain models. *Clinical Pharmacology & Therapeutics*, 20(4), 499-503.
- Cheung, C. W., Choi, W. S., Leung, Y. Y., Lui, F., Ng, J. K. F., Hei-Ho, A. M., & Irwin, M. G. (2012). A double-blind randomized crossover study to evaluate the timing of pregabalin for third molar surgery under local anesthesia. *Journal of Oral and Maxillofacial Surgery*, 70(1), 25-30.
- Qi, D. S., May, L. G., Zimmerman, B., Peng, P., Atillasoy, E., Brown, J. D., & Cooper, S. A. (2012). A randomized, double-blind, placebo-controlled study of acetaminophen 1000 mg versus acetaminophen 650 mg for the treatment of postsurgical dental pain. *Clinical therapeutics*, 34(12), 2247-2258.
- Hassan, S. S., Ahmed, A., Rai, M., & Kalappa, T. M. (2012). Analgesic efficacy of tramadol and butorphanol in mandibular third molar surgery: a comparative study. *J Contemp Dent Pract*, 13(3), 364-70.
- Moll, R., Derry, S., Moore, R. A., & McQuay, H. J. (2011). Single dose oral mefenamic acid for acute postoperative pain in adults. *Cochrane Database of Systematic Reviews*, (3).
- Raritan, N. J. (2008). Tapentadol [package insert]. Titusville, N. J. USA: Ortho-McNeil Janssen Pharmaceuticals, Inc.
- Cork, R. C., Isaac, I., Elsharydah, A., Saleemi, S., Zavisca, F., & Alexander, L. (2004). A comparison of the verbal rating scale and the visual analog

- scale for pain assessment. *The Internet Journal of Anesthesiology*, 8(1), 23-38.
18. Swadia, V. N., & Shah, M. B. (1999). Comparative evaluation of ketorolac, tramadol and diclofenac for postoperative pain relief in minor surgical procedures. *Indian J Anaes*, 43, 64-66.
 19. Wade, W. E., & Spruill, W. J. (2009). Tapentadol hydrochloride: a centrally acting oral analgesic. *Clinical therapeutics*, 31(12), 2804-2818.
 20. Afilalo, M., Etropolski, M. S., Kuperwasser, B., Kelly, K., Okamoto, A., Van Hove, I., ... & Haeussler, J. (2010). Efficacy and safety of tapentadol extended release compared with oxycodone controlled release for the management of moderate to severe chronic pain related to osteoarthritis of the knee. *Clinical drug investigation*, 30(8), 489-505.
 21. Singh, D. R., Nag, K., Shetti, A. N., & Krishnaveni, N. (2013). Tapentadol hydrochloride: A novel analgesic. *Saudi journal of anaesthesia*, 7(3), 322-326.
 22. Kleinert, R., Lange, C., Steup, A., Black, P., Goldberg, J., & Desjardins, P. (2008). Single dose analgesic efficacy of tapentadol in postsurgical dental pain: the results of a randomized, double-blind, placebo-controlled study. *Anesthesia & Analgesia*, 107(6), 2048-2055.
 23. Hawker, G. A., Mian, S., Kendzerska, T., & French, M. (2011). Measures of adult pain: Visual analog scale for pain (vas pain), numeric rating scale for pain (nrs pain), mcgill pain questionnaire (mpq), short-form mcgill pain questionnaire (sf-mpq), chronic pain grade scale (cpgs), short form-36 bodily pain scale (sf-36 bps), and measure of intermittent and constant osteoarthritis pain (icoap). *Arthritis care & research*, 63(S11), S240-S252.
 24. Williamson, A., & Hoggart, B. (2005). Pain: a review of three commonly used pain rating scales. *Journal of clinical nursing*, 14(7), 798-804.
 25. Fricke, J., Halladay, S. C., Bynum, L., & Francisco, C. A. (1993). Pain relief after dental impaction surgery using ketorolac, hydrocodone plus acetaminophen, or placebo. *Clinical therapeutics*, 15(3), 500-509.