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Clinical evaluation of analgesic efficacy of Tapentadol and Ketorolac in mandibular third molar surgery- A comparative study

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Abstract

Introduction: *The surgical removal of impacted mandibular third molars is one of the most commonly performed procedures in oral surgery. Postoperative complaints such as pain, trismus, and swelling affect the quality of life in patients.*

Materials and Methods: *A comparative study of the 32 patients, equally allocated to receive ketorolac and trapentadol respectively. As the data for this study were collected at different time points, analysis for the longitudinal study was done. Pain level was measured in five-ordered categories. As we had ordinal data in our study, we first checked for marginal homogeneity through Cochran-Mantel-Haenszel test.*

Results: *In the present study, the results show that there is no statistically significant difference between the two treatment groups (P = 0.2015). According to results, there is no significant group by time interaction, which means both drugs have shown almost equal efficacy at different time points. Similarly, there is no difference in efficacy of the two drugs across gender level.*

Conclusion: *The present findings showed that there is no statistically significant difference between the two treatment groups; however, ketorolac is more effective for immediate pain reduction.*

Keywords: *Impaction, mandibular third molar, Pain, nonsteroidal anti-infl ammatory drugs, opioid analgesics,*

Introduction

Pain is the most common discomfort perceived by human beings. Dental pain specifically after third molar extraction is said to be one of the most acute pain.[1] Extractions of the third molars require much planning and surgical skill during both preoperative diagnosis and postoperative management.[2]The pain experienced following the third molar surgery under local anesthesia has been shown to be of short duration and reaches its maximum intensity in the early postoperative period.[3]Treating the patient before the development of significant pain is consistent with the current trends toward more aggressive, preventive, and systematic approaches to pain management. Besides, it has been acknowledged that longer the pain remains uncontrolled, more sensitive patient may become to the painful stimuli.[4]Usually pain following the third molar surgery reaches moderate-to-severe intensity within the first 5h after surgery. On the other hand, there are some studies that show the postoperative pain reaches its peak intensity during the first 8 h after the surgery.[5]

Postoperative pain is usually treated using opiates. Most opioids produce analgesia by activating opioid receptors on neurons within the pain transmission pathway. Tapentadol is a centrally acting analgesic with a dual mode of action (i.e., m-opioid receptor agonism and norepinephrine uptake inhibition), distinguishing it from other commercially available opioids.[6]Opioid receptor binding has shown that tapentadol has higher binding affinity to m-opioid receptors than for delta(d)- and kappa(k)-opioid receptors.

In contrast, Ketorolac having prolonged analgesic activity (Power *et al*., 1990) has neither sedative nor anxiolytic properties (Brown *et al*., 1990).[7] With this context, the present research weights the comparison of the efficacy of two different analgesics after third molar extraction.

Materials and Methods

This study was conducted at the Department of Oral and Maxillofacial Surgery, involving 32 patients who required surgical extraction of impacted mandibular third molars. All the patients who were included in the study were given information regarding the procedure. The patients were randomly allocated to Group A and B respectively. Group A patients were given ketorolac 10 mg BD, and Group B patients were given tapentadol 50 mg BD postoperatively. Medically compromised patients, patients who have had any type of analgesic in the past

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48 h and patients allergic to the drugs were excluded from the study

All the procedures were performed under local anesthesia. Incision was given, and the operation site was exposed by reflecting mucoperiosteal flap, guttering of buccal bone, and sectioning of the third molar was done if required as per the standard impacted third molar surgery. After the surgery, operating site was irrigated with betadine and saline. The flap was primarily closed with 3-0 silk. Study participants were instructed to take medicine after 1 h of the surgery. Pain intensity was recorded at intervals of 1 h, 4 h, 10 h, 1 day, 2 day, and 3 day using the visual analog scale through telephonic conversation.

Results

Of the 32 patients, 16 were allocated to receive ketorolac and 16 patients were allocated to receive tapentadol. As the data for this study were collected at different time points, analysis for the longitudinal study was done. The main outcome variable, pain level was measured in five-ordered categories. Figure 1 shows the results of 1 h after surgery, Figure 2 shows the results of 4 h after surgery, Figure 3 shows the results of 10 h after surgery, Figure 4 shows the results of the 1st postoperative day, Figure 5 shows the results of the 2nd postoperative day, and Figure 6 shows the results of the 3rd postoperative day.

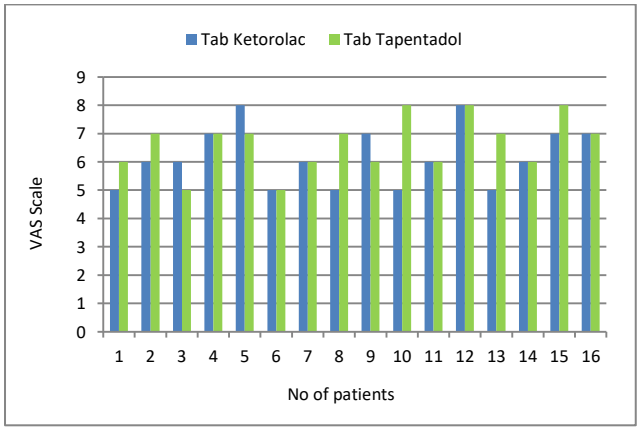

Figure 1: One Hour after surgery

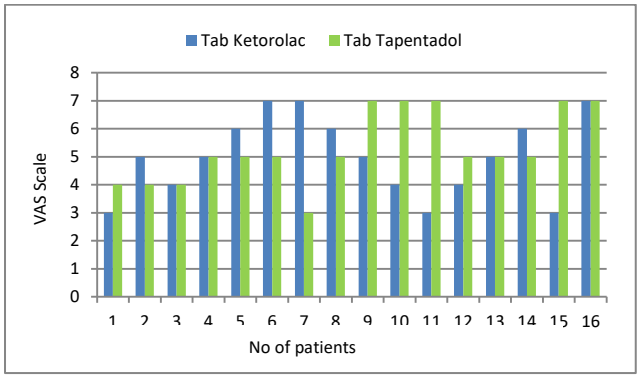

Figure 2: Four Hours after surgery

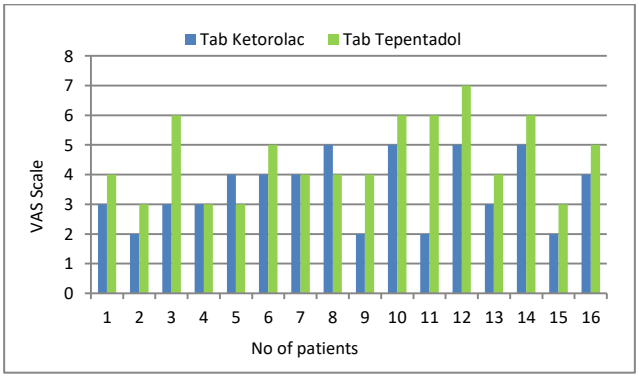

Figure3: 10 hours after surgery

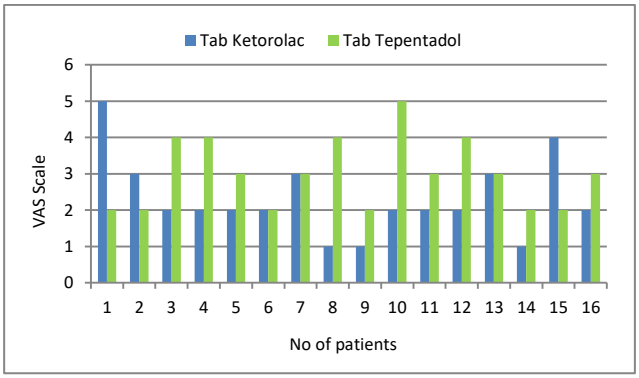

Figure4: First postoperative day

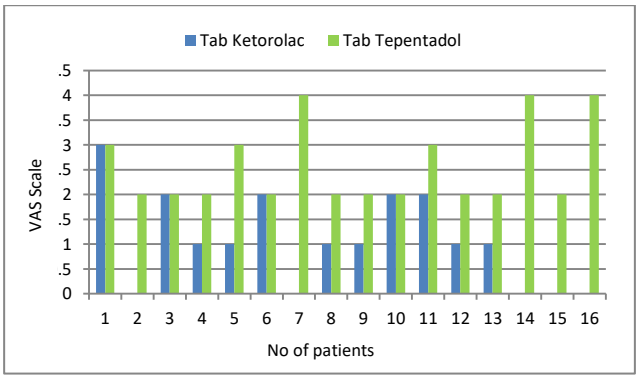

Figure 5: Second postoperative day

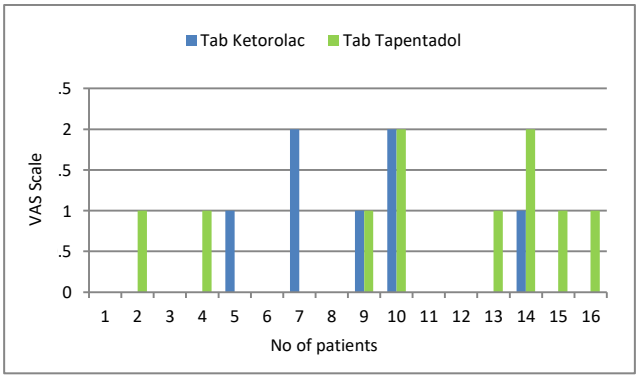

Figure 6: Third postoperative day

Discussion

Postoperative pain control is one of the imperative aspects of management of surgical patients.[8]Surgical removal of impacted third molar is followed by an inflammatory reaction characterized by pain, swelling, and trismus.[9]The management of this postoperative pain has been extensively studied with several NSAIDs.[10] NSAIDs reduce the biosynthesis of prostaglandins by inhibition of the enzyme cyclooxygenase (COX). Mechanism of action of NSAIDs prostaglandins, prostacyclin (PGI2), and thromboxane A2 (TXA2) are produced from arachidonic acid by the enzymes cyclooxygenase which exists in a constitutive (COX-1) and an inducible (COX-2) isoforms. COX-1 – "housekeeping" functions and present in most of the cells of the body. COX-2 – normally not present but induced by certain serum factors, cytokines, and other signal molecules at the site of inflammation.[11-15]Opioid analgesics act as agonists at opioid receptors in the central nervous system. Compared to pure agonists, agonist-antagonist drugs have less potential for abuse in 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, although caution is advised in this setting. However, agonist-antagonist medications have a ceiling effect for analgesia. In general, acute pain is best treated with short-acting pure agonist drugs, whereas chronic pain is best treated with longer-acting pure agonist drugs. Adverse effects related to opioids include sedation, constipation, nausea, vomiting, and pruritus. Respiratory depression is also possible but rare when opioids are given in appropriate doses.[16]

Ketorolac is a member of the pyrrolopyrrole group of nonsteroidal anti-inflammatory drugs.[16]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. In another study of the third molar extraction, Fricke *et al*.[17]found 30 mg of ketorolac was significantly better than 50 and 100 mg pethidine. Ketorolac exhibits analgesic activity mediatedby peripheral effects. At analgesic doses, it has minimal anti-inflammatory and antipyretic activities. It is also a potent platelet aggregation inhibitor. Ketorolac possesses no sedative or anxiolytic properties. It has been found that ketorolac is a useful substitute to opioid and other nonsteroidal analgesics in improving moderate-to-severe postsurgical pain.[17]

Tapentadol is a centrally active analgesic with a dual mode of action (i.e., m-opioid receptor agonism and norepinephrine uptake inhibition), distinguishing it from other commercially available opioids. Tapentadol is an immediate-release (IR) formulation for the relief of acute pain in adults, as an extended-release formulation for the management of chronic pain in adults. Tapentadol is also approved as an oral solution for the relief of acute pain in adults.[18,19] Clinical trials of patients with various types of moderate-to-severe acute pain have shown that tapentadol IR provides analgesia comparable to that of the pure m-opioid agonist, oxycodone IR, with improved gastrointestinal tolerability (lower incidence of nausea, vomiting, and constipation).[16]

We evaluated tapentadol IR for effects on moderate-to-severe pain after minor oral surgery, which is an established pain model for the assessments of analgesia, the results of which can be generalized to other surgical procedures. We evaluated both drugs comparison after 1 h which shows no significant difference with $P = 0.961$ and after 4 h also no significant difference with $P = 0.239$. Both drugs gave a significant different after 10 h, 1st day, 2nd day, and 3rd day with $P < 0.005$.

Of the 32 patients, 16 were allocated to receive ketorolac and 16 patients were allocated to receive tapentadol. As we had ordinal data in our study, we first checked for marginal homogeneity through Cochran–Mantel–Haenszel test. The results show that there is no statistically significant difference between the two treatment groups ($P = 0.2015$). According to the results, there is no significant difference between the groups by time interaction, which means both drugs have shown almost equal efficacy at different time points. Similarly, there is no difference in efficacy of the two drugs across gender level.

Conclusion

The overall reduction of pain using both groups has no significant difference, although ketorolac is more effective for immediate pain reduction than tapentadol.

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