THE EFFICACY OF PRE-EMPTIVE ANALGESIA IN CONTROLLING POSTOPERATIVE PAIN IN LOWER THIRD MOLAR SURGERY: A CLINICAL TRIAL

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ABSTRACT

Objective: The aim of this study was to evaluate the analgesic efficacy of preoperative versus postoperative administration of diclofenac sodium in the prevention of the postoperative pain following a lower third molar surgery.

Methods: A prospective randomized clinical trial was conducted on 73 patients who underwent surgical extraction of bilateral fully impacted lower third molars. Patients were randomised into two groups: group I were started on diclofenac sodium postoperatively, and group II were started on diclofenac sodium preoperatively, both groups were then prescribed a diclofenac sodium regimen for three days postoperatively and were advised to resort to an additional analgesic (paracetamol/codeine tablets) as a rescue medication when adequate relief from pain was not achieved. The analgesic efficacy of both regimens was tested.

Results: Results showed a significant difference between the two groups in terms of the analgesic efficacy in the first postoperative day. Significantly less pain and less need for additional analgesia was recorded in group II ($p<0.05$).

Conclusion: Preoperative treatment with diclofenac sodium provides effective relief from acute mild to moderate pain following third molar surgery compared to its postoperative administration.

Key words: Third molar surgery, Postoperative pain, Diclofenac sodium, Pre-emptive analgesia.

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Introduction

Third molar surgery is often performed on an ambulatory basis, and postoperative pain is a common complaint following this type of surgery. The trend towards day case surgery, with discharge on oral medication has highlighted the need for effective and safe analgesics using regimens that facilitate a rapid and swift recovery and quick discharge of patients. The ideal analgesic regimen for day case surgery management should provide good analgesia in the immediate period and enable early discharge without sedation, dizziness, or psychomotor impairment commonly found with opiates. This fact may need to be considered more seriously when we know that the standard of postoperative pain management on surgical wards is inadequate according to 50% of anesthesiologists, and 60% of inpatients report pain-related problems on hospital discharge.[1]

Excellent pain control following third molar surgery is essential for the delivery of optimal dental care and for the well-being of patients. Although the

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current armamentarium of local anesthesia and analgesic drugs are generally adequate, failure to control the immediate postoperative pain is frustrating to both patients and clinicians.[2]

It is well known that the natural metabolites of arachidonic acid, prostaglandins, and leukotrienes play a key role in the inflammatory process, since they act as mediators and modulators of that reaction by causing vascular dilatation, by increasing capillary permeability, by producing hyperalgesia, and by promoting the migration of leukocytes and macrophages to the site of inflammation. Since nonsteroidal anti-inflammatory drugs (NSAIDs) inhibit the enzyme cycolooxygenase and thus reduce the synthesis of prostaglandins PGE2 and PGI2, those drugs can be used for the control of pain, trismus, and swelling.[3,4]

The NSAIDs are considered the optimum choice for the management of postoperative pain following the surgical removal of third molars. The short acting opioids such as fentanyl or alfentanil are often used intra-operatively for more painful procedures; while the longer-acting opioids such as morphine are best avoided in the day case patients, as their side effects (nausea, vomiting, constipation and respiratory depression) are deleterious and expensive and may be more common than generally believed. Moreover the NSAIDs are superior to opioids in their anti-inflammatory action.[5,6]

Because pain after surgical removal of wisdom teeth is expected, prevention of pain is a better management strategy than treating the pain once it has occurred. Treating patients before they develop pain is considered a more humanitarian and enlightened approach to patient care and is consistent with the current trends toward more aggressive, preventive, and systemic approach to pain management. This approach will prevent or reduce the hyperalgesia state and inhibit inflammation and pain by reducing the synthesis of prostaglandins in response to surgical trauma. Moreover, it has become recognized that the longer pain remains uncontrolled, the more sensitive the patient becomes to painful stimuli. Once nociception is unregulated through both central and peripheral mechanisms, perception of pain is altered, and hyperalgesia can occur. Also, the rapid or preoperative analgesic intervention may prevent the upregulation (wind-up) of the nociceptve system within the central nervous system.[7,8,9]

The aim of this study is to compare the analgesic efficacy of preoperative versus postoperative administration of diclofenac sodium in the prevention of the postoperative pain following lower third molar surgery.

Methods

A prospective randomized clinical trial was conducted on 73 patients who underwent surgical extraction of bilateral fully impacted lower third molars at Prince Ali Military Hospital during the period between March and December 2003. All cases involved bone removal as part of the surgical procedure and were evaluated preoperatively by radiographs. All cases that showed only soft tissue impaction were excluded from our trial. All patients were verbally consented for the proposed surgical procedure and a full explanation was provided to them.

Patients were divided randomly into two groups in a simple alternate pattern. Group I (n=36) patients were given 100mg of a sustained release diclofenac sodium tablet one hour after surgery before leaving the day case ward, and advised to take another 50mg tablet of diclofenac sodium 8 hours later. On the second day they were requested to take 150mg of diclofenac in three divided doses for three consecutive days. Group II (n=37) patients received the same regimen except that they were given their first dose of 100mg sustained release diclofenac sodium tablet two hours prior to surgery, and then continued on the same analgesic regimen as the first group. Patients in both groups were requested to resort to an additional analgesic (paracetamol/ codeine tablets) as a rescue medication when adequate relief from pain was not achieved.

All surgeries were performed in the operating theatre by the same surgeon under local anesthesia and intravenous sedation. A standardized technique involving the classical envelope flap with a sulcus incision was used. All patients were discharged on the same day of surgery. The study was conducted in the morning so as to allow for a long evaluation period. The estimation of the complexity of the surgical procedure was based on duration of the operation.

Patients with history of peptic ulcer disease, asthma, haemorrhagic diathesis, or renal impairment were excluded from the study. All patients were given the same antibiotic regimen of 500mg oral amoxicillin three times daily, or erythromycin one gram twice daily.

The patients were requested to provide an overall evaluation of the pain intensity in a form of 4-point

Table I. Pain intensity in the two groups at different time points

Time Point / Pin Score	6 hrs. Post Op.		12 hrs. Post Op.	
Pain score	**0 & 1**	**2 & 3**	**0 & 1**	**2 & 3**
Group I	11 (30.55%)	25 (69.44%)	14 (38.88%)	22 (61.11%)
Group II	19 (51.35%)	18 (48.64%)	22 (59.45%)	15 (40.54%)

Table II. Need for additional analgesia in both groups

Rescue Analgesia / Group	Yes	No
Group I	19 (53.0%)	17 (47.0%)
Group II	11(29.7%)	26 (70.3%)

numerical scale, when pain is absent "0", slight "1", moderate "2", or intense "3" at the two time points: 6 hours following completion of surgery (the expected peak of pain in the first postoperative day) and 12 hours following completion of surgery. Each patient was given a special form to fill the pain score at the two above mentioned time points, besides recording any additional analgesia taken. All patients were reviewed on the second postoperative day in our outpatient clinics, and data of their pain scores was collected from them.

The pain-relieving efficacy for both regimens was tested by comparing the number of patients experiencing severe or moderate pain to the number of patients who reported slight or no pain at the two time points. Nonparametric statistical analysis of the results was done by means of a chi-square test.

Pain-relieving efficacy of each regimen was also assessed by comparing the number of patients who resorted to the additional rescue analgesia.

Results

In this trial we enrolled 73 patients (five patients were dropped from the study for failure to fill the pain score forms properly) who underwent surgical extraction of bilateral fully impacted lower third molars who managed to fill the pain score forms correctly and were reviewed on the second postoperative day; among them there were 32 male and 41 female patients. Their age range was 18-39 years (mean = 28).

There was no significant difference between the two groups in terms of the duration of the operations, which was used as an indicator for the complexity of the surgical procedure; the mean duration in minutes was 32 minutes for group I, and 30 in group II.

Table I summarizes data on the analgesic efficacy in both groups throughout the 12-hour period after surgery. The mean pain intensity scores at the first time point for the post treated group I was 2.45 and for the pretreated group II was 1.62, and at the second time point it was 2.40 for the post treated group, and 1.35 for the pretreated group. Statistical analysis of these results shows that patients pretreated with diclofenac sodium experienced significantly less pain throughout the 12-hour investigation period compared to those who received the diclofenac sodium only postoperatively ($p<0.05$).

The number of patients who resorted to rescue medication in both groups is shown in Table II. Among the pretreated group, 70.3% survived the first 12 hours following surgery without any need for rescue medication, while only 47.2% in the post treated group managed without the need for a rescue medication. Again these results show a significant difference ($p<0.05$) between the two groups in terms of the analgesic efficacy in case of preoperative administration of the nonsteroidal analgesic drug.

Discussion

Postoperative pain is considered a main reason for the delayed discharge and unanticipated hospital admission of outpatients. Efforts should be made to develop effective strategies for the prevention and treatment of postoperative pain in the ambulatory surgical patient.[10]

The debate on preoperative administration of analgesics is not new, but unfortunately it is not common practice among surgeons to start their patients on analgesia prior to surgery, Ong *et al.* in their study comparing the effectiveness of preoperative administration of a selective COX 2 inhibitor demonstrated a significant reduction in both the total analgesic consumption and the need for rescue medications when it was administered preoperatively compared to the postoperative treated

group.[11] This supports the concept of nociceptive upregulation of both peripheral and central nervous systems leading to more intense postoperative pain.[11,12]

In this clinical trial we focused on the operative day of surgery as there is a general consensus that this is the critical period during which the pain peak occurs and most patients tend to improve by the following days. The pain in this type of procedure usually starts two hours after the procedure as the effect of the residual local anesthetic wears off and the full inflammatory response to surgery evolves, usually becoming most severe between 6-8 hours following surgery. Futhermore, we excluded patients with serious diseases such as uncontrolled hypertension, diabetes mellitus, blood diathesis, or any illness that might confound the results of the study, as it is speculated that pain existing prior to surgery may lead to central sensitization, thus affecting postoperative pain evaluation.[13]

This study demonstrated that pre-emptive administration of diclofenac sodium one hour preoperatively resulted in lower pain experience compared to postoperative administration. The preoperative administration of diclofenac sodium allowed the drug to reach maximal plasma levels before the surgical incision, allowing enough time for large concentration of the drug to be achieved at the target tissues before the enzyme cyclooxygenase was expressed as a result to tissue injury. This is in agreement with previous research that studied the effect of preoperative administration of indomethacin, that resulted in significant reduction of postoperative pain and swelling.[14]

There is a lot of literature that contradicts the results of this study or similar studies that support the importance of pre-emptive analgesia. Campbell *et al*. who found no clinical significance between patients taking preoperative tenoxicam and alfentanil compared with those who did not take any in bilaterally symmetrical oral surgery,[15] however Katz explained this as failure of he surgeon to achieve a sufficient peri-operative nerve blockade or to the development of central sensitization once the pharmacological action of pre-emptive analgesia has worn off.[16]

Conclusion

NSAIDs are considered excellent analgesics for preventing postoperative pain in third molar surgery. Diclofenac sodium is an example of this group of analgesics. Preoperative treatment with diclofenac sodium provides effective relief from acute mild to moderate pain following third molar surgery.

We strongly recommend preoperative administration of diclofenac sodium for prevention of postoperative pain, as the analgesic and anti-inflammatory properties of non steroidal anti-inflammatory drugs are best employed when given preoperatively before tissue damage occurs and the whole inflammatory process takes place.

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