

A COMPARATIVE SPLIT MOUTH STUDY TO EVALUATE THE ANALGESIC EFFICACY OF “DICLOFENAC TRANSDERMAL PATCH” AND “DICLOFENAC INTRAMUSCULAR INJECTION” IN THE IMMEDIATE POST OPERATIVE PERIOD IN PATIENTS UNDERGOING IMPACTED MANDIBULAR THIRD MOLAR REMOVAL

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Abstract

Introduction: Successful surgical treatment is based on correct surgical techniques and the prevention and management of postoperative pain and complications. For postoperative analgesia, multimodal combinations are prescribed nowadays. **Aim:** The present study aims to evaluate the analgesic efficacy of diclofenac trans-dermal patch and diclofenac intramuscular injection in immediate post-operative patients after extraction of impacted mandibular 3rd molar and the objective is to evaluate the side effects associated with both the modalities and to compare the analgesic efficacy of two modalities. **Material and Methods:** In this study, eighty bilaterally impacted third molars were selected. The study drugs (trans-dermal Diclofenac patch and Diclofenac intramuscular injection) were divided into two groups Group A (40 cases) and Group B (40 cases). Post-operative self-evaluation by the patient for pain was done. It was recorded at intervals of 2 hours, 8 hours, 16 hours, 24 hours, 2nd day and 3rd day using the Visual Analogue Scale. **Results and Discussion:** Statistically significant higher pain score observed among group B at 8 hours (Mean rank = 28.20; p= 0.001), 16 hours (Mean rank= 30.25; p= 0.001), 24 hours (Mean rank=30.50; p= 0.001), 2 days (Mean rank= 27.05; p= 0.001) and 3rd day (Mean rank= 26.50; p= 0.001) respectively after extraction when compared with group A. **Conclusion:** Transdermal diclofenac patch is an effective, non-invasive, and cost-effective way of managing post-operative pain and can be used as a modality to control pain in an immediate post-operative period.

Keywords: Impacted third molar, analgesia, diclofenac transdermal patch, diclofenac intramuscular injection, postoperative pain control.

INTRODUCTION

Successful surgical treatment is based on correct surgical techniques and the prevention and management of postoperative pain that may be associated with oxidative stress and complications. Many factors may influence pain intensity, such as the nature, duration, extent of the surgery, and psychological aspects like stress and anxiety¹. Pain is a very predictable experience of the post-operative phase. If the post-operative pain was not treated, it may cause many clinical psychological changes which result in poor quality of life and may increase morbidity and mortality². Based on experimental studies, control or prevention of pain by analgesics is better than treatment of pain itself. NSAIDs are the most common choice analgesics in dentistry³. However, today NSAIDs toxicity (such as seizures, hypotension, apnoea, coma, and renal failure) is of major concern due to their widespread use of them⁴. NSAIDs are most widely used to relieve post-surgical pain.

For postoperative analgesia, multimodal combinations are prescribed nowadays,⁵ Many other modes like infiltration of wounds using LA, the use of steroids or NSAIDs and epidural opioids administration have been recommended for the treatment of post-operative pain^{6,7}. Out of all these modalities, the NSAIDs have increased in popularity in the management of post-operative pain⁸. These drugs can be administered in a variety of routes, including oral, parenteral, inhalation as well as trans-dermal. When the analgesic drug is administered by the oral route, then there is loss of its concentration occurs before its systemic absorption. This loss is because of first-pass metabolism. The parenteral route is painful and associated with various side effects

because the drug goes directly to the systemic circulation⁹. The trans-dermal route is well accepted by the patients. It is easy and simple. It has very minimal side effects. It is not painful and provides a slower and constant delivery of drugs. Trans-dermal patches were first developed in the 1970s and the FDA approved it first time in 1979 for treating motion sickness. Scopolamine was delivered in the form of a three-day patch¹⁰. Nitroglycerin patch was approved in 1981 and these days various drugs are available in the form of patches like fentanyl, nicotine etc¹¹.

The analgesic efficacy of transdermal diclofenac patch has been studied in clinical situations like laparoscopic surgeries, third molar impactions, and periodontal¹³. They offer various advantages: non-invasive, painless, and prevention of first-pass metabolism. Transdermal patches are an alternative for patients with cognitive impairment or handicapped who cannot self-medicate. For a comparative study of the role of a drug in achieving postoperative analgesia, it is important to have comparable, standardized, and near-identical surgical procedures in all the study groups^{14,16}. Impacted third molars extractions are one of the commonly performed oral surgical procedures which fulfill these criteria being bilateral in most cases, providing scope for the split-mouth study where the patient acts as his/her control. Hence, we have selected impacted third molar extraction. While studies exist in a similar clinical situation, they have been of small sample sizes, without a comparable dose of the drug and the rate of drug delivery was not standardized.

Aim and Objectives: The aim was “To evaluate the analgesic efficacy of diclofenac trans-dermal patch and diclofenac intramuscular injection in immediate post-operative patients after extraction of impacted 3rd molar.” The objective was to evaluate the side effects associated with both the modalities and to compare the analgesic efficacy of two modalities.

Material and Methods:

The present study was approved by the Institutional ethical committee and review board (SU/2017/1226(33)).

Study Design: Comparative Split Mouth Randomized Control Trial.

Sample: A total of forty patients within the age group of 18-30 years, indicated for surgical removal of bilateral impacted mandibular third molar teeth were included based on the following inclusion and exclusion criteria. The study drugs (trans-dermal Diclofenac patch and Diclofenac intramuscular injection) were divided into two groups as Group A (40 impacted third molars) and Group B (40 impacted third molars). Inclusion Criteria were, age between 18-30 years, Bilaterally impacted mandibular third molars (Class B and Type 2 of Pell and Gregory Classification), the willingness (informed consent) of subjects to comply for the operative procedure as well as the entire duration and availability for post-operative follow-up. Exclusion Criteria were Patients with acute inflammation, known history of allergy to diclofenac or other NSAIDs, Uncontrolled diabetes, blood dyscrasias, immuno-compromise, psychiatric disorders, and uncontrolled seizures. Individuals who used analgesics were not included, since variability in the effects of drugs on subsequent pain levels could not be assessed accurately. **Methodology:** After obtaining the complete history, patients were examined clinically; radiographic evaluation was done using Pell and Gregory classification and the difficulty was assessed using Pederson's difficulty Index. All patients were explained about the procedure, its complications and the follow-up period involved in the study. The patients who were willing were enrolled for the study. Informed consent was taken for each patient. Procedure was done following aseptic precautions. All the patients were anesthetized by 2% lignocaine hydrochloride with adrenaline in 1:80000 concentrations. Access was gained through a Modified Ward's Incision and a muco periosteal flap was raised. The ostectomy was carried out with a 701 SS White straight fissure bur and copious normal saline irrigation. With adequate ostectomy, elevation of the tooth was carried out and was followed by thorough debridement of the extraction socket. Sectioning of the tooth was carried out whenever necessary. Extraction was performed and post-operative instructions were given. The duration of procedure was measured by the time lapse between incision and completion of suturing. In Group A, Trans-dermal Diclofenac patch (100mg) was used (Fig.1). In Group B, Diclofenac intramuscular injection (75mg) was used (Fig. 4). Antibiotics were given postoperatively to patients after extraction. Group A – Immediately at the start of the procedure, Transdermal patch was placed. After 24 hour's patient advised to take Tablet Paracetamol 650 mg two times in a day. The patient was advised to take the rescue medication (Tablet Tramadol 50mg) if required. Group B - Immediately at the start of the procedure, Diclofenac intramuscular injection was administered. After 24 hours patient advised to take tablet Paracetamol 650 mg two times in a day. The patient was advised to take the rescue medication (Tablet Tramadol 50mg) if required. The extractions on both the sides were performed by the same operator. The patients were handed over the Performa and asked to fill it with the necessary information. The patient was given the rescue medication (Tablet Tramadol 50mg). The second extraction procedure was done following the protocols followed by the first extraction.

Follow up Protocol: The patient was recalled on the 1st and 3rd postoperative days after extraction. The filled Performa was collected on 3rd postoperative day of extraction. Follow up was done till the 3rd post-operative day.

Evaluation Criteria:Pain: Post-operative self-evaluation by patient for pain was done. It was recorded at intervals of: 2 hours, 8 hours, 16 hours, 24 hours, 2nd day and 3rd day using Visual Analogue Scale. The 10 cm long pain scale was subdivided into 5 equal parts, one end corresponding to no pain, the other to extremely severe pain. It was recorded at 2 hours, 8 hours, 16 hours, 24 hours, 2nd days and 3rd days. Additional Medications (Rescue Medication): The need for additional medications was determined if the patient required rescue analgesic provided. The patient was asked to note the time of rescue medication intake, number of times the additional tablets taken if any. It was recorded at intervals of: 2 hours, 8 hours, 16 hours, 24 hours, 2nd day and 3rd day.

Results:

In this study Out of forty cases(80 impacted third molars) ,14 were female and 26 were male and based on the distribution of mean age among different sex, the mean age for male was 33.53 and for female was 33.86. Based on the Pederson Difficulty Index among the two groups, 13 were having minimally difficult index, 27 were having moderately difficult index. The pain scores were calculated based upon the VAS, distribution of pain scores at 2hrs after extraction among 2 groups displayed that in Group A, out of 40 impacted third molars; ten cases were reported with score 0, eight cases were reported with score 1, twenty cases were reported with score 2 and two cases was reported with score 4. In Group B, out of 40 impacted third molars; twelve cases were reported with score 0, twelve cases were reported with score 1, fourteen cases were reported with score 2 and two cases were reported with score 3.

Table 1: Distribution of pain scores at different time intervals after extraction among two groups

| Groups | | N | Mean Rank | Mann-Whitney U | P Value |
|--|---------|----|-----------|----------------|---------|
| Hours_2 | Group A | 40 | 21.80 | 174.000 | .455 |
| | Group B | 40 | 19.20 | | |
| | Total | 80 | | | |
| Hours_8 | Group A | 40 | 12.80 | 46.000 | .001* |
| | Group B | 40 | 28.20 | | |
| | Total | 80 | | | |
| Hours_16 | Group A | 40 | 10.75 | 5.000 | 001* |
| | Group B | 40 | 30.25 | | |
| | Total | 80 | | | |
| Hours_24 | Group A | 40 | 10.50 | 0.000 | 001* |
| | Group B | 40 | 30.50 | | |
| | Total | 80 | | | |
| Hours_48 | Group A | 40 | 13.95 | 69.000 | 001* |
| | Group B | 40 | 27.05 | | |
| | Total | 80 | | | |
| Hours_72 | Group A | 40 | 14.50 | 80.000 | 001* |
| | Group B | 40 | 26.50 | | |
| | Total | 80 | | | |
| *Significance set at 0.05;N-number of samples | | | | | |

Similarly the distribution of pain scores at 8hrs after extraction among two groups displayed In Group A, out of 40 impacted third molars; two cases were reported with score 1, twenty six cases were reported with score 2, six cases were reported with score 3 and two cases were reported with score 4. In Group B, out of 40 impacted third molars; four cases were reported with score 2, eight cases were reported with score 3, sixteen cases were reported with score 4 and twelve cases were reported with score 5. Pain score was significantly less among Group A as compared to Group B. The p values obtained suggested statistically significant difference in the efficacy of transdermal patch (p= 0.001). At 8hrs, 16hrs, 24hrs, 2nd day and 3rd days pain score was higher in Group B in comparison of Group A which was statistically significant. Table-1 explains there is statistically

significant higher pain score observed among group B at 8 hours (Mean rank = 28.20; $p= 0.001$), 16 hours (Mean rank= 30.25; $p= 0.001$), 24 hours (Mean rank=30.50; $p= 0.001$), 2 days (Mean rank= 27.05; $p= 0.001$) and 3rd day (Mean rank= 26.50; $p= 0.001$) respectively after extraction when compared with group A (Table 1) there is no significant difference of pain score found between two groups at 2 hours after extraction. This indicates up to 2 hours after the extraction both Group A and Group B shows equally efficient in preserving analgesia. But when the time progresses the analgesic efficacy of group B diminishes drastically and shows both statistically and clinically significant difference with that of group A. Based on the statistical data, for the pain VAS, the P value indicated moderately significant pain relief in transdermal patch group over diclofenac injection compared to at the 8th, 24 hour, 48 hour and 72hours intervals. There was statistically significant difference observed in p values obtained in the efficacy of transdermal patch over the subsequent two days of administration. Out of 40 patients in Group A, 38 patients didn't take rescue medicine, 1 patient took one tablet and 1 patient two tablets. In Group B out of 40 patients, 6 patients did not took any rescue medicine, whereas 12 patients took one tablet, 14 patients took two tablets, 6 patients had to take three tablets. Moreover, two patients had to take four tablets.

Discussion:

Post-operative pain control is a never-ending field of research as pain in the postoperative period does not bear a direct relationship with the surgical injury. Currently, analgesic combination Regimens (multimodal analgesia) are recommended for post-operative management of pain. The NSAIDs are well known for their gastric disturbances. Our study was a split mouth cross-sectional study, a total of 40 patients (80 impacted third molar removals) were performed. For right third molar [Group A] diclofenac Transdermal patch was given for pain management and for left third molar [Group B] diclofenac intramuscular injection was used. Many studies have been conducted in past to fine out better modalities for management of post-operative pain. Arora P and Mukherjee B (2002)¹² found that EC:PVP 2:1 showed better permeation properties as well as pain relief. In A study by PredelHG et al (2003)¹⁴ the results showed that the diclofenac transdermal patch was a safe and effective modality for pain control and can be administered in traumatic soft tissue injuries cases. They divided the patients into two groups. A 140mg diclofenac patch was given to a group and the other group was given a placebo patch once daily for 3 days Joshi et al. (2004)¹⁵ did a double-blind study in 119 patients who required third molar removal, The pain was recorded using VAS and VRS scale at the time interval of 15 min, 30 min, 1 hr, 3 hrs, 6 hrs and 24 hrs post-operatively, they did not find any significant differences among the concluded that the efficacy of NSAIDs and codeine 60mg in post-operative pain management after removal of impacted third molars. Mason et al (2004)¹⁶ also concluded that topical and transdermal preparations produced better results.

Conclusion:

The purpose of our study was to determine a better modality for post-operative analgesia following mandibular third molar surgery. A transdermal diclofenac patch is an effective, non-invasive, and cost-effective way of managing post-operative pain and can be used as a modality to control pain in an immediate post-operative period. Even the result that we got was statistically significant and it was a cross-sectional study conducted on a modest sample of forty subjects, studies with larger sample sizes and more longitudinal studies need to be carried out in the future to endorse the results observed in our study.

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