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TRANSDERMAL DICLOFENAC PATCH FOR PAIN CONTROL AFTER PERIODONTAL OSSEOUS SURGERY: A COMPARATIVE CLINICAL TRIAL.

Dental Science

Dr. Huda Hussain* Postgraduate Scholar, Department of Periodontology, Government Dental College and Hospital, Srinagar, J&K. 190010.*Corresponding Author

Prof. Suhail Majid Jan Head, Department of Periodontology, Government Dental College and Hospital, Srinagar, J&K. 190010.

ABSTRACT

Contemporary standards of patient care entail a complete painless perioperative experience. While periodontal surgery does not result in more discomfort than other dental procedures, a significant inflammatory reaction can be expected when osseous reshaping or resection is involved. This study compares the pain control efficacy of transdermal route with the conventional oral route of the most commonly implicated NSAID, diclofenac. Twenty chronic generalized periodontitis patients were included in a split mouth study design. After periodontal surgery requiring osseous reshaping was performed in one quadrant, twice daily dose of 50 mg diclofenac was prescribed for 3 days. Two weeks later, surgery was performed in the other quadrant, and a 100 mg transdermal diclofenac patch was placed at hairless skin, which was replaced every 24 hours for 3 days. Patients were asked to record the pain intensity and pain relief immediately after surgery, at 2 hrs, 4 hrs, 8 hrs, 12 hrs, 24 hrs, 48 hrs and 72 hrs postoperatively, using a four point scale. Paired t-test was used to assess the responses. A significantly lesser pain intensity and better pain relief was noted with oral diclofenac as compared to the transdermal route during the initial 12 hours after surgery. However, thereafter, the difference between the two treatments was statistically non-significant, with progressive decline in pain intensity over the 3 postoperative days. It was concluded that though the transdermal route resulted in lesser adverse effects and response fluctuations, for osseous periodontal surgery, oral diclofenac results in better pain control initially. 100 mg Transdermal diclofenac, if used, should be in a higher concentration or supplemented with other analgesics during the early postoperative period

KEYWORDS

Transedermal Diclofenac, Oral Diclofenac, Periodontal Osseous Surgery

INTRODUCTION

The success of a surgical procedure is conditioned by many factors, which include appropriate pain control and management. With regard to periodontal surgery, pain is a common complain, presented by 79% of patients after open flap debridement, 89% after gingivectomy, and 93% after flap surgery with osseous resection[1], with the postoperative pain being significantly higher after osseous resection and gingivectomy, as compared to Modified Widman flap surgery.[2]Thoughmany factors such as anxiety and nature of the procedure influence the perceived intensity of postoperative pain, nevertheless, it has been recommended that analgesics be used after periodontal surgery to achieve maximum patient comfort and minimize postoperative pain. In the present era of 'painless surgery', it has been recommended thatfor surgeries involving slight tissue damage, as is the case with periodontal surgery, NSAIDS alone or combined with paracetamol should be used[3].

Non-steroidal anti-inflammatory drugs (NSAIDs) are most widely used to relieve oral postsurgical pain. Diclofenac sodium is commonly prescribed NSAIDs, which has an anti-inflammatory and analgesic property. Through oral route, only 50% of the absorbed dose of diclofenac becomes systemically available due to first pass metabolism. However,due to high plasma concentration, oral diclofenac causes significant adverse reactions, like gastric irritation, ulcers, and allergies.[3]

Recently, transdermal patches have been introduced to overcome these disadvantages of oral analgesics. Transdermal drug delivery is an innovative pharmacological approach, which provides a leading edge over injectables and oral routes by increasing patient compliance and avoiding first-pass metabolism. When it is applied to the unbroken skin, transdermal drug delivery releases a drug at a constant rate into systemic circulation via stratum corneum.[4]With regard to transdermal delivery system for diclofenac, a controlled release matrix has been introduced (NuPatch, Zydus Cadilla,India), with proven efficacy for postoperative pain management after conventional and transalveolar extractions [4,5], as well as root coverage procedures [6] and dental implant placement. [7] In comparison to orally administered diclofenac, transdermal diclofenac diethyamine patches were found to provide comparable pain relief and better patient acceptance, with an advantage over oral diclofenac of lesser GI complications.

With this background, the present study was designed to assess the feasibility and efficacy of transdermally delivered diclofenac in comparison with conventional orally administered diclofenac for postoperative analgesia, adverse reactions (gastric irritation, allergy), and patient compliance following periodontal osseous resective surgery.

MATERIALS AND METHODS

The study was designed as a prospective, split mouth investigation, involving chronic periodontitis patients in the age group of 25-50 years. A sample size of 20 patients was required in order to obtain 90% power with a *P* value set at 0.05. The study protocol was reviewed by the institutional ethical committee, and patients were recruited subsequent to fulfilment of the inclusion criteria and obtaining informed consent.

Inclusion Criteria:

Systemically healthy patients diagnosed with chronic generalized periodontitis requiring resective osseous surgery in at least two quadrants.

Exclusion Criteria:

- History of systemic diseases.
- Patients undergoing treatment with analgesics or corticosteroids during the trial period.
- History or clinical evidence of allergy to oral diclofenac or transdermal patch.
- Patients suffering from peptic ulceration.
- Pregnant/lactating females.
- Smokers and alcoholics.

Treatment procedures

After completion of phase I therapy, flap surgery was performed in one quadrant under local anesthesia(lidocaine 2% and epinephrine 1:100000). Thereafter, oral diclofenac sodium 50 mg tablets were prescribed to be taken twice daily for three days.The patients were advised to use 0.2 % chlorhexidine mouthwash for plaque control during the first postoperative week, subsequent to which, sutures were removed and toothbrushing was re-instituted. Another week was allowed for complete washout of the drug, after which periodontal surgery was performed in the other quadrant. This time, a100 mg transdermal Diclofenac patch (Nu Patch® - Zydus-Cadilla labs) was applied to the hairless deltoid region after completion of the surgery, which was to be replaced for three days on different areas. The matrix controlled diclofenac transdermal patch is a flat and transparent transdermal delivery system (TDS) that provides continuous and

systemic release of diclofenac and is designed to remain at the site of application for 24 hours. It is used to relievemild to moderate postoperative pain. The patch is to be applied onthe skin, preferably in an area devoid of hair. The 100mg patch is 50 squarecm in size and achieves plasma levelsranging between 20 and 50ng/ml, which islesser when compared to the oral route, butare sustained for a longer time, and are intended to provide long-term effectiveness and convenience.

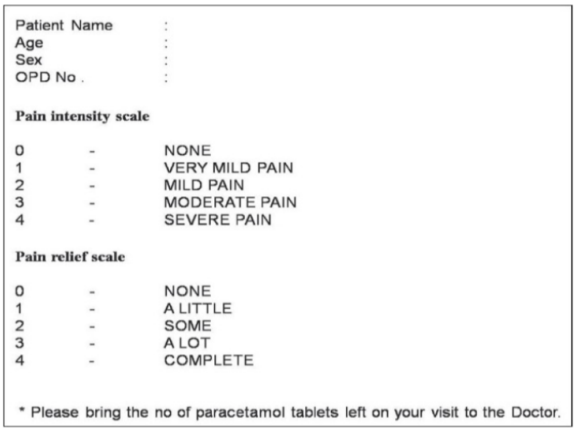
All surgical procedures were performed by a single operator and lasted an average of 60 minutes.

Data Collection

Each patient was given a Verbal Pain Intensity and Pain Relief Score Chart (both 5- point scales with values from 0 to 4) [Figure 1] for assessing pain intensity and pain relief at baseline (immediately before administration of tablet/application of transdermal patch), then 2, 4, 8, 12, 24, 48, and 72 hours postsurgically. In addition to pain intensity, adverse effects such as gastric discomfort, nausea, burning sensation, and pruritis were dichotomously recorded by noting the presence or absence of each adverse effect. Paracetamol 500 mg tablets were permitted to be used as rescue medication and a total of nine tablets were provided to each of the patients for the three postoperative days. The patients were asked to maintain a record of the number of paracetamol tablets consumed on the pain assessment charts and to return the remaining tablets to operator on their next visit. The patients' preference of oral diclofenac or transdermal patch was also assessed

Statistical analysis

The data hence obtained was statistically evaluated using the paired t-test. A P value of < 0.05 was considered to be statistically significant.


Patient Name :
Age :
Sex :
OPD No. :

Pain intensity scale

0 - NONE
1 - VERY MILD PAIN
2 - MILD PAIN
3 - MODERATE PAIN
4 - SEVERE PAIN

Pain relief scale

0 - NONE
1 - A LITTLE
2 - SOME
3 - A LOT
4 - COMPLETE

* Please bring the no of paracetamol tablets left on your visit to the Doctor.

Figure 1: Pain intensity and pain relief scores

RESULTS

The filled verbal pain intensity and pain relief score charts were collected from all the subjects and evaluated. An assessment of the intensity of pain revealed that there was a gradual decrease in the pain intensity scores from day one to day three with both the oral diclofenac tablets as well as with the transdermal patch. With regard to the variation in pain relief amongst the subjects, it was observed that all patients reported of complete or almost complete pain relief by the third day of therapy with either medication. In both groups of subjects, there was a gradual increase in pain relief scores over the three post operative days (Table-1,2; Figure 2,3).

Statistical analysis revealed that the difference in the pain intensity was significantly lower (Table 1) while the pain relief significantly higher (Table-2) with the oral tablets was higher for the first 12 hours after surgery, and not thereafter.

On comparing the temporal changes in pain intensity and pain relief, two peaks were evident for the oral treatment corresponding to the daily dose, whereas the graph for transdermal treatment was relatively smoother (Figure 2,3).

None of the patients on oral diclofenac therapy consumed paracetamol tablets, whereas two patients, when on transdermal patch therapy, consumed 2 paracetamol tablets each for pain relief.

Two patients when on oral diclofenac tablets complained of gastric acidity and burning sensation. Noadverse events were reported with the use of transdermal patch.

Table 1: Pain Intensity of test and control groups at different time points after surgery

	Mean		
Time point after surgery	Control	Test	P-value
0 (baseline)	3.65	3.72	0.122
2 hours	3.12	3.56	0.046*
4 hours	3.01	3.45	0.043*
8 hours	2.97	3.03	0.049*
12 hours	2.89	2.96	0.048*
24 hours	2.79	2.86	0.053
48 hours	2.40	2.45	0.123
72 hours	1.98	1.88	0.110

Table 2: Pain Relief in test and control groups at different time points after surgery

	Mean		
Time point after surgery	Control	Test	P-value
0 (baseline)	2.67	2.61	0.231
2 hours	3.34	2.92	0.048*
4 hours	3.25	2.98	0.045*
8 hours	3.12	3.01	0.049*
12 hours	3.45	3.13	0.045*
24 hours	3.52	3.43	0.102
48 hours	3.62	3.56	0.123
72 hours	3.71	3.80	0.110

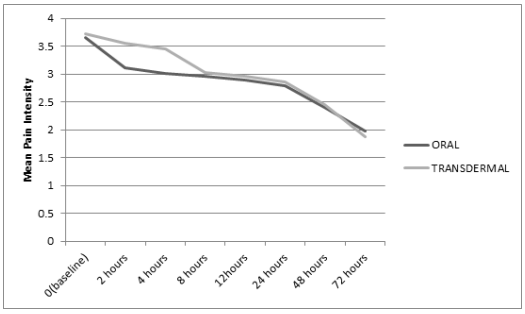


Figure 2: Changes in pain intensity over time

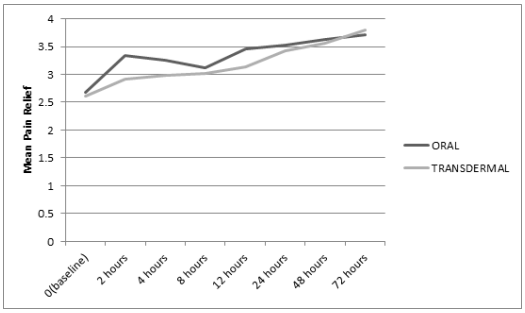


Figure 3: Changes in pain relief over time

Discussion

Dealing with post-operative pain remains an arena for never ending research with better formulations and modalities continuously being developed and tested. As far as periodontal resective surgery is concerned, the immense inflammatory response that follows decortication of bone results in considerable postoperative pain and swelling[2] , hence necessitating the need for proactive pain control measures to ensure patient comfort during the early postoperative hours. Diclofenac, a commonly precribed non-steroidal antiinflammatory drug is used to achieve this goal. In the present study, on evaluation of the effectiveness of two routes (oral and transdermal) of diclofenac administration, it was found that oral diclofenac may provide better pain relief than transdermal diclofenac patch during the early hours after osseous surgery. Similar results have been reported by **Bachilli et al (2009)**[8]. This may be due to the differences in peak plasma concentrations of the two routes, and the time taken to achieve them—the 50 mg tablet provides a maximum of 1.5µg/ml in 2-4 hours[9] whereas the 100 mg patch provides 0.05µg/ml in 10-12 hours[10], which is evidently insufficient to counteract pain after periodontal

osseous surgery. Pertinantly, this transdermal device (100mg) has been found superior to oral diclofenac for periodontal plastic surgery[6], and equivalent to it for extraction[4] and implant placement procedures[7], it seems that the inflammatory reaction provoked by decortication during osseous surgery may indicate the need for additional supplemental anti-inflammatory drugs, or a higher dose, if transdermal diclofenac is prescribed. Further studies are needed to verify these possibilities.

Statistical significant difference was noted between the treatments only for the first 12 hours, after which both treatments differed nonsignificantly from each other. It is known that post periodontal surgery, pain progressively lessens to almost diminish by 3 days[11]. As such, the decreasing pain intensity might have rendered it responsive to the sustained low dose delivered by the transdermal patch, and hence the efficacy of the two treatments became at par after the first postoperative day.

On the other hand, it was also seen that the fluctuations in pain intensity, necessitating a subsequent dose of medication, may be overcome by the use of transdermal delivery of diclofenac, as the latter maintains near uniform plasma concentrations for 24 hours [10]. Also it was possible to avoid the gastrointestinal side effects of diclofenac with this route of delivery. These are established advantages of transdermal medications. However, further research needs to identify the proper applications for new products, to be able to utilize pharmacological advances for patient benefit.

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