Original Research Article

Local anti-inflammatory and analgesic effect of 0.074% diclofenac mouthwash in post-operative periodontally treated patients

Roobal Behal[1*], Suhail Majid Jan[2]

[1]Consultant, [2]Professor and Head
Department of Periodontics, Government Dental College and Hospital, Shireen Bagh, Srinagar, Jammu and Kashmir, India
[*]Corresponding author email: **roobalbehal2006@yahoo.co.in**

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Abstract

Pain is the most pervasive and universal form of human distress. The costs of pain in human suffering and economic resources are extraordinary. It is the most common reason for seeking medical care, and it has been estimated that approximately 80% of physician office visits involve a pain component. Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most widely used class of drugs for the management of acute and chronic pain in dentistry. NSAIDs minimize edema, but they are associated with many adverse effects, like gastric irritability, as dyspepsia and gastric bleeding which lead to a number of contraindications. Diclofenac is a powerful anti-inflammatory and analgesic drug that is well suited for local use in the oral cavity. This study was conducted in order to determine the local anti-inflammatory and analgesic effect of 0.074% diclofenac mouthwash on patients with periodontal surgery. Twenty five chronic periodontitis patients (fifteen males and ten females) who were supposed to go for full quadrant flap surgery were selected for the study. The 10-point visual analog scale (VAS) was used to assess pain and the Modified Gingival Index (MGI). Additional parameters like swelling and burning sensation was evaluated on a 5-point scale (0=absent, 1=mild, 2=moderate, 3=intense, 4=not evaluated). Compared to baseline measurements, spontaneous pain was significantly reduced by diclofenac mouthwash on the first day of treatment which showed gradual decrease till 7th day. Other parameters, i.e. gingival inflammation, showed a highly significant reduction in the scores in the test group when compared to baseline. The new 0.074% diclofenac

mouthwash is an effective and tolerable medicinal product for post-surgical symptomatic relief. This topical formulation is sufficiently effective for pain relief after minor oral surgical procedures without subjecting the patients to systemic side-effects.

Key words

Diclofenac, Inflammation, Mouthwash, Pain, Periodontal surgery.

Introduction

Pain is primarily a psychological experience. It is the most pervasive and universal form of human distress and it often contributes to dramatic reductions in the quality of life. Episodes of pain can vary in magnitude from events that are mundane, but commonplace, to crises that are excruciating, sometimes intractable and not so common, but still not rare. The costs of pain in human suffering and economic resources are extraordinary. It is the most common reason for seeking medical care, and it has been estimated that approximately 80% of physician office visits involve a pain component. The etiology of post-operative pain is the progress of inflammation and swelling in the area of the procedure. The magnitude of this depends on the degree of tissue damage produced and on the extent of operative trauma. Tissue damage resulting from surgery induces the production of Cyclooxygenase-2 (COX-2), which in turn leads to the synthesis of prostaglandins (PGs), which sensitize pain fibers and promote inflammation [1]. Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most widely used class of drugs for the management of acute and chronic pain in dentistry. Managing acute post-operative pain is inherent to dental practice. NSAIDs affect the release of β-endorphin during post-operative pain [2]. Clinical trials have shown that NSAIDs are effective in the management of dental pain [2]. The post-operative sequel of dental procedures also includes inflammation due to tissue injury, most prominently edema. NSAIDs minimize edema, but they are associated with many adverse effects, like gastric irritability, which lead to a number of contraindications, as dyspepsia and more seriously gastric bleeding. Enteric coated formulations may reduce the likelihood of dyspepsia but they do not prevent gastric bleeding [3]. Thus, recent NSAID research has focused on the development of daily topical gels, toothpastes and rinses. In general, NSAIDs easily penetrate into the oral and gingival tissues to rapidly inhibit local gingival crevicular fluid PGE_2 levels within 1 h due to their lipophilic nature [3]. Data on the efficacy of a topical ketorolac rinse have also been reported [4]. According to these, rinsing twice daily with 0.1% ketorolac tromethamine significantly reduces alveolar bone loss and gingival crevicular fluid PGE_2 levels.

Diclofenac is a powerful anti-inflammatory and analgesic drug that is well suited for local use in the oral cavity. This results in decreased production of PG and thus reduces inflammation, swelling and pain. The drug also affects polymorphonuclear leukocyte function in vitro, thereby reducing chemotaxis, superoxide toxic radical production and neutral protease production and, thereby, reducing inflammation [5]. Thus, this study was conducted in order to determine the local anti-inflammatory and analgesic effect of 0.074% diclofenac mouthwash on patients with periodontal surgery.

Materials and methods

This randomized, double blind, placebo-controlled clinical trial was carried out and approved by the local research and ethical committee, Government Dental College and Hospital Srinagar, Jammu and Kashmir. Out-patients reporting to the Department of Periodontics were selected as per their availability after acquiring an Informed consent. Twenty five chronic periodontitis patients (fifteen males and ten females) who were supposed to go for full quadrant flap surgery were selected for the study. Subjects were in the

age range of 35–50 years and had minimum of 14 teeth with at least three posterior teeth in each quadrant. Patients who had systemic disease/condition that affected oral tissues, drug hypersensitivity to diclofenac and pregnant/ lactating women were excluded from the study. Patients who had been on systemic NSAID therapy during the last 3 months were excluded. A similar flap technique, i.e. modified flap operation by Kirkland, was performed, with a crevicular incision. Direct loop sutures were placed to close the flap edges. Periodontal pack was not given to prevent interference with the penetration of the drug into the gingival tissues. Subjects were randomized to receive either diclofenac mouthwash or placebo to rinse with 15 ml solution twice daily for 7 days after surgery. The 10-point visual analog scale (VAS) was used to assess pain and the Modified Gingival Index (MGI) [6] was used to assess the inflammation.

Additional parameters like swelling and burning sensation was evaluated on a 5-point scale (0=absent, 1=mild, 2=moderate, 3=intense, 4=not evaluated). Acceptability of the product was evaluated on a 4-point scale (0=unacceptable, 1=unpleasant, 2=acceptable, 3=pleasant). Spontaneous pain and burning were evaluated daily at 8AM for 7 days while redness and edema were evaluated after 3 and 7 days of treatment.

Data pertaining to the VAS score and swelling scores were analyzed using Mann-Whitney U-test for intergroup comparison. Data obtained for the MGI score was subjected to statistical analysis using Student's paired "t"-test for intergroup comparison. The level of significance was taken as 0.05 ($P<0.05$).

Results

Twenty five chronic periodontitis patients (fifteen males and ten females) with minimum of 14 teeth with at least three posterior teeth in each quadrant were selected by a convenience sampling method. All subjects completed the study. Compared to baseline measurements, spontaneous pain was significantly reduced by diclofenac mouthwash on the first day of treatment which showed gradual decrease till 7th day (**Table – 1**). After a week of treatment, the pain intensity was reduced to zero in 90% of the cases. While in the placebo group, slight worsening of the score was reported on the first day of treatment versus baseline (**Table – 1**). The difference between the two groups was statistically significant all throughout the course of the study. Comparing both the groups, reduction in pain score is significantly higher in the test group than in the control group (**Table – 1**). Other parameters, i.e. gingival inflammation, showed a highly significant reduction in the scores in the test group when compared to baseline at 7th day ($P <0.0467$) (**Table – 2**) and greater reduction in the control group when compared to baseline. However, when comparing both the groups, the difference was statistically significant at 7th day any time interval ($P <0.0467$) (**Table – 2**). Reduction in swelling was significant in the test group when compared to the control group (throughout the study period (**Table – 2**). Reduction in swelling with diclofenac was not significant ($P>0.05$) when compared to placebo group throughout the study (**Table – 3**). Mild burning was reported in few subjects rinsing with diclofenac mouthwash but none of the placebo group patients reported the same. Palatability was judged as pleasant/ acceptable in all cases.

Table - 1: Comparison of visual analog scale scores between the test and control groups.

	Baseline	**1st day**	**2nd day**	**3rd day**	**4th day**	**5th day**	**6th day**	**7th day**
Test Group	7.2	3.9	2.5	2.0	1.7	0.6	0.4	0.1
Control Group	7.3	7.4	6.4	5.8	4.9	3.9	3.1	2.4
***p*-value**	0.845	0.002*	0.0032*	0.045*	0.002*	0.001*	0.0002*	0.0001*
**** Significant using Mann-Whitney U-test (P≤0.05)***								

Table - 2: Comparison of modified gingival index scores between the case and control groups.

	Baseline	**3rd Day**	**7th Day**
Test Group	4.01±0.55	3.22±0.35	1.89±0.82
Control Group	3.87±0.65	2.98±0.37	2.21±0.21
P-value	**0.3242**	**0.4253**	**0.0467***
Significant using Student's unpaired t-test (P≤0.05)			

Table - 3: Comparison of swelling scores between the case and control groups.

	Baseline	**3rd Day**	**7th Day**
Test Group	1.75±0.65	0.85±0.76	0.07±0.09
Control Group	1.97±0.71	1.98±0.57	0.43±0.31
P-value	**0.07242**	**0.0853**	**0.34677**

Significant using Student's unpaired t-test (P≤0.05)

Discussion

The present study shows that diclofenac mouthwash 0.074% at a dose of 15 ml twice daily has a significant local analgesic effects (P<0.0001). The anti-inflammatory effect found was favorable although this was not significant. Diclofenac being soluble in water and its release is favored from aqueous solutions [7]. The new 0.074% diclofenac mouthwash has also overcome the previous disadvantages of insolubility and unpleasant taste. As most NSAIDs, diclofenac too appeared to be absorbed quickly when considering the brief contact of the solution with the oral mucosa, i.e. 1 min. The tolerability of the product has been confirmed to be good, with no adverse effects, except mild burning sensation in few subjects. In a previous study, the efficacy of 0.074% diclofenac mouthwash was evaluated in 79 patients with pain intensity at the end of anesthesia effect, equivalent to 54.8±15.1 of VAS. All parameters, i.e. spontaneous pain, redness and edema, showed significant improvement. The physician's and patient's final judgement recorded resolution/improvement in 94.1% of the cases, concluding that the mouthwash is efficacious and tolerable in the treatment of inflammatory condition of the buccal cavity following oral/periodontal surgery [8]. The gingival inflammatory condition were significantly improved by diclofenac mouthwash versus placebo (P<0.001). Both test and placebo formulations were found to be safe and palatable [9]. In a previous study which evaluated the efficacy of 0.074% w/v diclofenac mouthwash showed favourable results with diclofenac, although at the end of the treatment period no statistical differences were observed when compared to baseline [10]. Diclofenac-based formulations also had been evaluated for treatment of recurrent apthous stomatitis. Three percent diclofenac in 2.5% hyaluronan gel was found to have anti-inflammatory and pain-relieving effects [11] while Passàli, et al. [12], in his randomized, multicenter, study used undiluted BH 15 ml (22.5 mg) or KLS 10 ml (160 mg) diluted in 100 ml of water and reported that the differences between groups in the duration of analgesic effect after the first dose of drug and the time course of pain were found to be statistically significant (P=0.006 and P=0.017, respectively)while it was concluded that KLS mouthwash exerts a significantly longer first-application analgesic action with significantly greater local tolerability than BH mouthwash [12]. Another study concluded that in cases with mild postoperative pain following periodontal surgery, benzydamine HCl can be prescribed as an analgesic. However, in other cases, this mouthwash should be prescribed along with acetaminophen codeine to reduce systemic drug consumption [13], while other studies evaluated

the pain-relieving effect of 2% morphine oral solution in patients suffering from radiotherapy- and/or chemotherapy-induced oral mucositis and found that pain alleviation was significant ($P<0.001$), with duration of pain relief being 123.7±98.2 min for morphine. Results of these studies suggest a possible analgesic effect of topical morphine [14].

The results of the present study demonstrate that diclofenac mouthwash is characterized by excellent efficacy in relieving pain consequent to oral or periodontal surgical procedures. But, the anti-inflammatory effect may not be statistically significant. The new 0.074% diclofenac mouthwash is an effective and tolerable medicinal product for the management of post-surgical pain. This topical formulation is sufficiently effective for pain relief after minor oral surgical procedures without subjecting the patients to systemic side-effects.

Conclusion

The new 0.074% diclofenac mouthwash is an effective and tolerable medicinal product for post-surgical symptomatic relief. Thus, it can be an alternative drug for patients who cannot tolerate systemic NSAIDs. Also, by substituting systemic with topical NSAID, systemic drug interactions in patients on anticoagulants and asthmatics can be avoided. This topical formulation is sufficiently effective for pain relief after minor oral surgical procedures without subjecting the patients to systemic side-effects.

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