Original Article

Development and Clinical Evaluation of Transmucosal Mucoadhesive Patch of Lornoxicam for the Odontogenic Pain Management: A Preliminary Study

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Abstract

Background: Pain is the most common complaint of the patient that brings him/her to the dentist, pain often occurring in conjunction with inflammation and which considerably reduces the quality of patient's life. Nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly prescribed for the dental pain management. The gastrointestinal complications associated with NSAIDs can be effectively overcome if they are delivered by transmucosal route in the form of buccal patch. **Aim:** The study aimed to evaluate the efficacy of mucoadhesive lornoxicam patches in odontogenic pain management. **Materials and Methods:** The present study was conducted in 60 adult patients of either sex, diagnosed with odontogenic pain, and were attending the outpatient department. Informed consent was obtained from all the patients. A 1 cm × 1 cm mucoadhesive patch containing 4 mg of lornoxicam was applied on the attached gingival region of the tooth with pain. Pain was recorded using a ten-point visual analog scale score before and every 5 min till 30 min after the application of the patch. Statistical analysis was performed using repeated measure ANOVA with $P < 0.05$. **Results:** The results of the study revealed a statistically significant drop in the pain scores from baseline to the score recorded after 30 min ($P < 0.05$). **Conclusion:** The results of the present study conclusively suggested the suitability, safety, and efficacy of the transmucosal delivery of lornoxicam in the form of mucoadhesive patch for the management of odontogenic pain.

Keywords: Lornoxicam, odontogenic pain, pain scores, transmucosal mucoadhesive patches

Introduction

Pain is an unpleasant, subjective, sensational, and emotional experience associated with actual or potential tissue damage. The level of pain perception, threshold, and response varies under different conditions.[1] Pain is the most common reason for patients to come to the dental clinic; this pain usually originates in the tooth itself or its supporting structures.[2] Literature survey suggests that the overall estimated prevalence for dental pain ranges from 7%–66%.[3]

Dental pain may be defined as pain that originates from the innervated tissues within the tooth or immediately adjacent to it, and it has an impact on the individuals quality of life.[4]

The most commonly used drugs to manage dental pain are nonsteroidal anti-inflammatory drugs (NSAIDs), and mostly they are administered through peroral route. Diclofenac, meloxicam, etc., are the most commonly used medications in the world because of their demonstrated efficacy in reducing pain and inflammation. Numerous studies have clearly documented that the risk of upper gastrointestinal (GI) complications increases with increasing doses as well as increasing the frequency of use of NSAIDs.[5]

Lornoxicam, a congener of tenoxicam, is a new NSAID belonging to the oxicam class. It is a strong analgesic and anti-inflammatory NSAID as compared to other NSAIDs. Its analgesic activity is comparable to that of opioids. Studies have shown that it is more effective than 10 mg morphine when used at doses ≥8 mg to control pain after oral surgery.

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Lornoxicam combines the high therapeutic potency of oxicams with an improved GI toxicity profile. Clinical investigations have established it as a potent analgesic with excellent anti-inflammatory properties in a range of painful and/or inflammatory conditions, including postoperative pain and rheumatoid arthritis.[6]

In oral transmucosal drug delivery, drugs are directly exposed to the oral (buccal and sublingual) mucosa and permeate across the mucosal tissues to reach the systemic circulation. Mucoadhesion is a new emerging concept in drug delivery. Buccal drug delivery provides a numerous advantages over peroral delivery, such as abundant blood supply, robustness of the epithelium, more accurate dosing of the drug, short duration, satisfactory patient compliance, and bioavailability, is improved due to the avoidance of degradation in the GI tract and hepatic first-pass metabolism.[7] Buccal patches are greatly pliable and easily tolerated by the patient than tablets and more accurate than gels and ointments because of poor retention.

Lornoxicam binds extensively to plasma albumin (99%) and has a relatively short plasma half-life (3–5 h),[8] which makes it a good candidate for local delivery. Literature survey revealed the absence of any work on transmucosal delivery of lornoxicam for the treatment of odontogenic pain. Hence, the present work has been conducted with an aim to develop mucoadhesive transmucosal lornoxicam patches for the rapid and effective pain relief of odontogenic pain.

Buccal patches offer several advantages over peroral delivery of NSAIDs such as rapid onset of action, decreased local or systemic side effects, improved drug utilization, thereby reducing the total of the drug administered and also improves patient compliance and tolerance.[9]

Clinical implications of the study include rapid pain relief, no adverse effects, no allergenic effects, and beneficial in treatment of odontogenic pain. Hence, developed transmucosal patches are safe in the management of odontogenic pain.

Literature survey revealed the absence of any work on transmucosal delivery of lornoxicam for the treatment of odontogenic pain. Hence, the present work deals with the development of mucoadhesive buccal patches of lornoxicam for the rapid and effective pain relief.

Materials and Methods

This study was conducted in 60 adult patients of either sex, who were diagnosed with odontogenic pain, and were attending the Outpatient Department of Oral Medicine and Radiology, A.M.E's Dental College and Hospital, Raichur, Karnataka, India. Ethical clearance was obtained from the Institutional Review Board, A.M.E's Dental College and Hospital, Raichur. The informed consent from the patients was obtained before the study.

Clinical trial registry has done with a registration number - REF/2019/01/023371.

Inclusion criteria

Adult patients of either sex of age group between 18 and 55 years, clinically diagnosed with odontogenic pain (apical periodontitis and acute and chronic periapical abscess), mentally sound to answer the visual analog scale (VAS) score, and who had not taken any type of analgesic/anti-inflammatory drugs, or tranquilizers for 1 day before the study were included in the study.

Exclusion criteria

Patients allergic to the drug or patch material, pain due to ulcerated lesion or carcinomatous conditions, patients with any serious systemic diseases, patients with persistence mental confusion, or women who were pregnant and lactating were excluded from the study.

Preparation of patches

The mucoadhesive patches were prepared by solvent casting method. The known quantity of lornoxicam (1.2% w/v) was dissolved in 10 ml of alkalinized water (5 ml of 0.15 NaOH in 100 ml water). To this solution, HPMC K15M (4% w/v) and glycerol (0.5% w/v) were added as a mucoadhesive polymer and plasticizer, respectively, under stirring. The films were casted on a glass petridish and placed in the hot air oven maintained at 40°C for 24 h. The patches were cut into appropriate sizes (1 cm × 1 cm) packed in aluminum foil and stored in a glass dessicator till further use.[10] The patches were evaluated for drug content uniformity, weight uniformity, thickness, and folding endurance.[11]

Clinical evaluation

The patients were explained about the procedure and the VAS scores (0–10). The patients' data were collected on a detailed pro forma wherein the chief complaint, diagnosis, detailed medical history, VAS scores, and side effects in the next 24 h were also recorded through telephonic conversation. Pain intensity was measured by 10 mm VAS score with 0 being no pain and 10 being worst pain.

The patients were asked to describe the intensity of pain they experienced at baseline and every 5 min for 30 min [Figure 1]. The area with pain was mopped with cotton pallet, and then mucoadhesive patch was placed over the attached gingiva and alveolar mucosa of the offending tooth, as shown in Figure 2. The patients were advised to avoid talking, spitting, and to leave the applied area undisturbed for the next 30 min, and VAS score was recorded for every 5 min. After 30 min, patch was removed and discarded.[12]

Statistical analysis

Data obtained in the study were analyzed using the statistical package software for the social sciences version 19 (SPSS Inc., Chicago, IL, USA). Descriptive statistics such as mean, standard deviation, and percentage were used [Table 1]. Comparison of mean VAS score at different time intervals was carried out using repeated-measures ANOVA.

Results

In the present study, of 60 patients, 28 were female and 32 were male. The cases consisted of acute and chronic periapical abscess, apical periodontitis, and other pain of odontogenic origin. The baseline score was ranged from 2 to 10, with a mean of 6.07 ± 2.87 indicating the higher pain levels in most of the patients.

Pain reduction was noted starting from the first 5 min after the application of patch. The maximal pain reduction was seen in the first 10 min. Quick analgesic effect was achieved with the patch in all the patients and symptoms were also relieved with no adverse effect.

The mean VAS scores recorded at baseline was 6.07 which dropped down to 0.07 at the end of 30 min. The difference observed in VAS score between all the time intervals was found to be statistically significant ($P < 0.05$). The results of the VAS scores are given in Table 2 and depicted in Figure 1.

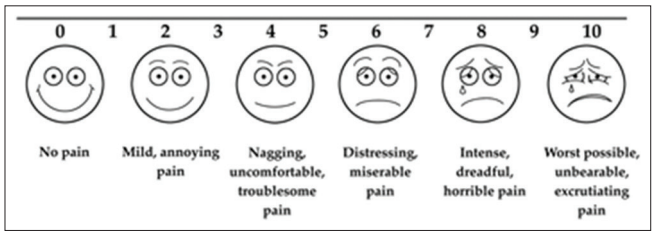


Figure 1: Assessment of pain (visually)

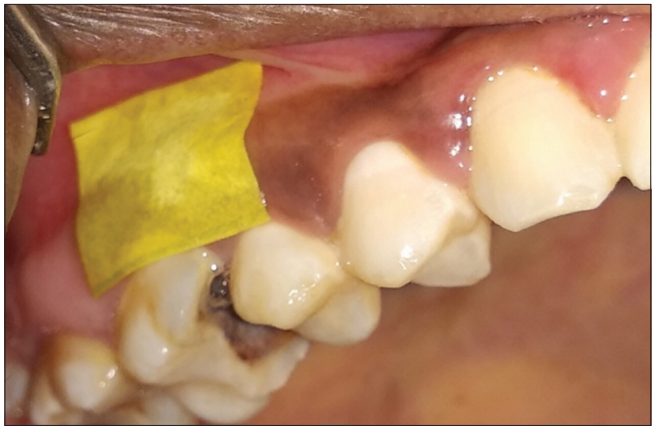


Figure 2: Mucoadhesive patch applied to the attached mucosa of maxillary first molar

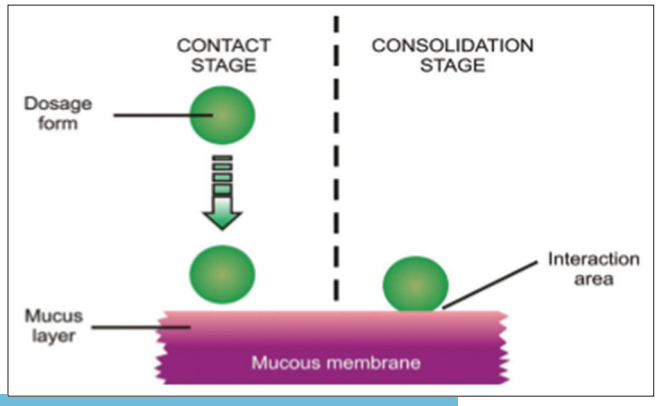


Figure 3: Two steps of mucoadhesion process

Discussion

Lornoxicam has an improved GI toxicity profile with the high therapeutic potency as compared to naproxen.[3] Although the usual oral dose of 4–8 mg of lornoxicam is well tolerated by the patients, several side effects have been reported such as stomach ache, nausea, vomiting, dizziness, somnolence, drowsiness, headache, and flushing.[13]

The parenteral route has its own flaws, and thus in recent years, there has been tremendous interest in the development of transmucosal delivery systems. One of the most common adverse effects of the most prescribed NSAIDs is gastritis, which could be changed with the help of newer techniques such as transmucosal drug delivery systems.

Buccal drug delivery provides numerous advantages over peroral delivery, such as abundant blood supply, robustness of the epithelium, more accurate dosing of the drug, short duration, and satisfactory patient compliance.[14]

It is estimated that the permeability of the buccal mucosa is 4–4000 times greater than that of the skin. The vessels drain absorbed drugs along with the blood into the major veins, which ultimately open into the jugular vein. Thus, the buccal route of drug delivery provides direct access to the systemic circulation painlessly and with a steady rate of delivery bypassing the stomach environment and first-pass metabolism, leading to high bioavailability.[15]

Transmucosal patch prepared soft and thin owing a comfort to the patient during the application and treatment period. Mucoadhesive formulations readily attached to the buccal cavity and retained for a longer duration and can be discarded at any time. The pain intensity was remarkably reduced within the first 5 min.

The mechanism of mucoadhesion is divided into two stages, namely the contact stage and the consolidation stage. In the contact stage, there is a contact between the mucoadhesive and the mucous membrane, along with spreading and swelling of the formulation, initiating deep contact with the mucus layer.[12] In the consolidation stage, due to the presence of moisture, the

Table 1: Mean pain scores at different time intervals

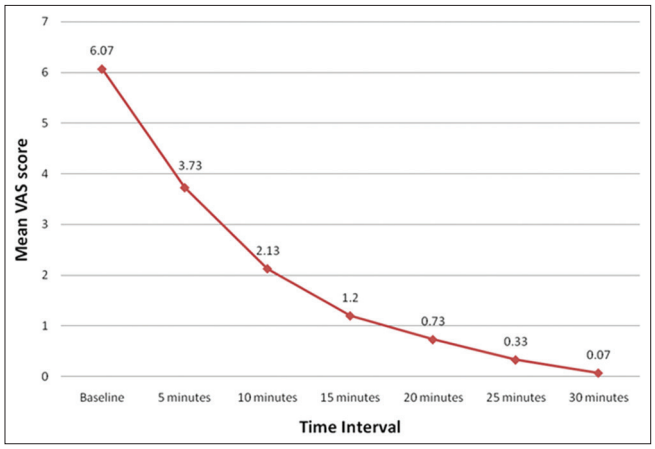
Time interval	*n*	Mean ± SD
Baseline	60	6.07±2.875
05 min	60	3.73±3.635
10 min	60	2.13±2.703
15 min	60	1.20±2.530
20 min	60	0.73±1.604
25 min	60	0.33±1.174
30 min	60	0.07±0.362

SD: Standard deviation

Table 2: Pairwise comparison of visual analog scale scores between all-time intervals

Time interval	Baseline	5 min	10 min	15 min	20 min	25 min	30 min
Baseline		<0.001[a]	<0.001[a]	<0.001[a]	<0.001[a]	<0.001[a]	<0.001[a]
5 min			<0.001[a]	<0.001[a]	<0.001[a]	<0.001[a]	<0.001[a]
10 min				<0.001[a]	<0.001[a]	<0.001[a]	<0.001[a]
15 min					0.106[c]	<0.05[b]	<0.05[b]
20 min						<0.05[b]	<0.05[b]
35 min							0.106[c]
30 min							

[a]Statistically significant at $P < 0.001$, [b]Statistically significant at $P < 0.05$, [c]Statistically nonsignificant ($P > 0.05$)



Graph 1: Mean pain (visual analogue scale) scores at different time intervals

mucoadhesive materials are activated. Moisture plasticizers in the system allow the mucoadhesive molecules to break freely and to make bonds by weak van der Waals and hydrogen bonds and after which the drug percolation occurs [Figure 3].[16]

In this study, baseline pain score was 6.07 and gradually decreases to 0.07 at different time of intervals, i.e., after 5 min – 3.73, after 10 min – 2.13, after 15 min – 1.2, after 20 min – 0.73, after 25 min – 0.33, and after 30 min – 0.07 [Graph 1] found statistically significant ($P < 0.001$).

In this study, the maximum decline was observed within the first 10 min after which it became more gradual. Furthermore, the difference in VAS score between all-time intervals was found to be statistically significant.

On telephonic conversation, a maximal of 4–6 h of analgesic effect was noted before the patient had taken next analgesic, and this effect was noticed in all patients.

The results of the present study were in accordance with another study wherein mucoadhesive indomethacin patches used showed rapid and effective analgesic effect in 65 patients diagnosed with various oral conditions associated with pain,[17] and mucoadhesive meloxicam patches in 55 patients diagnosed with dental pain and had the analgesic effect for about 4–5 h.[12] Future studies can be conducted with larger sample size; this research opens a new panorama in the field of pain relief.

Conclusion

Our study established the efficacy of lornoxicam mucoadhesive patch in dental pain management with no side effects, and the patient had the analgesic effect for about 4–6 h. The study revealed statistically significant results suggested that the transmucosal drug delivery system can be safe, promising, and therapeutic system for buccal delivery to avoid the disadvantage of parenteral and oral routes.

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Conflicts of interest

There are no conflicts of interest.

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