Original Article

A randomized placebo-controlled trial to evaluate a novel noninjectable anesthetic gel with thermosetting agent during scaling and root planing in chronic periodontitis patients

ABSTRACT

Aim: To study the efficacy of a noninjectable anesthetic gel with a thermosetting agent in the reduction of pain during scaling and root planing (SRP) in untreated chronic periodontitis patients.

Materials and Methods: This study is a randomized, double-masked, split-mouth, placebo-controlled trial. Thirty patients were enrolled who underwent SRP in a split-mouth (right side/left side) manner. Before commencement of SRP, both quadrants on each side were isolated and had a randomized gel (either placebo or test gel) placed in the periodontal pockets for 30 s. The pain was measured using numerical rating scale (NRS) and verbal rating scale (VRS).

Results: The median NRS pain score for the patients treated with the anesthetic test gel was 1 (range: 0-4) as opposed to 5 (range: 3-7) in the placebo treated patients. The mean rank of pain score using NRS in test gel was 16.18 as compared to 44.82 in placebo treated sites. Hence, significant reduction in pain was found in test gel as compared to placebo using NRS ($P < 0.001$). The VRS showed that the majority of patients reported no pain or mild pain with a median of 1 as compared to placebo treated sites with a median of 2 suggestive of moderate pain.

Conclusions: The NRS and VRS pain scores showed that the side treated with anesthetic gel was statistically more effective than the placebo in reducing pain during SRP.

Key words: Anesthesia, intra-pocket, pain, scaling root planing

Introduction

The pathogenesis of the periodontal disease is complex involving interactions among microbial species, host immune response, and environmental factors which results in tissue inflammation and bone destruction.[1] The clinical consequence of which may be pocket formation and loss of attachment. Bacteria are considered to be the primary etiological factor. The goal of periodontal therapy is to arrest the inflammatory disease process by eliminating the microbial etiology and contributing risk factors for periodontitis, preserving the dentition in a state of health, comfort, and function with appropriate esthetics and preventing recurrence of periodontitis.[2] Treatment protocol aims at the mechanical removal of the sub gingival biofilm, and the establishment of a local environment and microflora compatible with periodontal health. The gold standard for treating periodontal disease is mechanical scaling and root planing (SRP) which forms integral

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components of the periodontal treatment plan.[3] Carried out efficiently, SRP reduces pocket depth, bleeding on probing, gingival inflammation, and stabilize attachment levels. SRP is performed using hand instruments or sonic devices or a combination of both. In either case, patients may experience little pain associated with the instrumentation that requires the use of some kind of local anesthesia. Common procedures for pain management in periodontics are infiltration anesthesia or topical anesthesia. Disadvantages of infiltration anesthesia include needle phobia, pain associated with injections, or the long, and inconvenient duration of soft-tissue anesthesia.[4] Alternative to infiltration anesthesia, topical anesthetics has been developed to provide patients with needle free anesthesia. Topical anesthetics used are in the form of jellies, sprays, ointments, and patches. Different techniques such as transmucosal patch containing 10% or 20% lidocaine are been used to produce anesthesia for nonsurgical periodontal therapy. Disadvantages include costs and adherence of patch in posterior regions.[5] Hence for effective SRP, anesthetics must be characterized by convenient and painless administration, fast onset, adequate, and profound anesthesia. An intra-pocket anesthesia gel (Oraqix, Dentsply Pharmaceuticals) containing lidocaine (2.5%) and prilocaine (2.5%) with thermosetting agent proved to be practicable alternative to control intra-operative pain during mechanical SRP.[5] At room temperature, intra-pocket anesthetic (Oraqix, Dentsply Pharmaceuticals) is low-viscosity fluid, whereas at body temperature it transforms into an elastic gel. In the periodontal pocket, it remains at the application site, thereby limiting the risk of its spreading to adjacent areas. The scales used to measure pain in this study were verbal rating scale (VRS) and numerical rating scale (NRS). The NRS is a single 11-point numeric scale in which respondent selects a whole number (0-10 integers) that best reflects the intensity of their pain. With 0 representing — "no pain" and 10 representing — extreme pain, e.g., "pain as bad as you can imagine" and "worst pain imaginable."[6] Hence, the aim of this study was to evaluate the efficacy of an intra-pocket anesthetic gel (Oraqix, Dentsply Pharmaceuticals) in the reduction of pain during SRP in individuals with untreated periodontitis.

Materials and Methods

This study was a randomized, double-masked, split-mouth clinical trial comparing the action of anesthetic gel and placebo in a group of untreated periodontal patients. Two investigators were required (Investigator A and Investigator B).

Study population

Thirty participants (20 males and 10 females) aged between 18 and 65 years with chronic periodontitis (pocket depths >5 mm) were recruited from Department of Periodontology, Sullia, DK, Karnataka, India in relation to their periodontal condition. This study was conducted in accordance with the Helsinki Declaration of 1975, as revised in 2000.

Inclusion criteria

1. Patient aged between 18 and 65 years of age.
2. Patients needed to have a minimum of two incisors, one canine, one premolar, and one molar in all four quadrants.
3. Patients should not have undergone SRP or any periodontal treatment in the previous 12 months.

Exclusion criteria

1. Those requiring prophylactic antibiotics before periodontal SRP.
2. Those suffering from any psychiatric disorders or chronic pain problems.
3. Patients with coagulation disorders or on anticoagulation therapy.
4. Female patients those were pregnant or lactating.
5. Patients with congenital or idiopathic methemoglobinemia or those receiving treatment with methemoglobin-inducing agents.
6. Patients allergic to dental anesthetics.
7. Those taking nonsteroidal anti-inflammatory drugs in the 3 days before participation in the study.
8. Patients are having acute periodontal pain, pulpitis, abscesses, or other acute infections.

Screening visit

Investigator A performed the screening visit. This visit comprised of routine dental history (including presenting complaint, medical history, dental history) and examination (including extra-oral and intra-oral examinations, examination of dental hard tissues, and when indicated radiographic tests and vitality testing. Of the 42 patients examined, 30 met the entry requirements, and agreed to participate in the study and were subsequently invited to a second "test visit."

Test visit

This study was performed in a split-mouth manner, incorporating left and right sides. One side of the mouth would receive the "test gel" (Oraqix, Dentsply Pharmaceuticals) and the other side would receive placebo gel. At baseline, every patient underwent a periodontal examination including probing pocket depth (PPD) recorded by Williams Graduated Probe at six sites per tooth. Before the treatment was started, the patients were educated on the usage of VRSs (0 = none, 1 = mild, 2 = slightly moderate, 3 = moderate, 4 = strong) and NRS (patient was asked to choose a score between 0 and 10 which represents the pain). No interim descriptors were used. A third party, not participating in the study randomized

the side of the mouth to receive either the test or placebo gel. Gels were placed in 2 ml graduated syringes with plastic needle applicator. They were then placed in envelopes with "RIGHT" or "LEFT" written on the envelope with an identifier number. Neither the patients nor the investigator doing SRP was aware of which gel was in which envelope until the treatment was completed.

Anesthetic procedure

Examiner A began with the upper right side, opening the first envelope marked RIGHT. The quadrant was dried and isolated with cotton rolls. 2 ml of prefilled syringe with a blunt-tip plastic applicator was used to apply the test gel (Oraqix, Dentsply Pharmaceuticals) or placebo subgingivally at sites in the chosen quadrant with probing depths ≥5 mm on the facial and lingual aspect starting from the most posterior tooth of the selected quadrant and continuing anteriorly [Figure 1]. The gel was left undisturbed in the pocket for a period of 30 s after application. After 30 s, the pockets were irrigated with water, and thereafter, SRP procedure was initiated by Investigator B. If there was an interruption due to pain, re-application of the gel was done into the pockets of the same tooth and debridement resumed 30 s later. In case, after second application patient reported of pain then infiltration anesthesia was given and the subject was excluded from the study. Investigator A then proceeded to the lower right quadrant and the same procedure was repeated with the same gel as for the upper right quadrant. After commencement of SRP in the right quadrant, pain assessment was done within 5 min after treatment using NRS and VRS. The same procedure was carried in an identical manner with the second envelope marked "LEFT." The patient then completed a second NRS and VRS corresponding to SRP on the left side of the mouth. By compiling results in this manner, each patient was effectively acting as their own control, producing two separate pain scores for SRP on both the right and left sides of their mouth. After completion of SRP, the masking of which gel (either test or placebo) was in which envelope was lifted, and the envelope numbers were matched. The identifier number changed with every patient.

Statistical analysis

Descriptive statistics and data analyses were performed using statistical software. Mann-Whitney U-test was used to analyze pain perception. All analysis was carried out with SPSS 15.0 software (SPSS Inc., Chicago, IL, USA). $P \leq 0.05$ were considered to indicate statistical significance.

Results

A total of 30 eligible individuals were recruited in this study. The patients included were 20 males and 10 females. The average age was 43.67 ± 7.85with a range of 30-56 years [Table 1]. There was no statistical significance found in pain scores between males and females in the placebo side or test side using NRS and VRS [Table 2]. In the placebo side, the mean score was found to be 5.17 ± 1.29, whereas the median score with interquartile range was found to be 5 ± 2 with a minimum value of 3 and maximum value 7. Whereas, the test side the mean score was found to be 1.37 ± 1.24, the median score with interquartile range was found to be 1 ± 2.25 with minimum value of 0 and maximum value 4 [Table 3]. The box plot represents the NRS and VRS for both test and placebo gels [Figures 2 and 3]. The pain scores showed highly statistically significance between the test gel and placebo with $P < 0.001$ [Table 4]. All 30 patients who

Table 1: Patient demographics

Sl. No	Mean	SD	Range
Age	43.67	7.85	30-56 (>0.05) NS
Gender	10 (females)/20 (males)		

SD: Standard deviation; NS: Not significant

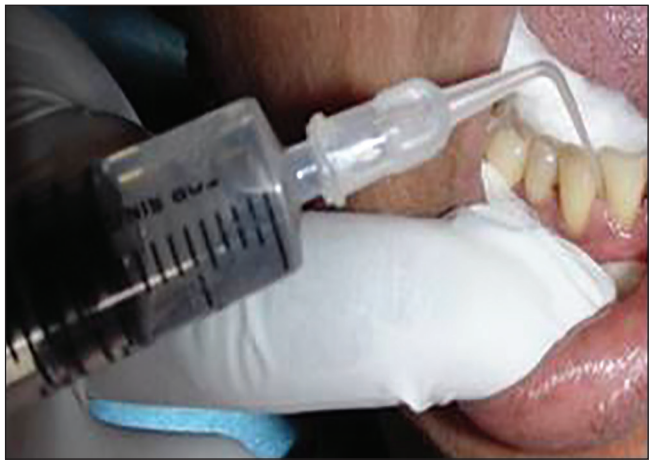

Figure 1: Area isolated and gel applied

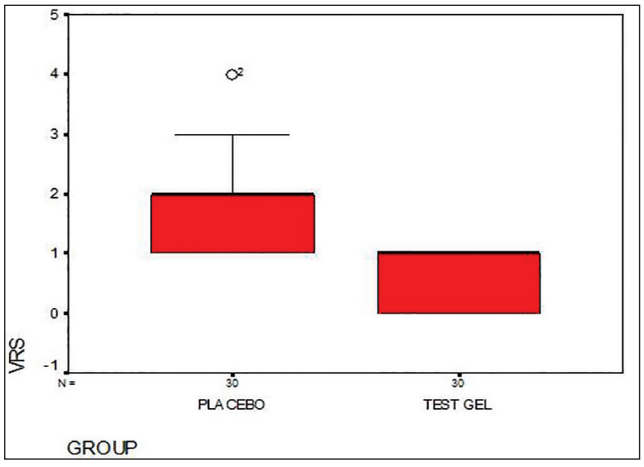

Figure 2: Box plots of placebo and test gels verbal rating scale

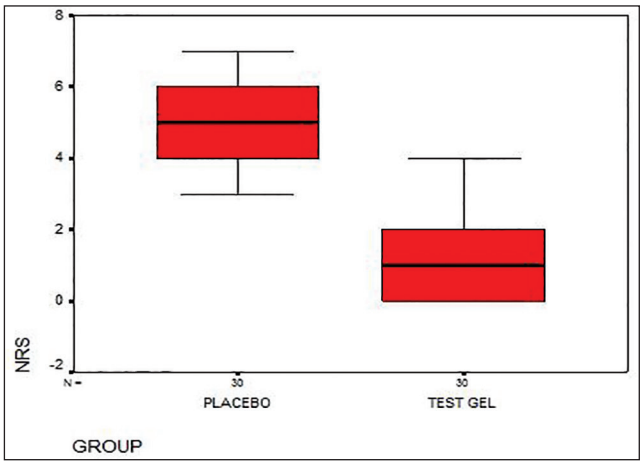

Figure 3: Box plots of placebo and test gels numerical rating scale

participated in the study completed the treatment, with no adverse events being reported.

Discussion

The primary objective of this study was to evaluate the efficacy of an intra-pocket anesthetic gel (Oraqix, Dentsply Pharmaceuticals) as compared to a placebo in the reduction of pain during SRP in individuals with untreated periodontitis in Indian population. The results demonstrated highly significant reduction in patient's perception of pain for the side of the mouth having the test gel as compared to the side of the mouth having the placebo, reported through NRS and VRS scoring $P < 0.001$. The primary means of determining gel efficacy was the measurement of treatment-associated pain. The scales used were NRS and VRS. In NRS respondent is asked to indicate the numeric value on the segmented scale that best describes their pain intensity. Scores range from 0 to 10. Higher scores indicate greater pain intensity.[7] Advantages include easy using and scoring, requires minimal language translation, hence, can used across the globe. Often, periodontal therapy is associated with high levels of anxiety. Erten *et al*.[8] indicated that periodontal therapy is associated with low levels of discomfort, but some patients become anxious and avoid treatment. Hence, to overcome the anxiety and pain during SRP and to provide patients with needle free treatment topical anesthetics may be used instead of injected anesthetics. The disadvantages of topical anesthesia for SRP are limited efficacy due to inadequate depth of penetration, too short duration of action, difficulties of administration, uncontrolled spreading, and undesirable taste,[9] which limits the usage of topical agents. Hence, to overcome this disadvantage and to maximize the effect many topical agents have been introduced. Evaluate the efficacy local anesthetic (EMLA) cream 5% is a 1:1 oil/water emulsion of a eutectic mixture of lidocaine (2.5%) and prilocaine (2.5%) bases.[10]

Table 2: Comparison of pain scale values between test and placebo in males and females

Sl. No	Mean	SD	Range	Median	IQR	*P*
NRS placebo						
Male (20)	5.30	1.342	3-7	5	2.25	>0.05 NS
Female (10)	4.90	1.197	3-7	5	2	
NRS test						
Male	1.50	1.395	0-4	1	3	>0.05 NS
Female	1.10	0.876	0-3	1	0.5	
VRS placebo						
Male	1.95	0.826	1-4	2	1	>0.05 NS
Female	1.60	0.516	1-2	2	1	
VRS test						
Male	0.65	0.489	0-1	1	1	>0.05 NS
Female	0.70	0.483	0-1	1	0	

NS: Not significant ($P > 0.05$); IQR: Interquartile range; SD: Standard deviation; NRS: Numerical rating scale; VRS: Verbal rating scale

Table 3: Comparison of pain scales between test gel and placebo

Group	Mean	SD	Median	IQR	Minimum-maximum
NRS					
Placebo	5.17	1.29	5.0	2.0	3-7
Test	1.37	1.24	1.0	2.25	0-4
VRS					
Placebo	1.8	0.74	2.0	1.0	1-4
Test	0.67	0.48	1.0	0	0-1

NRS: Numerical rating scale; VRS: Verbal rating scale; SD: Standard deviation; IQR: Interquartile range

Table 4: Difference in pain scales between test gel and placebo

Group	Mean rank	*P*
NRS		
Placebo	44.82	<0.001 HS
Test	16.18	
VRS		
Placebo	42.17	<0.001 HS
Test	18.83	

HS: Highly significant ($P < 0.001$); NRS: Numerical rating scale; VRS: Verbal rating scale

EMLA has been shown to reduce pain during probing,[11] hand scaling,[12,13] ultrasonic scaling,[14] rubber dam clamp application,[15] and palatal injection.[10] Chung *et al*. conducted a study to EMLA cream on pain perception during scaling. Forty subjects with chronic gingivitis or periodontitis were enrolled, which was a randomized, split-mouth, controlled, masked clinical trial, the mean VAS, and VRS; when EMLA cream was applied (18.39 ± 14.47 mm and 0.95 ± 0.69) was significantly lower ($P < 0.001$ for VAS and VRS) compared to when EMLA cream was not used (26.54 ± 16.46 mm and 1.30 ± 0.75). Hence, concluding significant reduction of pain is achieved by using EMLA cream and ultrasonic scaler.[14] However, EMLA is not registered for intra-oral use. Hence, a new thermosetting topical intra-pocket anesthetic gel

(Oraqix, Dentsply Pharmaceuticals) has been developed for the intra-oral application. Introduced in 2004, in the United States, and in 2010, in Canada, it is a microemulsion of 25 mg/g lidocaine and 25 mg/g prilocaine gel. It is a colorless liquid, containing hydrochloric acid, purified water along with the thermosetting agent. The addition of thermosetting agent causes the solution to change from the liquid state at room temperature to gel form at the temperature of the oral cavity.[14] It is available in cartridge form. One cartridge contains 1.7 g of anesthetic gel (Oraqix, Dentsply Pharmaceuticals), which is usually sufficient for one quadrant of the dentition. The maximum recommended a dose of anesthetic gel at one treatment session is five cartridges, that is, 8.5 g gel containing 212.5 mg lidocaine base and 212.5 mg prilocaine base. Efficacy and safety of the intra-pocket anesthesia gel (Oraqix, Dentsply Pharmaceuticals) containing lidocaine and prilocaine (25 mg G1 each) are well-documented.[16,17] Friskopp and Huledal proved a large safety margin with respect to systemic effects following the application of the anesthesia gel in periodontal pockets.[18] Friskopp *et al*.[5] showed that the anesthetic gel provided onset of anesthesia within approximately 30 s when placed into periodontal pockets and duration of anesthesia was approximately 20 min. Three previous multicenter, double-masked, randomized, placebo-controlled clinical trials studied the efficacy of the anesthetic gel for purposes of SRP procedures.[16,17,19] The three studies included 337 individuals at 18 study centers. This studies used Hodges-Lehmann point estimate of treatment differences and found that the results favor the anesthetic gel by reducing VAS pain scores by magnitudes of 8,[16] 4,[19] and 10,[17] The present study was carried out in Sullia, located at a distance of 89 km from Mangalore, Karnataka, India with maximum average temperature range of 37°C to minimum of 14°C. India is a hot tropical country, except the northern states of Himachal Pradesh, Jammu and Kashmir in the north, and Sikkim in the northeastern hills, which have a cooler, more continental influenced climate. Canada is often associated with cold weather and snow. The intra-pocket anesthetic (Oraqix, Dentsply Pharmaceuticals) became gel within the cartridge in <10 min as soon as it came in contact with the external environment and had to be refrigerated again for it to become liquid again. Limitation of the present study included smaller sample size and posttreatment parameters such as PPD for both test side and placebo were not assessed. The scales used for measuring pain were of a subjective type, and a more objective method should be used.

Conclusions

The anesthetic gel, 25 mg/lidocaine plus 25 mg/g prilocaine with thermosetting agents provides a statistically significant reduction in pain on SRP in patients with untreated periodontitis. It suggests that the gel may be alternative with patients who associate SRP to be painful and avoid dental treatment. Such a product is not available in the Indian market; hence, pharmaceutical companies should develop a product similar to it with modification of temperature changes. Additional further studies need to be conducted to determine the efficiency of the gel with larger sample size.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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