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Effectiveness of a transmucosal lidocaine delivery system for local anaesthesia during scaling and root planing

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Abstract

Objective: This study compared the efficacy of transmucosal anaesthetic patches containing lidocaine (46.1 mg/2 cm^2) to placebo for local anaesthesia during quadrant scaling and root planing using periodontal clinical indices and patient perception of pain.

Material and Methods: Forty healthy adults with moderate periodontal disease and moderate subgingival calculus were scaled at weekly intervals, two quadrants randomized to treatment patches and two quadrants randomized to placebo patches. Bleeding, probing depths and attachment levels were evaluated prior to treatment and 1 month after quadrant scaling was completed. Subjects completed 100 mm visual analogue pain scales 15 min. after patch placement and at the end of treatment, and were asked for verbal assessment of perceived pain.

Results: Subjects' verbal ratings demonstrated consistently greater pain relief with active patches than placebo ($p < 0.0001$). Visual analogue scales demonstrated significantly greater pain relief with the treatment patches after 15 min. ($p = 0.0003$) and at the end of treatment ($p = 0.0149$). Efficacy of periodontal therapy was equivalent for treatment and control groups. No adverse events were observed; localized minimal gingival irritation was noted in three subjects.

Conclusion: Transmucosal lidocaine patches provided sufficient anaesthesia for therapeutic quadrant scaling and root planing procedures.

Key words: local anaesthesia; pain; periodontitis; scaling and root planing; transmucosal drug delivery

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Periodontal diseases are a group of inflammatory diseases of microbial etiology (Socransky 1970). Pathogenic bacteria in dental plaque are responsible for the initiation and progression of periodontal disease largely through their abilities to induce a host-mediated inflammatory response (Socransky & Haffajee 1992, Zambon 1996). If the disease is untreated, it will lead to attachment loss, loss of supporting structures of the teeth, and eventual tooth loss (Harris 2003, Rowe 1996). Long-term studies support the removal of plaque and calcified plaque (calculus) both above and below the margin of the gingiva to promote healing and prevent further progression of inflammation and periodontal tissue destruction (Ramfjord 1990, Renvert & Persson 2002).

Effective therapeutic scaling and root planing requires the use of injected local anaesthesia to make the procedure comfortable for the patient and to facilitate the clinician's ability to provide care. Many patients are apprehensive about receiving local anaesthesia through needle injection (Malamed 1997, Matthews et al. 2001). Other patients who might benefit from injected local anaesthesia during scaling and root planing may not receive it because of the inability to inject local anaesthetic because of regional licensing restrictions, as is the case for many dental hygienists. Thus, the use of an effective, long lasting form of topical anaesthetic could make treatment more comfortable and convenient for both patients and clinicians. A patch delivered local anaesthetic, lidocaine transmucosal delivery system (LTDS), DentiPatch,™ (Noven Pharmaceuticals, Inc., Miami, FL, USA) has been developed to provide topical gingival and mucosal anaesthesia. The patch systems

are currently FDA approved in the USA to achieve mild topical anaesthesia prior to dental procedures. Patch delivered local anaesthesia would be a great asset to both dental clinicians and patients if it provided sufficient pain control for therapeutic scaling and root planing. The purpose of this study was to evaluate the efficacy and safety of transmucosal anaesthetic patches for providing local anaesthesia during therapeutic scaling and root planing procedures performed to treat moderate periodontal disease.

Materials and Methods

This study was a single-centre, single-blind, randomized, four period, two treatment, placebo controlled, crossover design comparing anaesthetic effects of active transmucosal patches (46.1 mg lidocaine each in 2 cm^2) to control patches (no lidocaine). Forty healthy adult subjects with moderate periodontal disease and clinically detectable subgingival calculus were enrolled. Subjects were required to have at least six posterior sites with probing depths >5 mm and a Gingival Index (Löe 1967) of $\geqslant 2$ in those same sites, but no probing depths exceeding 8 mm. Subjects had full-mouth intra-oral radiographs taken, a baseline periodontal evaluation, and four treatment visits (each consisting of ultrasonic scaling and root planing of one quadrant using randomly assigned placebo or lidocaine transmucosal patches). Subjects then returned 1 month after treatment was completed for a periodontal evaluation of healing. Subjects also received instruction and practice in using visual analogue scales (VAS) at the beginning of the study.

Each active transmucosal patch is 2.0 cm^2 and contains 46.1 mg of lidocaine in the adhesive. Non-active ingredients include karaya gum. Placebo and active patches were randomly assigned in pre-determined sequences by quadrant, two quadrants received active patches and two quadrants received placebo patches, with one active and one placebo treatment for each jaw. The first quadrant treated was randomly selected, as was the patch type, active or placebo. At the second visit, the alternate patch type was used during treatment of the opposite side on the same jaw. Treatment sequences were balanced so half the subjects had the mandible treated first and half the maxilla; half had the left side treated first and half the right side; and half the subjects received the placebo treatment first and half the active treatment. Thus, among the 20 subjects randomly assigned placebo first, five were assigned to each quadrant. Patches were pre-labeled with subject number, visit number and treatment quadrant so clinicians and subjects were blinded to anaesthetic treatment received. Clinicians were trained to place the patches according to manufacturer's instructions (Fig. 1). Patches were placed one or two at a time, first drying the mucosa for 30 s, applying the patch with light pressure for 30 s, and then leaving it in place for 5 min. At each treatment visit the patches were placed, scaling begun 5 min. after patch placement, and patches removed 15 min. after placement. Rescue medicine, injected local anaesthetic, was offered when scaling and root planing treatment was begun and at any time the subjects reported pain. Four experienced dental hygienists placed the patches and provided the scaling and root planing treatment. Clinicians were blinded to the patch type (active or placebo) but could ascertain anaesthetic effects from the patient.

A complete periodontal examination was performed at baseline and the exit examination by one trained and experienced periodontist who was also blinded to the patch type. Baseline and exit examinations consisted of measure-

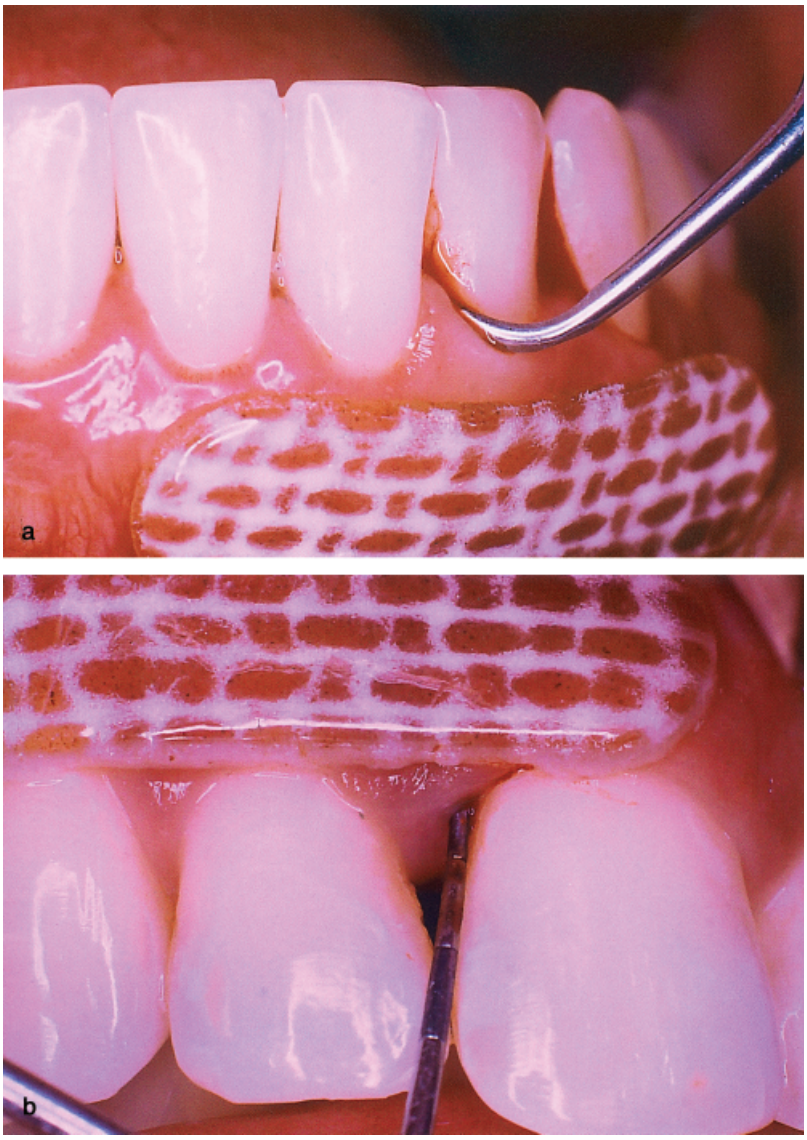

Fig. 1. Picture of lidocaine transmucosal delivery system in place, or quadrant of patches. (a) Mandibular anterior patch placement with scale in place. (b) Maxillary anterior patch placement with probe in place.

ments of probing depths, clinical attachment loss, Gingival Index, Plaque Index (Löe 1967), gingival irritation, and global assessments describing pain and anxiety designed for the study. Data collected during treatment visits included subject measurements of pain on 100 mm VAS 15 min. after patch placement and at end of treatment, verbal description of the amount of pain felt, and subject comments. The duration of the therapeutic scaling and root planing was recorded by the clinicians, and as well as observation of gingival irritation at the location of the patches both after removal and at the end of each treatment visit.

Statistical analysis

Data were analysed using mixed effects regression models using random person within sequence effects (Littell et al. 1996). Treatment visit and quadrant effects were used in all models; rescue medication, age, gender, and baseline percent bone loss were evaluated along with carryover (first order), treatment-by-visit, and visit-by-quadrant effects. Time elapsed since treatment was examined as a covariate for the change in periodontal attachment loss and probing depth measures. Regression model fit was checked via residual examination. Natural logarithmic transformations were used for the VAS measures to give normally distributed model residuals. Since an interim analysis was performed with half the subjects, using an O'Brien–Fleming procedure (e.g. Koch & Gansky, 1996) at $\alpha = 0.0001$, the final analyses were performed with $\alpha = 0.0499$. Exit exam global assessment questionnaire items were assessed with one-sample chi-square tests of one proportion *versus* 0.50 (equal probability).

Results

Subject characteristics

Forty healthy adult subjects started and completed the protocol, 23 female subjects and 17 male. The mean age was 39 ± 9.7 (median 35; range 25–63) years old. At the baseline examination there was no surface irritation present on the gingiva of any subject, based on a scale of 0 (no irritation), 1 (mild), 2 (moderate), and 3 (severe). Bone loss, evaluated by full-mouth radiographic survey ranged between 30% and 50%, with a mean of $36.1 \pm 7.8\%$ (median 30.2%). The baseline and treatment visits occurred 1 week apart, and the exit examination was performed 4 weeks after the last treatment visit was completed. There were several minor deviations in the timing because of scheduling changes (three subjects had 14 days between two visits and one subject had 18 days between two visits) but subjects adhered to the appointment schedule very well.

Subject anxiety

Subjects were asked, at the baseline examination, to describe their level of anxiety regarding dental visits of various types, about pain during dental visits, and types of anaesthetics they had previously received. Most (70%) were not very anxious or not at all anxious about dental visits. Their anxiety level for various procedures was generally low except for root canal therapy and extraction of teeth. Of those experiencing anxiousness on typical dental visits, 73% responded that it was most often related to the anticipation of discomfort or pain. Although the subjects generally received injected local anaesthetics for typical dental visits, most had not previously received therapeutic scaling and root planing treatment. Of those who previously received therapeutic scaling and root planing, 33.3% of respondents to the questions reported the procedure as extremely or fairly painful, 28.6% required anaesthesia for the procedure. In addition, 85.7% of the subjects in the study found the traditional forms of local anaesthesia (injections, topical, or both) to be either fairly effective or extremely so.

Patch and treatment timing

According to manufacturer's instructions, it takes 2 min. for the transmucosal patch to begin to take effect, and a maximum transfer of anaesthetic to oral tissues occurs within 15 min., providing about 45 min. of good topical anaesthesia. The patches were placed and allowed to remain for an average of 15 (range 5–20) min. Therapeutic scaling and root planing procedures began 5–13 min. after initial placement of the patches, and required 15–75 (mean: 38) min. to complete. Rescue medication was offered shortly after the scaling procedures began, and any time the subjects indicated intolerable pain or requested injected anaesthetic. Treatment time was not defined in order to more closely simulate clinical practice and permit the clinicians to scale until calculus was removed. The patches remained in place 15 min. unless they were taken off sooner in order to deliver rescue medication.

Seven subjects, with a total of nine quadrants out of 160 treated, required rescue medication, with six quadrants (7.5%) receiving scaling and root planing with placebo patches and three quadrants (3.8%) treated using active patches.

Irritation of gingival tissues

Topical irritation of gingival tissues after removal of transmucosal patches with active ingredient has been reported in a small number of cases (Hersh et al. 1996). In this study, the examiner evaluated gingival irritation at the baseline and exit examinations and clinicians were trained to evaluate the gingival condition prior to patch placement, after patch removal and at the end of each treatment visit. Gingival irritation was measured on a scale of 0 (none), 1 (minimal), 2 (moderate), and 3 (severe). Any comments from the subjects were recorded. Minimal irritation, rated on the scale as 1, was observed in three subjects. In two cases the tissue immediately beneath the patch system appeared slightly reddened when the patches were removed, and the redness disappeared by the end of the treatment visit. For the third subject, slight reddening of the gingival tissue was visible at the end of the treatment visit but not immediately after patch removal. In each case, the irritation was localized and appeared to be associated with one patch rather than spreading around the gingiva of the entire quadrant being treated. There were no comments about irritation of the gingiva from any of the subjects. Irritation was evaluated at the exit examination to determine if any changes to the gingiva occurred subsequent to treatment. There was no evidence of gingival irritation seen at the exit examination for any of the 40 subjects (95% one-sided confidence interval: 0.075).

Subject overall assessment of anaesthetic effectiveness

All subjects were asked to rate the efficacy of the patches at the end of every treatment visit using a 5-point

Table 1. Verbal assessment of efficacy at end of treatment visits*

Visit	Placebo (SE)	LTDS (SE)	Area treated
1	3.6 (0.31)	3.8 (0.31)	First quadrant
2	2.1 (0.31)	3.7 (0.31)	Second quadrant, same arch
3	2.4 (0.31)	2.7 (0.32)	Third quadrant, opposite arch
4	2.6 (0.31)	4.0 (0.31)	Fourth quadrant

*Scale 1–5

SE, standard error; LTDS, lidocaine transmucosal delivery system.

scale: poor = 1, fair = 2, good = 3, very good = 4, and excellent = 5. The overall mean ($\pm$ standard error) difference score was 0.8 ± 0.2 as a combined group. Scores were consistently and significantly higher for the active patches, indicating better pain relief with the active than the placebo patches, $p = 0.0001$, but the magnitude of the differences varied from the initial treatment on one jaw to the treatment on the other side of the same jaw. At the first treatment visit, scores were similar for both placebo and active patches, but the second treatment on the same jaw showed dramatic differences in scores. The data for the treatment visits are presented in the Table 1.

Subjects had the opportunity to comment about pain when the patches were removed, after 15 min. in place, and at the end of treatment for each visit. Most subjects, 89.7%, did not comment. Most of the comments indicated that mild-to-moderate pain was felt, sometimes localized to one area. Of the 33 comments recorded from all subjects over four treatment visits, 21 comments reported mild but tolerable pain, while one case reported no pain. Five comments were related to severe pain and/or needing rescue medication, and seven comments related to taste or other non-pain issues.

Exit examination global assessment questions

Three questions addressed subject choice of local anaesthetic at future dental visits. Most subjects, 85%, could correctly guess the difference between the active and the placebo patches ($p < 0.0001$). 30.8% of subjects reported the active patches to be extremely effective in controlling pain during the therapeutic scaling and root planing treatments, and an additional 56.4% found them to be fairly effective, accounting for 87.2% of all subjects ($p < 0.0001$). The large majority of subjects, 87.3% reported they were extremely likely or fairly likely to choose the transmucosal patches at future visits requiring therapeutic scaling and root planing ($p < 0.0001$). Almost as many, 84.6% stated they were extremely likely or fairly likely to request transmucosal patch anaesthetic even if not offered by the dentist or dental hygienist ($p < 0.0001$). And 85% reported they were not at all likely or not very likely to ask for another form of local anaesthesia if offered the transmucosal patches ($p < 0.0001$).

VAS were completed by each subject 15 min. after patch placement, which was approximately 10 min. after scaling was begun. Subjects were also asked to complete a second VAS at the end of each treatment appointment. Each subject marked a line on the 100 mm scale indicating the level of pain felt. The reported pain scores were significantly lower for LTDS at every visit, both 15 min. after patch placement ($p = 0.0003$) and at the end of treatment ($p = 0.0149$), than those reported for the placebo. The overall comparison log (VAS) for 15 min was -0.4 ± 0.1 log mm (mean $\pm$ SE) and end of treatment was -0.3 ± 0.1 log mm, both statistically significant. Presented as control (log placebo) – experimental (log active), the mean differences translated to mm were 5.7 mm for 15 min. and 3.9 mm for end of treatment. The same interesting phenomenon occurred with these VAS data as with the overall verbal assessment made at the end of each treatment visit. Subjects better distinguished between active and placebo treatments at the second visit in the sequence treating the same jaw, so that visits 2 and 4 assessments showed greater distinction in pain perception. VAS scores are presented in Table 2.

Subjects were asked to report verbally the amount of pain that was felt 15 min. after patch placement, about 10 min. after scaling had begun, then again at the end of the treatment visit. Each subject specifically described the pain on a scale with the response none = 0, mild = 1, moderate = 2, severe = 3, and very severe = 4. Overall mean differences were statistically significant, -0.3 ± 0.1 ($p = 0.0019$) at 15 min. (mean $\pm$ SE), and -0.3 ± 0.1 ($p = 0.0103$) at the end of treatment**.** Subjects again appeared better able to distinguish relief between placebo and active patches at visits 2 and 4, during the second treatment on either the maxillary or mandibular arch. It is of interest to note that one subject never reported any pain at any visit (VAS = 0 and verbal score = 0), while two other subjects reported no pain verbally (verbal score = 0) at all visits while providing VAS scores between 1 and 12 mm. Mean verbal scores, by visit, are presented in the Table 3.

Healing of the periodontal tissues was expected to mirror documented clinical changes assessed in many studies (Armitage 1980, Antczak-Bouckoms et al. 1993, Baderstein et al. 1985, Carranza 2002, Loomer & Perry 2003, Perry & Schmid 2002, Tinoco & Gjermo 1992). Subjects were evaluated 4 weeks after therapeutic scaling and root planing procedures were completed and indices compared with baseline examination

Table 2. Visual analogue scale (VAS) scores

	Placebo mean (SE)	LTDS mean (SE)
VAS 15 min. after placement		
Visit 1	21.1 (4.6)	17.8 (4.6)
Visit 2	33.8 (4.6)	16.2 (4.6)
Visit 3	27.0 (4.6)	22.6 (4.6)
Visit 4	30.4 (4.6)	14.4 (4.6)
VAS end of treatment visit		
Visit 1	22.2 (4.3)	19.4 (4.3)
Visit 2	33.7 (4.3)	22.0 (4.3)
Visit 3	22.0 (4.3)	20.8 (4.3)
Visit 4	21.7 (4.3)	13.5 (4.3)

SE, standard error; LTDS, lidocaine transmucosal delivery system.

Table 3. Verbal pain scores

	Placebo mean (SE)	LTDS mean (SE)
Verbal score 15 min. after placement		
Visit 1	0.9 (0.2)	0.8 (0.2)
Visit 2	1.6 (0.2)	0.8 (0.2)
Visit 3	1.3 (0.2)	1.2 (0.2)
Visit 4	1.4 (0.2)	0.8 (0.2)
Verbal score at end of treatment visit		
Visit 1	1.0 (0.2)	1.0 (0.2)
Visit 2	1.5 (0.2)	0.8 (0.2)
Visit 3	1.2 (0.2)	1.2 (0.2)
Visit 4	1.2 (0.2)	0.9 (0.2)

SE, standard error; LTDS, lidocaine transmucosal delivery system.

data in order to assess the efficacy of the scaling and root planing treatment. There were no differences in clinical indices noted between the quadrants treated with active and those treated with placebo patches after treatment.

Discussion

The results of this study show that transmucosal patches with lidocaine provided adequate anaesthesia so that therapeutic scaling and root planing treatment could be performed, without the use of injected local anaesthetics. The transmucosal patches did not alter periodontal healing in any way. The use of the patches made subjects more comfortable, but most subjects receiving the placebo were also able to tolerate the pain associated with therapeutic scaling and root planing. Twice as many subjects treated with placebo found the pain intolerable and required rescue medication, although this number was not statistically significant.

Subject evaluations indicated that transmucosal patch delivered anaesthetic provided pain relief that ranged from fairly effective or extremely effective for the duration of the treatment appointments. Most individuals, more than 80%, reported that they were likely to choose transmucosal anaesthetic patches or ask for it in preference to injected local anaesthetics for future scaling and root planing treatments. Subject comments were overwhelmingly favourable about the patch delivery system, indicating a strong preference during treatment for pain relief that was adequate and did not involve injections.

Transmucosal lidocaine patches were found to be a safe form of anaesthetic administration. No adverse events related to the use of the patches were seen. Mild gingival irritation, redness appearing at the patch placement sites occurred in 7.5% of the 40 subjects, during 1.9% of the 160 treatment visits.

Periodontal therapy provided to the subjects in this study was thorough ultrasonic scaling and root planing and resulted in healing responses consistent with those seen in other therapeutic scaling and root planing studies using conventional injected local anaesthetics.

Subjects who received scaling and root planing procedures were much more comfortable when transmucosal lidocaine patches were used for pain control than when placebo patches were used. This was confirmed by both VAS and verbal assessments of pain felt during treatment and at the end of each treatment.

Overall, LTDS provided sufficient anaesthesia necessary for therapeutic scaling and root planing, and was preferred over traditional injected anaesthetics. Future studies may determine the adequacies of these patches compared with other forms of anaesthetic, and for providing anaesthesia for other dental procedures.

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