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ORIGINAL ARTICLE

The analgesic effect of benzocaine mucoadhesive patches on orthodontic pain caused by elastomeric separators, a preliminary study

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Abstract

Objectives: To study the effect of benzocaine mucoadhesive patches (20%) on orthodontic pain caused by elastomeric separators. ***Subjects and methods.*** A split-mouth design was used in 30 patients (12 female, 18 male, aged 23 ± 3.75 years). They were instructed to apply benzocaine and placebo patches randomly for right or left first permanent molars of maxillary/mandibular arches for 20 min and repeat this procedure every 6 h with a similar type patch. A 10 cm Visual Analogue Scale (VAS) was used for pain perception assessment in patients who were given benzocaine (benzocaine group) or placebo (placebo group) patches. Pain perception (VAS) was recorded immediately after separator placement and after 2, 6, 12, 18, 24, 48 and 72 h. ***Results.*** The mean VAS (SD) for the placebo and benzocaine groups were 2.28 (1.08) and 1.63 (0.67), respectively. The pain peaked at 24 h. Significant pain perception differences were observed between groups at 2, 18, 24, 48 and 72 h. Pain perception was not different between genders or jaws investigated ($p > 0.05$). The Friedman test revealed significant differences in pain perception among various time intervals for benzocaine ($\chi^2 = 99.84$, $p = 0.000$) and placebo ($\chi^2 = 102.361$, $p = 0.000$) groups. Significant negative correlations (ρ) were found only between pain perception scores and patient's ages in the placebo group at 18 (−0.438), 24 (−0.526), 48 (−0.565) and 72 h (−0.458). ***Conclusion.*** The recorded mean VAS values were relatively low; however, the benzocaine 20% patches significantly reduced the post-separation orthodontic pain.

Key Words: *pain, orthodontics, benzocaine patch, orthodontic separators*

Introduction

The experience or fear of pain is the most important concern for patients and orthodontists [1,2], the worst aspect of treatment and the main discouraging reason for seeking orthodontic care [3,4]. Approximately 90–95% of patients experience some pain following placement of arch wires or elastomeric separators. Pain occurs within the first 4 h, reaches its peak at 24 h and lasts for 7 days [5,6]. However, 25–45% of patients continue to report pain even after a week [5,7]. The highest pain level in 95% of patients was reported after a day, caused by elastomeric separators and arch wires, and, still 40% experienced some pain after 1 week, but on a relatively lower pain level [8]. There is no standard method for reducing orthodontic pain and various methods have been used, such as low-level laser therapy, vibratory stimulation of the periodontal ligament, transcutaneous electrical nerve stimulation, as well as the pre- and postoperative use of medications (i.e. non-steroidal anti-inflammatory drugs (NSAIDs)) [1,9,10]. Orthodontic pain can negatively influence treatment outcome, oral hygiene and co-operation [11,12] and nearly 10% of patients choose to discontinue treatment because of the initial painful experiences [5]. Pain is a subjective response, with contributions from cultural

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background, experience, pain threshold, emotional state, stress level, gender, age, motivation and the appliances used [1,2,5,9,13,14].

Benzocaine (ethyl 4-aminobenzoate) has been used as a topical anaesthetic with minimal systemic adverse side-effects [15]. Benzocaine differs from other anaesthetics as it is not injected and applied directly to the area to be anaesthetized. It acts locally and is rapidly metabolized by esterases into an inactive compound [16], blocking the initiation and conduction of nerve impulses by decreasing the neuronal membrane permeability to sodium ions [17], which increases the pain thresholds [18,19]. Benzocaine has been used locally as a wax [20] or gel [21] to reduce the orthodontic pain, but, to our knowledge, the use of benzocaine mucoadhesive patches (for this study we simply call them benzocaine patches) has not been reported yet. Therefore, the objective of the present study was to investigate the effect of benzocaine patches (20%) on post-separation orthodontic pain and assessing the relationship between patient's age and pain perception.

The null hypothesis

Benzocaine patches (20%) have no significant effect on the perceived pain level for the first 72 h following placement of elastomertic separators.

Subjects and methods

Ethical approval for this study was granted by the Medical Ethics Committee of the Shahid Beheshti University of Medical Sciences. Subjects were 35 patients who were scheduled for orthodontic treatment either at the Orthodontic Department, School of Dentistry, Shahid Beheshti University of Medical Sciences, or in a private practice in Tehran, Iran. Patients were advised about the objectives of the study and written informed consent was obtained. The inclusion criteria for the subjects who participated in this study were:

(1) 15 years or older, in good general health without any reported systematic diseases;
(2) No concurrent use of analgesics and anti-inflammatory drugs;
(3) Requiring banding of posterior teeth and placement of two or more elastomeric separators as a part of orthodontic treatment;
(4) Caries-free dentition with healthy periodontium and without any endodontic problems in the posterior part of the mouth;
(5) Presence of antagonist teeth in the opposite arch and absence of posterior open bite and interdental spaces; and
(6) It was decided that the crowding for the dental arch under investigation should be moderate (4–8 mm).

Patients were excluded from the study if they used analgesics and anti-inflammatory drugs during the study, did not complete the questionnaire, did not use or improperly used benzocaine or placebo patches, removed elastomeric separators, or showed sensitivity or allergy to benzocaine. Of the 35 patients, five patients did not follow instructions and were excluded from the study. Overall, 30 patients (18 males, 12 females, aged 23 ± 3.75 years) completed the study and orthodontic separators were placed for 17 maxillary and 23 mandibular arches.

Interventions and assessment of pain perception

Elastomeric separators (Dentarum, Springen, Germany) were placed for either two (only one arch) or four first permanent molars (maxillary and mandibular arches). The patches sized 0.5 × 1.5 cm, containing 20 mg benzocaine (equal to one puff of 20% benzocaine sprays), dichloromethane, poly vinyl pyrolydyne, propylene glycol, ethanol, hydroxyl propylene methylcellulose and aspartame. Identical placebo patches (size, appearance and taste) were prepared, but without benzocaine. A senior orthodontic resident performed this study and was blinded to the type of patches. In allocating patches, a split-mouth design was used. Patients were instructed to apply benzocaine patches on the buccal attached gingivae and embrasure of either the right or left first molar for 20 s and then repeat this procedure with a similar patch every 6 h. The placebo patch was placed on the first molar on the opposite side of the same arch. The choice of the first molar to apply a benzocaine or placebo patch was determined randomly. The patches remained in place until they resolved.

Patients were asked to rate the pain after elastomeric separator placement, using a 10 cm Visual Analogue Scale (VAS). The VAS consisted of marked horizontal lines from 0 (no pain) to 10 cm (agonizing pain). They were advised to discontinue using the patches if they developed any symptoms (e.g. headache, fatigue). Patients were given post-treatment instructions and advised against the concurrent use of analgesic drugs. After placing the orthodontic separators, patients were asked to fill out a pain questionnaire for 72 h that included information on the age, gender, and the involved dental arch (s) (maxilla and/or mandible) as well as data on the pain VAS score. They were asked to mark the pain level on the 10 cm VAS for the involved jaws immediately after separator placement and after 2, 6, 12,18, 24, 48 and 72 h.

Statistical analysis

The analysis was performed using the Statistical Package for Social Sciences (SPSS) Version 17.0 (SPSS Inc., Chicago, IL). Mean, standard deviation (SD)

Table I. Mean, standard deviation (SD) and mean ranks for pain scores (VAS) as well as the result of the Wilcoxon Signed Ranks test.

	Benzocaine group		Placebo group		
Pain evaluation interval, Time (h)	Mean (SD)	Mean rank	Mean (SD)	Mean rank	*p*-value
0	0.77 (0.50)	2.47	1.03 (1.16)	2.13	0.163
2	1.10 (0.71)	3.20	1.77 (1.10)	3.43	0.007
6	1.57 (0.90)	4.30	2.10 (1.56)	4.00	0.087
12	1.87 (1.11)	5.03	2.43 (1.63)	4.73	0.059
18	2.10 (1.03)	5.75	2.77 (1.61)	5.47	0.019
24	2.50 (1.14)	6.58	3.40 (1.38)	6.65	0.019
48	2.13 (1.11)	5.82	3.03 (1.45)	6.13	0.003
72	0.97 (0.85)	2.85	1.67 (0.92)	3.45	0.002
Total	1.63 (0.67)		2.28 (1.08)		

and mean ranks for pain scores (VAS) were calculated. The Wilcoxon signed-rank test was used to determine the differences in pain perception after orthodontic separator placement between two groups (placebo and benzocaine) at different time intervals. Any difference in the pain score for the involved jaw and gender in both groups was analysed using the Mann-Whitney U-test. The Friedman test of multiple comparisons was used to compare the longitudinal pain level in both groups. The Spearman's correlation coefficient (ρ) was used to assess the relationship between patient's age and pain perception scores. Any $p < 0.05$ was considered as statistically significant.

Results

The retention of mucoadhesive patches was satisfactory and participants did not report any adverse side-effects for the entire study. The pain peaked at 24 h when the mean pain scores (SD) were 3.40 (1.38) (mean rank = 6.65) and 2.50 (1.4) (mean rank = 6.58) for the placebo and benzocaine groups, respectively (Table I). A decline in the pain perception was observed after 48 h in both groups. The Wilcoxon signed-rank test demonstrated significant differences in pain perception between groups at 2, 18, 24, 48 and 72 h (Table I). Therefore, the null hypothesis was partially rejected. The mean pain score (SD) for the placebo and benzocaine groups were 2.28 (1.08) and 1.63 (0.67), respectively. The Friedman test revealed significant differences in pain perception among various time intervals for benzocaine ($\chi^2 = 99.84$, df = 7, $p = 0.000$) and placebo ($\chi^2 = 102.361$, df = 7, $p = 0.000$) groups.

The mean pain score (SD) for females and males in the placebo group were 2.28 (1.17) and 2.27 (1.00), respectively. The corresponding pain scores for the benzocaine group were 1.54 (0.66) and 1.73 (0.69), respectively. The results of the Mann-Whitney test did not show any significant gender differences in the pain perception in the placebo ($p = 0.67$) or benzocaine groups ($p = 0.58$). There were only significant negative correlations (ρ) between pain scores and patient's ages in the placebo group at 18 (−0.438), 24 (−0.526), 48 (−0.565) and 72 h (−0.458) (Table II). However, no significant correlation was found in the benzocaine group (ρ ranged between −0.004 and 0.184). In the mandibular arch, the mean pain scores (SD) for the placebo and benzocaine groups were 2.27 (1.00) and 1.73 (0.69), respectively. The corresponding mean pain scores in the maxillary arch were 2.28 (1.17) and 1.54 (0.66), respectively. No significant jaw difference in pain perception was observed in the placebo ($p = 0.91$) and benzocaine ($p = 0.54$) groups.

Discussion

This study used placebo and benzocaine patches with a split-mouth design to eliminate inter-individual biologic and anatomical variations as well as force magnitude differences [22]. To control for crowding

Table II. Correlation coefficients (ρ) between pain scores and the patient's ages at different time intervals.

Time intervals (h)	0	2 h	6 h	12 h	18 h	24 h	48 h	72 h
ρ (placebo)	−0.166	−0.182	−0.328	−0.355	−0.438	−0.526	−0.565	−0.458
p-value	0.382	0.335	0.077	0.054	0.016	0.003	0.001	0.011
ρ (bezocaine)	−0.004	0.022	0.151	0.184	−0.034	0.033	−0.170	−0.047
p-value	0.983	0.907	0.424	0.331	0.857	0.864	0.369	0.805
n	30	30	30	30	30	30	30	30

patients with moderate crowding selected assuming they had tight contact points for permanent molars. Both groups were homogenous for pain perception and no significant differences were observed between groups immediately after the orthodontic separator placement, giving reliability to the post-therapeutic findings. A 10 cm VAS tool with graded linear horizontal scale was used to assess the pain, which is a method previously used in the literature [8,23–26]. The VAS has been shown to be a reliable and accurate tool in evaluating subjective experiences, such as pain [27], to meaningfully compare groups or individuals [28,29]. This method provides more variety in responses [20] and gives a more sensitive and accurate representation of pain intensity than do descriptive pain scales [27].

The pain peaked at 24 h in both groups. Perhaps this coincided with the more accentuated inflammatory stage, indicating that experimental pain initiated by orthodontic separators, was an effective method that followed the physio-pathological pattern [30–32]. Our findings agree with studies [1,4,8–11,20,33] that reported a delayed pain emergence following orthodontic separator placement. Giannopoulou et al. [34] showed the pain scores increased 1 and 24 h after placement of separators and related this to an inflammatory response mediated by cytokines and Prostaglandins (the increase of PGE2 and IL-1β).

Benzocaine apparently works by blocking nerve signals; however, pain was present at all time intervals and significant differences were observed between groups at 2, 18, 24, 48 and 72 h. According to VAS scores, the benzocaine group experienced significantly less pain. These findings bear similarities with the work of Kluemper et al. [20] that used benzocaine wax and conventional orthodontic wax as a placebo. Hersh et al. [35] concluded that mucoadhesive patches containing 12 mg benzocaine (for 60 min) were effective in the relief of spontaneous toothache pain, but the outcome in comparison to the placebo group, was not significantly different. The designs of these studies are not similar to the present study and comparison is difficult, i.e. study sample, pain origin (i.e. pain caused by archwires, spontaneous toothache or separators), the delivery system and the amount of benzocaine delivered to the tissue, as well as the location of patches and the duration of their contact with tissue. The recorded mean VAS values were low, suggesting the pain due to elastomeric separators was not really a clinical problem. However, these findings have implications for orthodontic treatment, as benzocaine patches used in this study were effective in reducing the pain perception and can be useful in reducing anxiety in orthodontic patients [36].

Consistent with several studies [4,7,9,12,32,37-39], no gender differences were found in the mean pain scores in both groups. Nonetheless, a few studies [14,40] reported higher pain experience in women, which contrasts with our findings. Pain is a subjective response to a noxious stimulus with individual variations [37] and its intensity depends on factors such as the sleep quantity, psychological condition, levels of depression, genetic and hormonal differences and previous painful experience [30,40–42]. Further, McGrath and Craig [43] concluded that puberty led to the emergence of different pain experiences for genders and that women had higher levels of pain scores compared to men after puberty.

Similar to studies that studied pain perception after placing archwires, we did not observe a difference in pain perception between maxillary and mandibular arches [12,44]. Fernandes et al. [12] investigated the pain perception during the initial phase of orthodontic movement caused by two types of aligning archwires. In the first 11 h after inserting archwires, a higher pain level was recorded in the mandibular arch and the differences were significant, but that was not true for the whole study period. Jones and Chan. [44] reported no relationship between pain scores and the dental arches during orthodontic treatment for two initial arch wires. It appeared differences of the maxillary and mandibular arches were not important in perceiving orthodontic pain following separator placement.

There was no significant association between pain level and age in the quadrant that received benzocaine patches, but significant correlations were observed in the placebo sides. Ngan et al. [9] used the separator and archwires induced orthodontic pain and the pain levels experienced by two age groups (patients more than 16 years and those of 16 years and under) were not different. Bergius et al. [5] also reported no correlation between the post-separation pain level and age in patients aged 12–18 years. In contrast, there are other studies that showed an age gradient in the pain perception [12,14,44–46]. The resent study had participants aged 15–31 years and, therefore, comparison with the mentioned studies is difficult. Nonetheless, the younger patients showed higher pain perception scores in a few time points in the placebo side, compared to the older ones. Although the cause and effect link between the malocclusion and psychosocial well-being [47] or dental health [48] has not been established yet, the older patients usually are aware of these perceived psychosocial and functional issues and have sufficient internal motivation to face orthodontic pain. Although a preliminary study in nature, it was adequately powered to detect the lower pain perception level induced by benzocaine patches for most time points. This reduced pain perception could lead to increased comfort level, reduced anxiety, a positive attitude among orthodontic patients about their treatment and improved compliance [20,37].

The compliance to use the patches was good and they were well tolerated. Case reports of adverse events such as methemoglobinemia associated with the use of

benzocaine sprays in the mouth and throat have been occasionally reported, although its mechanism is not well-understood [49]. Although not seen in this study, this clinical situation, unless reversed with methylene blue, can be associated with increased morbidity and mortality. There was no taste difference between benzocaine and placebo patches following application in this study, which might have influenced blinding. Further, Benzocaine is an odourless powder and, due to its numbing effect on taste buds [50], the effect of likely taste difference on blinding seems to be minimal. According to some authors, the placebo effect of short-duration existed [51] and could be observed at 2 h in the placebo group. As this study did not assign a group as a control group, we were not able to assess the placebo effect. Further, the orthodontic elastic separators have an effect that is not similar to orthodontic tooth movement, owing to the amount of displacements of the teeth in the periodontal ligament space and the likely occurring bone metabolic changes. Therefore, the present findings cannot be applied to orthodontic tooth movement. A limitation of this study is that patches were placed on the buccal attached gingiva of the maxilla or mandible, but information on the thickness of the attached gingiva and the underlying alveolar bone was not collected. Consequently, future investigations aimed at determining the relationship between the efficacy of benzocaine patches and the thickness of attached gingival or the underlying alveolar bone is needed.

Conclusion

The mean VAS values recorded in this study were relatively low. The pain peaked at 24 h and started to decrease 48 h after placement of separators. The use of benzocaine patches (20%) during the first 3 days following separator placement significantly reduced the pain level for most time intervals. Pain perception was not different between genders or jaws investigated.

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***Declaration of interest*:** The authors report no conflicts of interest.

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NOTICE OF CORRECTION

The Early Online version of this article published online ahead of print on 10 Jan 2013 containded errors in the author list. This has been corrected for this version.