Original Article

Effectiveness of metronidazole gel and mobile telephone short-message service reminders on gingivitis in orthodontic patients: *A double-blind randomized controlled trial*

Hafiz Taha Mahmood[a]; Farheen Fatima[b]; Mubassar Fida[c]; Rashna Hoshang Sukhia[d]; Sarah Irfan[e]; Durreshahwar Malik[e]; Ashfaq Younus[f]; Erum Afzal[e]

ABSTRACT

Objectives: To compare the effectiveness of metronidazole gel and mobile telephone short-message service (SMS) reminders on gingivitis in patients undergoing fixed orthodontic treatment.

Materials and Methods: The trial was double blinded (patient and investigator), and only the clinical trial unit pharmacist was unblinded. Data were collected from patients undergoing fixed orthodontic treatment for at least 6 months. A total of 66 patients were randomly assigned to either 0.8% metronidazole gel (n = 22), SMS reminder and placebo gel (n = 22), or placebo (control) group only (n = 22). Gingival index (GI), bleeding index (BI), and orthodontic plaque index (OPI) were evaluated on several teeth at baseline (T_0) and after 4 weeks (T_1). Paired-sample *t*-tests were used to compare mean differences of indexes at T_0 and T_1 in the groups, and independent-sample *t*-tests were used to determine the effects of interventions compared with the controls.

Results: Data from 64 patients were analyzed; there were 2 dropouts. There were statistically significant ($P < .05$) reductions in GI, BI, and OPI scores from T_0 to T_1 for each intervention. However, there were no significant differences between each intervention and the control group. There were no adverse effects.

Conclusions: The null hypothesis could not be rejected. There is no difference between interventions (application of 0.8% metronidazole gel and SMS reminder for reinforcing oral hygiene) in reducing gingival inflammation in orthodontic patients. (*Angle Orthod.* 2021;91:220–226.)

KEY WORDS: Gingivitis; Metronidazole; Orthodontic appliances; Oral hygiene; Text messaging

INTRODUCTION

Fixed orthodontic appliances allow extensive accumulation of plaque on teeth, leading to gingivitis, periodontitis, and enamel demineralization.[1,2] Several studies[3,4] reported an elevation in the plaque index scores within 1–3 months of appliance placement. Naranjo et al.[5] reported the changes in bacterial composition within 12 days, and Zachrisson and Zachrisson[6] reported the development of gingivitis in 1–2 months of fixed appliance treatment.

A common strategy to improve plaque removal in patients is to incorporate chemo-therapeutic agents.[7] The localized delivery allows maximum concentration of the drug at the target site and minimizes potential systemic effects.[8] Metronidazole has been used by several researchers because of its selective antimicrobial activity against the obligate anaerobes. A meta-analysis conducted by Pavia et al.[9] showed the effectiveness of localized use of metronidazole as an adjunct to scaling and root planing. Miani et al.[10]

[a] Consultant Orthodontist and Senior Registrar, Hamdard University Dental Hospital, Karachi, Pakistan.

[b] Consultant Orthodontist and Senior Registrar, Bahria University Medical and Dental College, Karachi, Pakistan.

[c] Consultant Orthodontist, Associate Professor, Program Director Orthodontics Residency Program, Section of Dentistry, Department of Surgery, The Aga Khan University Hospital, Karachi, Pakistan.

[d] Consultant Orthodontist and Assistant Professor, Section of Dentistry, Department of Surgery, The Aga Khan University Hospital, Karachi, Pakistan.

[e] Resident in Orthodontics, Section of Dentistry, Department of Surgery, The Aga Khan University Hospital, Karachi, Pakistan.

[f] Instructor in Orthodontics, Section of Dentistry, Department of Surgery, The Aga Khan University Hospital, Karachi, Pakistan.

Corresponding author: Dr Hafiz Taha Mahmood, BDS, FCPS, Consultant Orthodontist/Senior Registrar, Hamdard University Dental Hospital, Plot # S.T-2, Block-L, North Nazimabad Karachi, Pakistan
(e-mail: dr.tahamahmood@gmail.com)

Accepted: October 2020. Submitted: May 2020.
Published Online: December 30, 2020

concluded that the use of metronidazole gel significantly reduced the total bacterial count in the gingival crevicular fluid.

Another modality to improve plaque control in patients is by instigating positive behavioral changes and increasing patient compliance via mobile telephone SMS reminders.[11] SMS reminders give instructions to the patients and reinforce oral hygiene maintenance.[11,12] Eppright et al.[12] reported the effectiveness of short-message service (SMS) reminders in orthodontic patients and found significantly lower bleeding index (BI), gingival index (GI), and orthodontic plaque index (OPI) scores in the SMS reminder group compared with controls.

The application of metronidazole gel is effective in the management of periodontal disease.[8,10] In addition, the constant reminder therapy at weekly intervals would also lead to improvements in oral hygiene.[12] No previous study has been conducted to compare the effectiveness of SMS reminders and the use of metronidazole gel to reduce gingival inflammation in orthodontic patients.

Specific Objectives and Hypotheses

The aim of this study was to compare the effectiveness of application of 0.8% metronidazole gel or mobile telephone SMS oral hygiene reminders with placebo gel on gingivitis in 66 adult patients for a period of 4 weeks. The null hypothesis was that there would be no difference between the interventions (0.8% metronidazole gel and mobile telephone SMS reminders) on reducing the gingival inflammation in orthodontic patients.

MATERIALS AND METHODS

Trial Design

This study was a three-arm parallel, randomized, double-blind controlled trial with an allocation ratio of 1:1:1. Ethical approval was obtained from the Ethics Review Committee of the Aga Khan University Hospital (5320-Sur-ERC-18). The trial was registered in the clinical trials registration database (ClinicalTrials.gov; NCT03508999). There were no deviations to the protocol after trial initiation. The study was conducted according to the World Medical Association's Declaration of Helsinki and the principles of Good Clinical Practice.

Participants, Eligibility Criteria, and Settings

The sample was collected from the outpatient orthodontic clinic from May 2018 to November 2018. Eligibility criteria included patients aged between 18–40 years with moderate to severe crowding undergoing orthodontic treatment for at least 6 months with all teeth mesial to the first molars bonded; systemically healthy patients with no comorbidities such as rheumatic fever, blood dyscrasias, congenital heart disease, or diabetes mellitus; and patients with gingivitis as assessed by GI (score $\geq$ 2), BI (score = 2), and OPI (score $\geq$ 2) on any three standard teeth (teeth numbers 13,15, 21, 33, 35, 41). Only those patients who gave written consent were included in the study.

The exclusion criteria were women who were pregnant or lactating and patients with histories of surgical or nonsurgical periodontal therapy in the past 6 months, use of antibiotic or anti-inflammatory drugs in the past 30 days, smoking, or allergy to metronidazole; clinical attachment loss of greater than 2 mm at two sites; or removable or fixed dental prosthesis.

Interventions

All patients were treated with the same fixed orthodontic appliances using metal brackets (Di-MIM Bracket System, Ortho Organizers, Carlsbad, Calif) on the incisors, canines, and premolars and bands on the first molars. Bonding of the brackets was completed by orthodontic residents (H.T.M., F.F., S.I., D.M., E.F.) with a direct bonding approach and use of chemical cure adhesives (3M Transbond, Saint Paul, Minn). The type of ligation for each patient was conventional (elastomeric ligatures). General oral hygiene instructions were given verbally as well as provided in a brochure to each participant of the study by the treating clinician.

Group A participants were given 0.8% metronidazole gel. Group B participants were given placebo gel and biweekly SMS reminders for reinforcing oral hygiene ("Please keep brushing twice daily with a soft bristle toothbrush and fluoridated toothpaste."). Group C participants were given placebo gel (control) only. All patients were instructed to apply a pea-sized amount of gel on the gingiva twice daily for 4 weeks. Patient compliance for gel use was assured by providing a log sheet and further checked by having them return the tubes of gels. Another log sheet given to each participant was used to confirm whether they received the reminder SMS at biweekly intervals.

The 0.8% metronidazole gel contained metronidazole tablets and 2% carboxy-methyl cellulose as a base solution. The placebo gel contained similar ingredients except the metronidazole tablet. The preparation, packing, labeling, storage, and dispatch of the gel were performed by the clinical trial unit (CTU).

Outcomes

The primary outcome was measurement of the indexes during the study period from baseline (T_0) to 4 weeks (T_1) of metronidazole gel/reminder SMS therapy (Figure 1). GI[13] and BI[14] were evaluated by

Scoring	Gingival Index (GI)
0	No inflammation
1	Mild inflammation, slight change in color, slight edema, no bleeding on probing
2	Moderate inflammation, moderate glazing, redness, bleeding on probing
3	Severe inflammation, marked redness and hypertrophy, ulceration, tendency to spontaneous bleeding
Scoring	**Bleeding Index (BI)**
0	Absence of bleeding after 30 seconds
1	Bleeding observed after 30 seconds
2	Immediate bleeding
Scoring	**Orthodontic Plaque Index (OPI)**
0	No plaque deposits on the tooth surfaces surrounding the bracket base
1	Plaque deposits on one tooth surface at the bracket base
2	Plaque deposits on two tooth surface at the bracket base
3	Plaque deposits on three tooth surface at the bracket base
4	Plaque deposits on four tooth surface at the bracket base

Figure 1. Scoring criteria for the evaluation of gingival,[13] bleeding,[14] and orthodontic plaque[15] indexes.

assessing and probing the gingiva. OPI was evaluated by using plaque disclosing tablets (Produits Dentaires SA, Vevey, Switzerland).[15]

Six standard sites on the incisors, canines, and premolars were used in this study as described by Gettinger et al.[16] The banded first molars were not included because banding itself was expected to lead to a compromise in periodontal conditions. The study sites were assessed using a Williams probe and included six proximal line angles on the following teeth: right maxillary second premolar, mesiobuccal line angle; right maxillary canine, distobuccal line angle; left maxillary central incisor, distopalatal line angle; right mandibular central incisor, distolingual line angle; left mandibular canine, distobuccal line angle; and left mandibular second premolar, mesiobuccal line angle. If a study tooth was missing, the corresponding tooth on the contralateral side was examined. There were no changes in the outcome assessment after trial initiation.

The patients were included in the trial if GI, BI, and OPI scores were found to be $\geq$2 on any three or more of the six teeth that were evaluated in the trial. The cumulative GI and BI indexes were obtained by calculating the average of the measured values at T_0 and T_1. For OPI, the score at each time interval was obtained by counting the number of teeth with plaque accumulation.

Sample Size

Sample size was calculated using an OpenEpi (version 3.01 developed by Emory University, Atlanta, GA.) sample size calculator. Martin et al.[17] reported that a mean GI at 4–6 weeks in the gel group was 1.56 $\pm$ 0.14, whereas in the control group it was 1.68 $\pm$ 0.12. With that difference at a level of significance (α) of 5% and power of (1-β) 95%, at least 19 observations were needed for each arm. The sample size was inflated by 10% to get 21 participants per arm for any loss to follow-up or noncompliance. Because there were three experimental groups, a total of 63 participants were needed.

Interim Analyses and Stopping Guidelines

None.

Randomization (Sequence Generation, Allocation Concealment, Implementation)

Participants were assigned to one of the three study groups using a computer-generated randomization list. The randomization was performed by CTU using a random permuted block sampling of 6 and 9.

Patients recruitment was performed by one pair of investigators (H.T.M. and F.F.) who explained the aims and objective and the design of the study to the patients. Allocation was concealed from the patients and investigators by labeling the gels with the same prescription and using sequentially numbered codes. All of the measurements at T_0 and T_1 were recorded by the second set of investigators (S.I., A.Y., and E.F.) on separate T_0 and T_1 sheets. The reminder SMS was sent by another clinician (D.M.) who was not part of the recruitment stage.

Blinding

The trial was double blinded (patient and investigator), and only the CTU pharmacist was unblinded in the study. The randomization codes were not revealed until data analysis was performed.

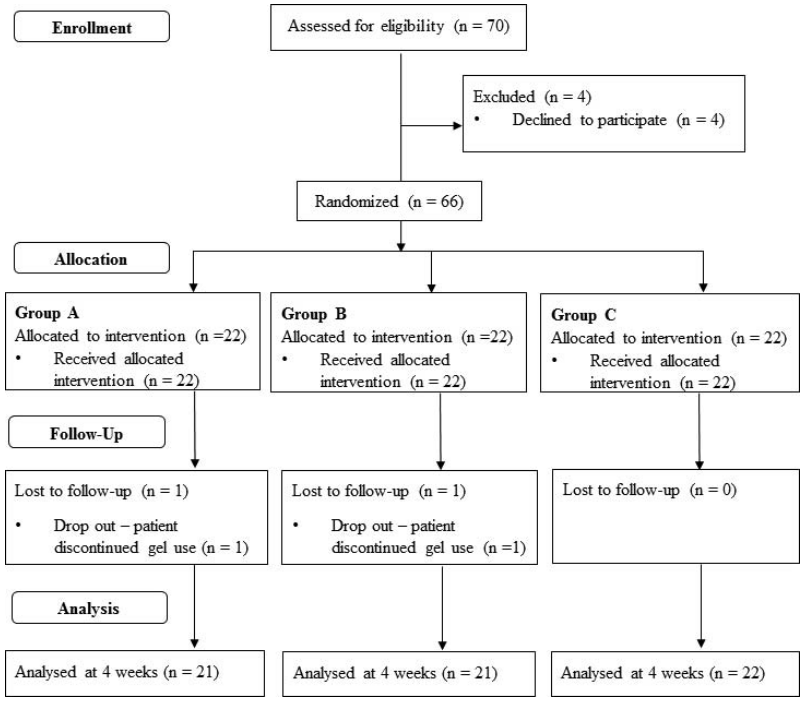

Figure 2. Consolidated Standards for Reporting of Trials flow diagram of the progress of participants through different stages of the trial.

Statistical Methods

Data were analyzed using SPSS version 22.0 (UNICOM Systems, Inc., Los Angeles, Calif.). Descriptive statistics for all baseline clinical parameters such as GI, BI, and OPI scores were calculated. To test the normality of data, the Shapiro-Wilk test was applied, and it showed normal distribution; hence, parametric tests were applied. Paired-sample *t*-tests were applied to compare the mean differences (T_0–T_1) of GI, BI, and OPI in groups A, B, and C. To evaluate the effect of interventions with controls, independent-sample *t*-tests were applied among the GI, BI, and OPI variables in groups A vs C and group B vs C. The level of significance was kept at $P \leq .05$.

RESULTS

Participant Flow

A total of 70 patients were assessed for eligibility in the trial, of which 4 declined to participate. Thus, 66 patients were randomly assigned with 22 patients per group. There was one drop out in both groups A and B (Figure 2).

Table 1. Baseline Demographic Characteristics of the Participants[a]

Variable	Group A	Group B	Group C
Total	21	21	22
Male	2	6	9
Female	19	15	13
Age	23.41 ± 6.54	22.01 ± 3.92	23.17 ± 5.32
Mean GI T_0	1.23 ± 0.55	1.30 ± 0.49	1.40 ± 0.4
Mean BI T_0	1.25 ± 0.04	1.25 ± 0.55	1.40 ± 0.4
Mean OPI T_0	3.76 ± 0.43	3.86 ± 0.35	3.59 ± 0.66

[a] N = 64.

Baseline Data

The number of female participants was higher in each group because of the fact that a greater number of women sought orthodontic care. The mean ages of the participants in each group were comparable (Table 1).

Numbers Analyzed, Outcomes, and Estimation

The means and standard deviations (SDs) at T_0 and T_1 of groups A, B, and C are given in Table 2. There were statistically significant differences ($P < .05$) in the values at T_0 and T_1 of GI, BI, and OPI in all groups. The values at T_1 showed improvements in all indexes for each intervention. All interventions showed resolution of gingival inflammation. Greater reductions in OPI scores further improve the GI and BI indexes.

Although there were statistically significant differences within each intervention between T_0 and T_1, the group-wise (group A vs group C and group B vs group C) comparisons of GI, BI, and OPI values showed no significant differences (Tables 3 and 4). Hence, all interventions were similarly effective in the resolution of gingivitis.

Harms

None.

Table 2. Comparison of Means and SDs of GI, BI, and OPI Scores in Metronidazole Gel, Reminder SMS, and Control Groups at T_0 and T_1[a]

	Group A					Group B					Group C				
	Mean ± SD		95% CI[b]		*P*	Mean ± SD		95% CI[b]		*P*	Mean ± SD		95% CI[b]		*P*
Variable	T_0	T_1	Lower	Upper	Value	T_0	T_1	Lower	Upper	Value	T_0	T_1	Lower	Upper	Value
GI	1.23 ± 0.55	0.75 ± 0.70	0.13	0.83	.010	1.3 ± 0.49	0.58 ± 0.55	0.41	1.02	<.001	1.4 ± 0.4	0.74 ± 0.54	0.42	0.89	<.001
BI	1.25 ± 0.44	0.74 ± 0.63	0.19	0.81	.003	1.25 ± 0.55	0.61 ± 0.5	0.35	0.92	<.001	1.4 ± 0.4	0.75 ± 0.58	0.47	0.85	<.001
OPI	3.76 ± 0.43	2.71 ± 1.38	0.38	1.71	.004	3.86 ± 0.35	2.76 ± 1.44	0.36	1.82	.005	3.59 ± 0.66	2.05 ± 1.49	0.9	2.18	<.001

[a] Group A = metronidazole gel (n = 21), group B = reminder SMS + placebo gel (n = 21), and group C = placebo gel (n = 22). Paired-sample *t*-test; $P \leq .05$.
[b] CI indicates confidence interval.

Table 3. Comparison of Means and SDs of GI, BI, and OPI Scores in the Metronidazole Gel and Control Groups[a]

Variable	Group A, Mean ± SD	Group C, Mean ± SD	*P* Value
GI	0.48 ± 0.77	0.65 ± 0.53	.36
BI	0.50 ± 0.67	0.66 ± 0.43	.39
OPI	1.57 ± 2.20	2.09 ± 1.92	.41

[a] Group A = metronidazole gel, and group C = placebo gel. N = 43; independent-sample *t*-test; $P \leq .05$.

DISCUSSION

Main Findings and Interpretations

In this trial, no significant differences were found in the effectiveness of either metronidazole gel or reminder SMS therapies. The comparison of metronidazole gel and reminder SMS therapy with the control group did not lead to superior results for any intervention. Effective reductions in all index scores were also found in the placebo group. As standard oral hygiene instructions were given to each participant of the trial, the similar positive effects with all interventions could also have been attributed to patients' proficient compliance and management of oral hygiene.

The factors related to the clinically acceptable effects in the placebo group could have been attributed to patient expectations toward outcome, patient–doctor relationships, or the Hawthorne effect.[18–20] This effect was frequently reported in various studies as the sole criterion for oral health improvements of control groups that received placebo treatments.[21,22] Feil et al.[21] also reported a reduction in plaque scores with intentional application of the Hawthorne effect and changes in patients' behavior and compliance. The effective reduction in all indexes in each group could have been attributed to the Hawthorne effect.

Numerous researchers have reported significant improvement in the GI, BI, and plaque index with the topical application of 2% chlorhexidine,[23] 0.4% stannous fluoride,[24] and antioxidant-essential oil gels.[25] Pradeep et al.[26] reported a reduction in the GI and plaque index and microbiological count after 24 weeks of application of 10 mg metronidazole gel. Perinetti et al.[27] reported a decrease in bleeding on probing, probing depth, and clinical attachment levels after four

Table 4. Comparison of Means and SDs of GI, BI, and OPI Scores in Reminder SMS and Control Groups[a]

Variable	Group B, Mean ± SD	Group C, Mean ± SD	*P* Value
GI	0.72 ± 0.67	0.65 ± 0.53	.88
BI	0.64 ± 0.62	0.66 ± 0.43	.73
OPI	1.95 ± 2.39	2.09 ± 1.92	.83

[a] Group B = reminder SMS + placebo gel, and group C = placebo gel. N = 43; independent-sample *t*-test; $P \leq .05$.

weekly applications of 1% metronidazole gel. In the current study, improvements in the GI, BI, and OPI scores was also found after 4 weeks of application of 0.8% metronidazole gel. Nevertheless, the previous studies were conducted in nonorthodontic patients, and no other study had previously evaluated the effects of this gel in orthodontic patients.

In orthodontics, active reminders are persuasive in keeping up the good rapport between doctors and patients, decreasing the level of self-reported pain by the patient and improving oral hygiene compliance.[12,28] Bowen et al.[29] sent biweekly SMS reminders for 4 weeks about oral hygiene compliance and found significantly lower plaque coverage around teeth. Iqbal et al.[30] sent weekly SMS reminders for 3 months and found significantly lower BI and plaque and modified gingival index scores in their studied population. In the current trial, biweekly SMS reminders were sent for 4 weeks and similarly resulted in significantly lower GI, BI, and OPI scores.

Limitations

The main limitation of this study was the relatively short follow-up period. There were more female participants in each arm, and their presence may have confounded the results as women have previously been shown to be generally more compliant.[31] Metronidazole gel may result in a metallic taste, which may cause nausea. Participants were informed of the taste in the written consent form, and compliance with using the gel was ensured by having them fill the log sheets. The concentration of metronidazole gel that was used was also unique and not readily available in every health care setting.

Generalizability

The generalizability of the results could be limited because the study was conducted in one center only. The strength of the study was that there was limited attrition of the sample. The double blinding of the trial reduced observational and detection biases. In addition, a pair of clinicians was involved in the recruitment stage and another set of clinicians were involved in obtaining the measurements of the indexes, leading to further reduction in selection and measurement biases. Furthermore, the clinician who sent the reminder SMS was not part of the trial participant recruitment.

Recommendation

Additional trials for testing the efficacy of metronidazole gel and reminder SMS at biweekly intervals with a greater follow-up period are needed to confirm the reported findings of this study and to determine the maximum effectiveness of such interventions.

CONCLUSIONS

- There were significant improvements in the indexes in all intervention groups. Gingival inflammation was reduced with the topical administration of 0.8% metronidazole gel, reminder SMS at biweekly intervals, and placebo gel.
- The improvement in the gingival scores could be attributed to better oral hygiene maintenance by the patients or attributed to trial participation itself (Hawthorne effect).
- The null hypothesis could not be rejected. There was no difference between interventions or compared with a placebo in reducing gingival inflammation in orthodontic patients.

ACKNOWLEDGMENTS

The authors thank Dilshad Begum and Sadaf Gul from clinical trials unit of our hospital for helping us in protocol write-up, drug dispensing, and randomization of the study participants. The trial was sponsored by the Department of Surgery at our hospital.

Protocol

The protocol is available on request from the corresponding author.

Declaration of Conflicting Interests

The authors declare no conflicts of interest.

REFERENCES

1. Mitchell L. Decalcification during orthodontic treatment with fixed appliances: an overview. *Br J Orthod*. 1992;19:199–205.
2. Atack NE, Sandy JR, Addy M. Periodontal and microbiological changes associated with the placement of orthodontic appliances. A review. *J Periodontal*. 1996;67:78–85.
3. Karkhanechi M, Chow D, Sipkin J, et al. Periodontal status of adult patients treated with fixed buccal appliances and removable aligners over one year of active orthodontic therapy. *Angle Orthod*. 2012;83:146–151.
4. Liu H, Sun J, Dong Y, et al. Periodontal health and relative quantity of subgingival Porphyromonas gingivalis during orthodontic treatment. *Angle Orthod*. 2011;81:609–615.
5. Naranjo AA, Triviño ML, Jaramillo A, Betancourth M, Botero JE. Changes in the subgingival microbiota and periodontal parameters before and 3 months after bracket placement. *Am J Orthod Dentofacial Orthop*. 2006;130:275–217.
6. Zachrisson S, Zachrisson BU. Gingival condition associated with orthodontic treatment. *Angle Orthod*. 1972;42:26–34.
7. Ainamo J. Control of plaque by chemical agents. *J Clin Periodontol*. 1977;4:23–35.
8. Loesche WJ. Antimicrobials in dentistry: with knowledge comes responsibility. *J Dent Res*. 1996;75(7):1432–1433.
9. Pavia M, Nobile CG, Bianco A, Angelillo IF. Meta-analysis of local metronidazole in the treatment of chronic periodontitis. *J Periodontol*. 2004;8:830–838.

10. Miani PK, do Nascimento C, Sato S, Filho AV, da Fonseca MJ, Pedrazzi V. In vivo evaluation of a metronidazole-containing gel for the adjuvant treatment of chronic periodontitis: preliminary results. *Eur J Clin Microbiol Infect Dis*. 2012;31:1611–1618.
11. Fjeldsoe B, Marshall A, Miller Y. Behavior change interventions delivered by mobile telephone short-message service. *Am J Prev Med*. 2009;36:165–173.
12. Eppright M, Shroffb B, Bestc AM, Barcomad E, Lindauere SJ. Influence of active reminders on oral hygiene compliance in orthodontic patients. *Angle Orthod*. 2014;84:208–213.
13. Loe H. The Gingival Index, the Plaque Index and the Retention Index Systems. *J Periodontol*. 1967;38:610–616.
14. Saxton CA, van der Ouderaa FJ. The effect of a dentrifice containing zinc citrate and Triclosan on developing gingivitis. *J Periodontal Res*. 1989;24:8–80.
15. Beberhold K, Sachse-Kulp A, Schwestka-Polly R, Hornecker E, Ziebolz D. The orthodontic plaque index: an oral hygiene index for patients with multibracket appliances. *Orthodontics (Chic)*. 2012;13:94–99.
16. Gettinger G, Patters MR, Testa MA, et al. The use of six selected teeth in population measures of periodontal status. *J Periodontol*. 1983;54:155–159.
17. Martin BJ, Campbell PM, Rees TD, Buschang PH. A randomized controlled trial evaluating antioxidant–essential oil gel as a treatment for gingivitis in orthodontic patients. *Angle Orthod*. 2016;8:407–412.
18. Adler HM. Toward a biopsychosocial understanding of the patient-physician relationship: an emerging dialogue. *J Gen Intern Med*. 2007;22:280–285.
19. Crum A, Zuckerman B. Changing mindsets to enhance treatment effectiveness. *JAMA*. 2017;317:2063–2064.
20. Jeffcoat MK. Principles and pitfalls of clinical trials design. *J Periodontol*. 1992;63:1045–1051.
21. Feil P, Grauer J, Gadbury-Amyot C, Kula K, McCunniff M. Intentional use of the Hawthorne effect to improve oral hygiene compliance in orthodontic patients. *J Dent Educ*. 2002;66:1129–1135.
22. Gilbert GH, Duncan RP, Campbell AM. Evaluation for an observation effect in a prospective cohort study of oral health outcomes. *Community Dent Oral Epidemiol*. 1998;26:233–240.
23. Jamilian A, Ghasemi M, Gholami D, Kaveh B. Clinical effects of 2% chlorhexidine gel on patients undergoing orthodontic treatment. *Orthod Waves*. 2008;67:162–166.
24. Boyd RL, Chun YS. Eighteen-month evaluation of the effects of a 0.4% stannous fluoride gel on gingivitis in orthodontic patients. *Am J Orthod Dentofacial Orthop*. 1994;105:35–41.
25. Martin BJ, Campbell PM, Rees TD, Buschang PH. A randomized controlled trial evaluating antioxidant–essential oil gel as a treatment for gingivitis in orthodontic patients. *Angle Orthod*. 2016;86:407–412.
26. Pradeep AR, Kumari M, Priyanka N, Naik SB. Efficacy of chlorhexidine, metronidazole and combination gel in the treatment of gingivitis—a randomized clinical trial. *J Int Acad Periodontol*. 2012;14:91–96.
27. Perinetti G, Paolantonio M, Cordella C, D'ercole S, Serra E, Piccolomini R. Clinical and microbiological effects of subgingival administration of two active gels on persistent pockets of chronic periodontitis patients. *J Clin Periodontol*. 2004;31:282–285.
28. Keith D, Rinchuse D, Kennedy M, Zullo T. Effect of text message follow-up on patient's self-reported level of pain and anxiety. *Angle Orthod*. 2013;83:605–610.
29. Bowen TB, Rinchuse DJ, Zullo T, DeMaria ME. The influence of text messaging on oral hygiene effectiveness. *Angle Orthod*. 2015;85:543–548.
30. Iqbal J, Awan R, Parvez A, Zahid AUH, Gardezi AA, Irfan S. Effectiveness of text message instructions on oral hygiene for orthodontic patients. *Pakistan Oral Dent J*. 2017;37:278–282.
31. Cucalon III A, Smith RJ. Relationship between compliance by adolescent orthodontic patients and performance on psychological tests. *Angle Orthod*. 1990;60:107–114.