

Pain Experience with Micro-osteoperforations during Initial Orthodontic Alignment: A Randomized Clinical Trial.

Experiencia de dolor con micro-osteoperforaciones durante la alineación ortodóncica inicial: Un ensayo clínico aleatorizado.

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Abstract: Objective: The objective of this clinical trial was to investigate the perception of pain during initial maxillary alignment with an adjunctive procedure of micro-osteoperforations (MOPs) compared to conventional orthodontics. **Material and methods:** This study design was a single-centre, two-arm parallel prospective randomised clinical trial. Thirty consecutive adult subjects (25 females and 5 males; mean age \pm SD, 22.66 \pm 3.27 years) with 5-8mm moderate upper labial segment crowding were randomly allocated using block randomisation into intervention and control group. All subjects had first premolar extractions, bonded conventional fixed appliances and 0.014-inch nickel-titanium archwire was placed for initial alignment. The intervention group received a 3-mm deep MOPs procedure under local anaesthesia using a Propel device (PROPEL Ortho Singapore) on the labiogingival aspect between the maxillary incisors. Both groups received a set of 100 mm visual analogue scale to complete over the first week, recording pain at 24 hours, 3 days and 1 week. Data were analysed using repeated-measures analysis of variance (ANOVA). **Results:** There was a statistically significant difference observed in perceived pain levels between MOPs and the control group on day 1, day 3 and day 7 postoperatively. Pain perception was significantly lower in the intervention group at all time points. **Conclusion:** Accelerating orthodontic tooth movement with MOPs did not accentuate pain perceived during initial maxillary alignment with fixed appliances.

Keywords: Tooth movement techniques; minimally invasive surgical procedures; pain; orthodontics, corrective; dental care; prospective studies.

Resumen: Objetivo: El objetivo de este ensayo clínico fue investigar la percepción del dolor durante la alineación maxilar inicial con un procedimiento adyuvante de micro-osteoperforaciones (MOP) en comparación con la ortodoncia convencional. **Material y Métodos:** El diseño de este estudio fue un ensayo clínico aleatorizado prospectivo paralelo de dos brazos y un solo centro. Treinta sujetos adultos consecutivos (25 mujeres y 5 hombres; edad media \pm DE, 22,66 \pm 3,27 años) con apiñamiento moderado del segmento labial superior de 5-8 mm se asignaron al azar mediante la asignación al azar en bloques en el grupo de intervención y de control. A todos los sujetos se les realizaron extracciones

de los primeros premolares, se colocaron aparatos fijos convencionales adheridos y se colocó un arco de níquel-titanio de 0,014 pulgadas para la alineación inicial. El grupo de intervención recibió un procedimiento de MOP de 3 mm de profundidad bajo anestesia local utilizando un dispositivo Propel (PROPEL Ortho Singapore) en la cara labial de los incisivos superiores. Ambos grupos recibieron un conjunto de escala analógica visual de 100 mm para completar durante la primera semana, registrando el dolor a las 24 horas, 3 días y 1 semana. Los datos se analizaron mediante análisis de varianza de medidas repetidas (ANOVA). **Resultados:** Se

observó una diferencia estadísticamente significativa en los niveles de dolor percibido entre los MOP y el grupo de control el día 1, el día 3 y el día 7 del postoperatorio. La percepción del dolor fue significativamente menor en el grupo de intervención en todos los momentos. **Conclusión:** La aceleración del movimiento dental de ortodoncia con MOP no acentuó el dolor percibido durante la alineación maxilar inicial con aparatos fijos.

Palabra Clave: Dolor; técnicas de movimiento dental; procedimientos quirúrgicos mínimamente invasivos; ortodoncia correctiva; atención odontológica; estudios prospectivos

INTRODUCTION.

Pain and discomfort are the most common experiences associated with fixed appliance treatment.¹ Pain experienced during orthodontic therapy is multifactorial and individually different. For instance, a study reported that there were no significant variations in pain perception based on age among adolescents (13-19 years old) compared to adult (19-26 years old), where males reported to have higher pain levels compared to females both at baseline and after 24 hours of treatment.² Several studies have reported on the different pain experiences associated with different types of orthodontic treatment modalities. Fixed appliances were reported to have higher pain responses due to their constant force compared to removable devices.^{3,4}

Pain associated with clear aligners due to tray deformation resulted in less pain intensity as compared to pain elicited by wire deformation in fixed appliances treatment.⁵ Comparing pain between self-ligating brackets and conventional ligation, no significant difference was reported.⁶ A study reported that pain during initial orthodontic alignment was similar between three different nickel-titanium (NiTi) archwires irrespective of gender, age and severity of crowding.⁶

The comprehensiveness of orthodontic treatment planning and mechanics is essential not only for attaining satisfying outcomes but also for abridging the duration of treatment, where literally could increase compliance among patients. One way of minimizing the iatrogenic effects caused by fixed appliances is to reduce the treatment length by accelerating the rate of tooth movement. Numerous adjunctive modalities that can facilitate orthodontic tooth movement have been

suggested and reported. These include surgical methods, device-assisted therapies, mechanical stimulation methods, and pharmacological approaches.⁶⁻⁸ Several forms of corticotomy have demonstrated an increased in the rate of orthodontic tooth movement.⁹ However, the nature of its invasiveness is associated with several surgical side effects, such as pain, swelling¹⁰ which limit its use routinely in practice.

Micro-osteoperforations (MOPs) have been introduced to lessen the invasive complexity of surgical tension applied to alveolar bone. To date, two methods of MOPs implementation were reported either by using a disposable Propel device or a miniscrew perforated into the alveolar bone.¹¹ The first clinical trial by Alikhani *et al.*,⁸ demonstrated that MOPs significantly increase the velocity of canine retraction, comfortable, and safe but the study duration was performed for a short period of one month only. Following this, considerable increase in interest has developed mainly focusing on the rate of space closure by means of canine or en-masse retraction.¹¹⁻¹³ A meta-analysis disclosed that MOPs were statistically significant in facilitating the rate of canine retraction; nevertheless, from the clinical perspective, it was not exceptionally significant with an increase of only 0.45mm per month.¹⁴ The latest evidence suggests that there is inadequate evidence to conclude whether a single use of MOP can expedite orthodontic tooth movement.¹⁵

Differing from the previous trials, this study aimed to compare the pain experienced during orthodontic alignment of maxillary anterior crowding following the initial placement of a conventional preadjusted edgewise bracket system with and without adjunctive procedure of MOPs.

MATERIALS AND METHODS.

Trial design and setting

A two-arm, single-centre, prospective randomized, clinical trial was conducted at the Orthodontic Clinic of Faculty of Dentistry, UiTM from 1st October 2017 to 1st October 2018. Ethical approval was obtained from the board of Research Ethics Committee UiTM 29th September 2017 [Reference: 600-IRMI (5/1/6); REC/297/17]. This trial is registered at ISRCTN registry with the study ID ISRCTN15080404.

Participants and eligibility criteria

Voluntary participants who matched the inclusion criteria were recruited, and their informed written consent was obtained prior to the commencement of the study. The participants' rights were protected throughout the trial phase. Inclusion and exclusion criteria for this study were as follow:

Inclusion criteria

- Moderate crowding of maxillary anterior region.
- Extraction of the first upper premolars with or without anchorage control.
- Healthy periodontal status.
- All permanent maxillary teeth present, except third molars.

Exclusion criteria

- Previous orthodontic treatment involving either removable or fixed appliances.
- Presence of systemic disease or compromised periodontal health.
- Taking medications that could interfere with tooth movement such as anti-inflammatory drugs, systemic corticosteroids, or calcium channel blockers.
- Craniofacial or dental abnormalities (e.g. hyperdontia, supernumerary, cleft lip and palate).
- Smoking.

Enrollment

The size of the sample was calculated based on a calculation using Power and Sample Size Calculations (PS software) version 3.1.2. The statistical power was set at 80% with a significance level of 0.05. Results from a previous study that compared the pain during initial alignment at day 1 were used to detect the mean pain difference of 10.4mm between the trial and control groups, and it was determined a sample size of 10 participants were required.¹⁶

Considering the possibility of dropouts, a total of 15 consecutive patients were recruited for each group. Verbal and written information regarding the study

was meticulously explained and made to be clearly understood to the participants.

Allocation

Sequentially numbered sealed, opaque concealed envelopes were used for randomisation of group allocation and were held by the central trial coordinator (NHN). Odd-numbered participants were allocated to the MOP group, whereas even-numbered ones were included as controls. Both the operator and participants were unaware of the therapy assignment until the envelope seals were opened. The study flow is following CONSORT 2010 statement¹⁷ as shown in Figure 1.

Appliance design

A standardised procedure was used with a conventional, preadjusted edgewise orthodontic bracket system on 0.022 x 0.028-inch slot brackets of McLaughlin, Bennett and Trevisi prescription (Victory Series, 3M Unitek). Patients in the MOP group additionally underwent the MOP therapy regimen following bracket placement. Initial archwire used was a 0.014-inch nickel-titanium (NiTi) archwire followed by 0.018-inch NiTi (TruFlex NiTi archwire, Ortho Technology).

MOPs Procedure

Perforation dimensions were 1.5-mm wide and 3-mm deep, using the MOP device from PROPEL Ortho Singapore (PTE LTD), were conducted by a single operator. Following bracket placement, additional to the MOP group, they underwent surgical perforations. Participants were asked to rinse with chlorhexidine digluconate 0.12% antiseptic mouthwash prior to MOPs. The tiny perforations of MOPs were performed under atraumatic local anaesthesia infiltration (Lignocaine with 1:100,000 adrenaline) with a 30-gauge short needle to deliver the anaesthetic agent. Two perforations were performed on the alveolar bone equidistant between the anterior teeth from the upper right third to upper left third, except at the midline alveolar bone to prevent trauma to the soft tissue frenum (Figure 2).

Postoperatively, they also were prescribed 0.12% chlorhexidine digluconate (Oradex) mouthwash to be used twice a day for 1 week at home.

Pain score with visual analogue scale

Participants were asked to evaluate their pain level by using the Visual Analogue Scale (VAS) (Figure 3).

A diary comprising three pages of VAS was given to each participant for them to record their pain level at the time intervals highlighted. Participants were asked to assess and mark their level of pain on the scale of

VAS at 24 hours (D1), 3 days (D3) and 1 week (D7) after the bracket placement visit and return the pain diary during the one month review session. The mark was then measured with a 10-cm ruler, with 1 mm equal to 1 point on the scale; 0 point indicated the lack of pain, while 10 points would mean the worst pain conceivable. Participants were refrained from taking analgesics, especially anti-inflammatory group as this may affect pain perception and could cause confounding bias in result interpretation, following similar previous studies within the same domain.^{7,8}

Statistical methods

Descriptive and analytical statistical analyses were performed using SPSS IBM version 20.0. The significance level was 0.05, with a power of 80% to detect the difference between the MOPs and control group. The examiner was blinded to the treatment allocation during data analysis; identifying details of the VAS scale were concealed before measurement; however,

it was impossible to blind the operator and subjects to the adjunctive procedure being performed, after the envelope was broken.

Repeated-measure analysis of variance (ANOVA) was employed to analyse the data obtained with a Bonferroni correction for intragroup difference (*i.e.* time effect). When the *p*-value was significant, a pairwise comparison with confidence interval adjustment was performed accordingly. Overall comparison of pain among the groups regardless of the time was employed based on the F-test, with a significance level of less than 0.05. Finally, a profile plot was produced to interpret the interaction.

One examiner was calibrated and performed the measurements. Reproducibility of the VAS measurements within the same outcome assessor were determined using intraclass correlation coefficient (ICC) by repeated measures of 15 VAS in random order in two weeks apart. The reliability was excellent with an intraclass correlation coefficient of 0.96, indicating a low-level of random error.

Figure 1. CONSORT study flow diagram.

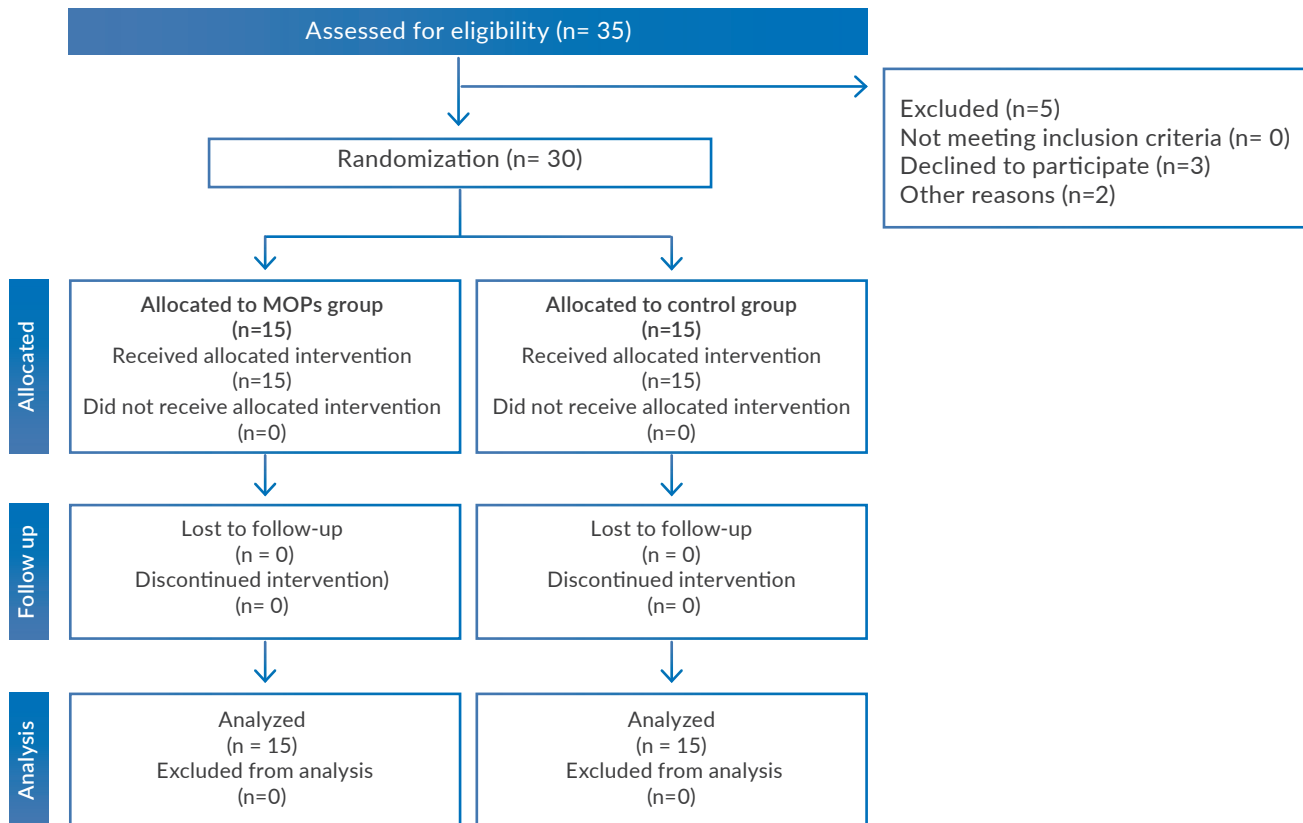
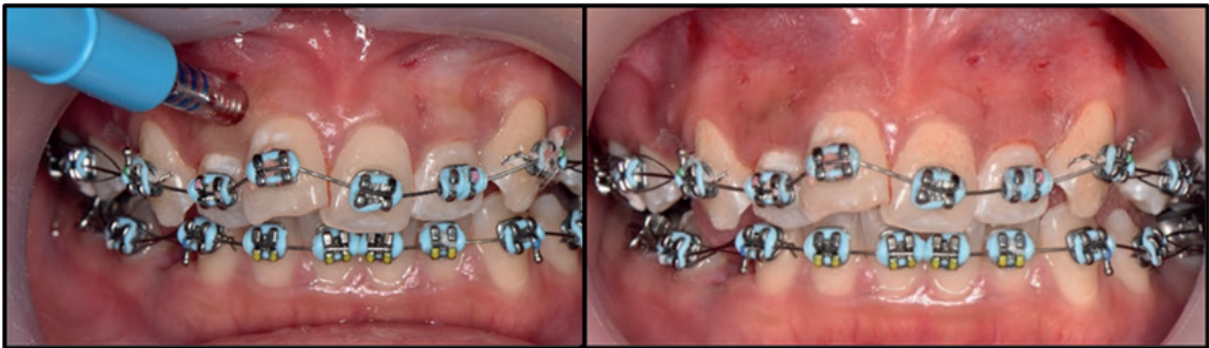


Figure 2. Experimental model.



A: MOPs procedure with Propyl. Device *in situ*. Dimension of perforation was 1.5 mm wide and 3 mm deep. B: Post MOPs, two small perforations between UR3 to UL3 at every interdental alveolar bone except at the midline, was seen with minimal bleeding and trauma

Figure 3. Visual Analogue Scale.

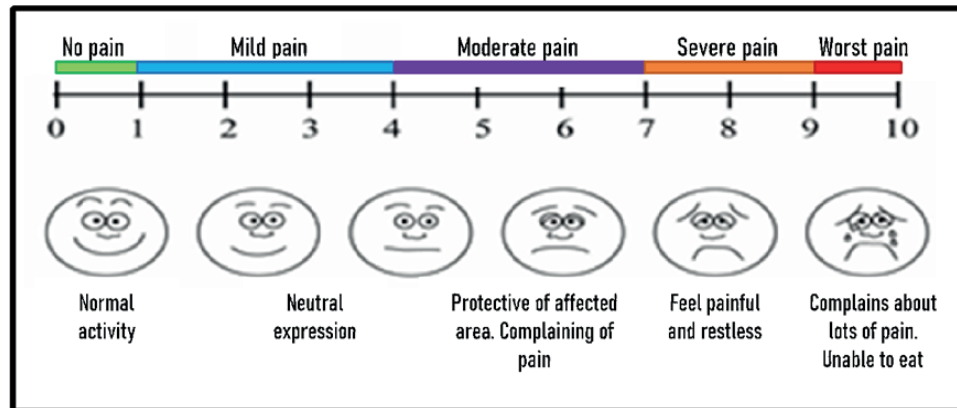


Figure 4. Profile plot of mean pain score between groups over time

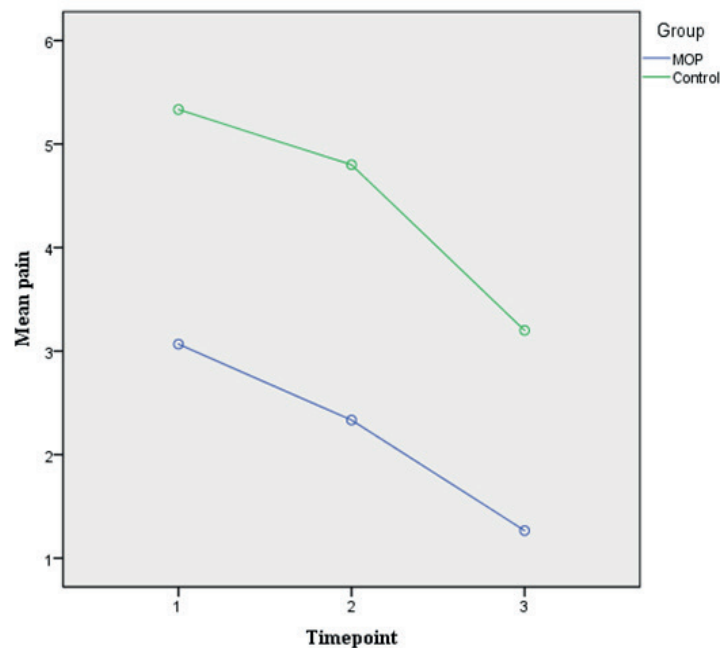


Table 1. Demographic Characteristics of the Participants.

Variable		MOPs n=15(%)	Control n=15(%)
Age (years)	Mean (SD)	22.80 ±3.78	22.50 ±2.74
	<i>p</i> -value	0.810	
Ethnicity	Malay	15(100)	13(86.7)
	Chinese	0(0)	2(13.3)
Gender	Male	(13.3)	3(20)
	Female	13(86.7)	12(80)

Table 2. Comparison of mean pain within each group according to incremental time.

Comparison	MOPs		Control	
	MD (95% CI)	<i>p</i> -value	MD (95% CI)	<i>p</i> -value
D1- D3	0.73 (0.113, 1.353)	0.019	0.53 (-1.38, 2.44)	1.000
D1- D7	1.80 (0.70, 2.9)	0.002	2.13 (-0.02, 4.29)	0.052
D3- D7	1.07 (0.39,1.74)	0.002	1.60 (0.39, 2.81)	0.009

Note: Repeated measures ANOVA within-group analysis was applied, followed by pairwise comparison with confidence interval adjustment. MD: mean difference, significant at the 0.05 level.

Table 3. Comparison of Mean Pain Among Two Groups Over Time.

Time	Group	Mean pain	95% CI	Significant
D1	MOPs	3.07	1.73, 4.40	Significant
	Control	5.33	4.00, 6.67	
D3	MOPs	2.33	0.96, 3.70	Significant
	Control	4.80	3.43, 6.17	
D7	MOPs	1.27	-0.09, 2.63	Significant
	Control	3.20	1.84, 4.56	

Note: Repeated measures ANOVA between groups.

RESULTS.

Demographic Characteristics

The subjects' participation is shown in the CONSORT flow diagram in Figure 1. A total of 35 participants were eligible for this trial. However, five were excluded consisting of three patients declined to participate, and another two were moving away.

30 participants who had met the inclusion criteria were

enrolled for the trial, consisting of 25 females and 5 males (mean ± SD age, 22.66 ± 3.27 years). Fifteen participants in each group continued to undergo follow-up appointments. Table 1 shows the participants' demographic characteristics, in which the age between groups being found to be not significant ($p>0.05$).

The baseline data demonstrated that there were fewer male subjects in both groups compared to females.

Comparison of Mean Pain Score

A significant difference in mean pain was noted within each group based on time ($F= 9.569, p<0.05$). The ensuring pairwise comparison with confidence interval adjustment was performed and presented in Table 2. The results showed that there was a significant reduction level of pain ($p<0.05$) within the MOPs group at all time points. Meanwhile, the control group displayed a significant difference of mean pain for D3 versus D7 (mean difference = 1.60, 95% CI: 0.39, 32.81; $p=0.009$).

Mean pain was measured for the inter- and intra-groups for the time intervals of Day 1, Day 3 and Day 7. The measurements constituted a within-group factor (*i.e.* repeated measures factor) and the treatment groups (a between-group factor), which is presented in Table 3.

Furthermore, the p -value for time-treatment interaction based on the F-test was significant ($p<0.05$), in which the analysis was then followed by producing the adjusted means (estimated marginal means) with its adjusted confidence interval. The mean pain scores for the MOPs group did not overlap with the confidence interval of the control group, with the measurement indicative of a significant difference between groups as observed in D1, D3, and D7. Additionally, the pain intensity was found to be reduced significantly from post-op until day 7 in the MOPs group.

Profile Plot of Mean Pain Score

In general, the average intensity of pain was gauged to be between low to moderate, with none of the participants reporting severe pain (>75 mm) over the days of initial alignment (Figure 4). Both groups had a similar pattern of pain reduction until day 7, with peaked pain occurring on day 1 postoperatively. Overall, the control group demonstrated a higher level of mean pain compared to the trial group.

DISCUSSION.

Pain Experience

Alignment and levelling occur in the first stage of orthodontic therapy, in which light and continuous forces are applied using highly flexible and round archwires. The light force may minimise tissue hyalinisation and undermine resorption, but it may also cause pain and discomfort to the patient.^{18,19}

The results of this study are in agreement with others,¹¹⁻¹³ that MOPs do not exacerbate pain in conjunction with fixed appliances treatment.

Patients testified only bearable discomfort at the site

of the MOPs, with no harm reported. They investigated the rate of tooth movement by means of canine or en-masse retraction. In those studies, one to three MOPs were performed in the extraction spaces. The perforations were equidistant from the canine and second premolar. Meanwhile, in this study, a total of eight MOPs was performed on the anterior maxillary segment. We found that regardless of the number of perforations performed, it did not exacerbate pain perceived by participants. The study protocol adapted from previous trials where participants refrained from taking analgesics especially anti-inflammatory groups as this may affect pain perception and could cause in a confounding variable result interpretation.^{7,8} Adopted by previous trial, timing for recording of VAS score in this study involved the exception of the first 24 hours because local infiltration that was given could affect the interpretation of outcomes.¹⁶ The time frame for VAS scoring in this study showed a similar common trend of proven consistency of the pain pattern.³ Similarly, pain related to postoperative appliance manipulation was reduced tolerably to near-baseline levels by day 7, after spiking on days 1 to 3.

All participants reported good healing process for the multiple tiny perforations, with no incidence of infection or scarring occurring. To date, regardless of the procedure, pain is a subjective symptom of various dimensions that cannot be measured objectively. The subjectivity is influenced by the personality, recollections of painful events, emotional state, age, culture, context, and other factors' impact on an individual's responses to, and for the description of pain.²⁰

Therefore, the best option is to let the patients report and evaluate the intensity themselves. Pain evaluation in this study was following the well-defined classification by Burstone²¹ for orthodontic pain proposed. The classification is based on pain perception in response to the orthodontic force applied, which is divided into three degrees. The first degree of pain, in which the patient is not aware of the pain and second degree is, pain or discomfort, which is caused during clenching or force gauge, by the patient, is still capable of masticating a normal diet regardless of it.

The third degree of pain is when the patient may be unable to masticate food of normal consistency due to the pain.²¹ This interpretation was described accordingly to the participants when explaining how they were expected to mark a location on the VAS line, which was

by conforming to the amount of personal experience of pain. Poor compliance and treatment discontinuation have been credited towards the patient's displeasure caused by appliance therapy during the initial stage.²²

Thus, in comparison with the conventional treatment, any adjunctive modality towards accelerating orthodontic tooth movement should not exaggerate any pain perception. Minimally invasive surgical procedures to facilitate orthodontic tooth movement have attracted increased attention recently, and this reflects a great interest in this topic.

The conservative nature of these approaches can be translated to the fact that no mucosal flap elevation or suturing is required,²³ as well as the lack of any significant adverse effects reported in several clinical trials within the domain.^{8,12,13} Besides, the first clinical trial for MOPs in humans have demonstrated a reduction in orthodontic treatment duration by 62%,⁸ but its short length has indicated that further study on the effect of the number, frequency, and long-term ramifications of MOPs is recommended.

This is supported by Attri *et al.*,¹² reported that MOPs are effective to enhance velocity of tooth movement. In contrast, Alkebsi *et al.*,¹³ concluded that MOPs did not enhance the rate of tooth movement. In addition, the cost-benefit ratio also needs to be considered before implementing any adjunctive procedures for accelerating orthodontic tooth movement.

Cell Kinetics

Orthodontic tooth movement is considered as a periodontal phenomenon involving dynamic compression of the periodontal ligament, as it generates histological and bio-molecular modifications triggering vibrant crestal bone resorption and apposition.²⁴ Pain following orthodontic force application is a component of the inflammatory reaction that causes changes in blood flow. This reaction inevitably results in the release of various chemical mediators eliciting a hyperalgesic response.

Almost all procedures in orthodontic treatment can cause pain such as placement of separator, archwire insertion, and activation, application of orthopaedic forces and debonding procedure.¹ Pain perception is part of an inflammatory reaction that triggers the changes in blood flow following orthodontic force application.

This study shows that both groups had acceptable degrees of pain which is significantly lower in the MOPs group compared to the control group. This could

be explained by the gate control theory proposed by Melzack *et al.*,²⁵ It suggests that control of pain may be achieved by selectively influencing the large, rapidly conducting neuron fibres.

Following MOPs, disruption of cortical bone elicits regional acceleratory phenomenon (RAP).⁸ RAP healing is a complex physiological process with dominating features connecting accelerated bone turnover and decreases in regional bone densities.

Tissue reorganisation and healing then occur through transient bursts of localised soft and hard tissue remodelling associated with transient catabolic conditions.²⁶ The gate may be closed by decreasing the small-fibre input and by enhancing the large neuron fibre input resulting in hypoalgesia.

Limitation of the study

In this study, the age, amount of crowding, the magnitude of force applied, and treatment approaches were similar for all participants. However, it is recommended that future studies assess gender differences in terms of pain perception associated with MOPs, which was not performed in this study due to the low number of male participants.

CONCLUSION.

The adjunctive procedure of MOPs for accelerating orthodontic tooth movement did not exaggerate the pain experienced during the initial dental alignment with an orthodontic appliance.

MOPs are expected to yield better acceptance among patients due to being minimally invasive and less pain presumed to be experienced.

Conflict of interests: The authors declare that they have no competing interests.

Ethics approval: This study was approved by the Universiti Teknologi Mara (UiTM) Research and Ethics Committee [Reference: 600-IRMI (5/1/6); REC/297/17]. This trial also was registered at ISRCTN registry with the identifier number ISRCTN15080404.

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Authors' contributions: AAS performed the MOPs procedure, participated in patient's recruitment, analysed the data and drafted the manuscript. SHAG participated in the design of the study, analysed the data and helped to draft the manuscript. NAH participated in consent taking, application of the study ethics, randomization and manuscript write up. All authors have approved the manuscript for submission.

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