The effect of micro-osteoperforations on the rate of orthodontic tooth movement in animal model: A systematic review and meta-analysis

Ebrahim Eini [a], Mehrnaz Moradinejhad [a], Rayan Chaharmahali [a], Fakher Rahim [b],*

[a] Department of Orthodontics, School of Dentistry, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
[b] Thalassemia and Hemoglobinopathy Research Center, Research Institute of Health, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

ARTICLE INFO

ABSTRACT

Introduction: The long passing time for tooth movement (TM) is one of the challenges in orthodontic. complications such as gingival recession, root resorption, and caries are common in orthodontic. To address this, there is an increased tendency to find safe and effective methods to accelerating tooth movement. A surgical method such as micro-osteoperforations (MOP) accelerating the TM. The current meta-analysis aims to investigate the outcome of MOP in accelerating TM in animal studies.
Methods: In the present meta-analysis, we evaluated 6 studies that focused on the effect of MOP on TM with the following keywords: (((MOP* OR micro-osteoperforations*) AND (("accelerating tooth movement " OR " tooth movement" AND " orthodontic tooth movement " OR " orthodontic ")) until May 2021.
Results: The results have shown there is significant difference in TM after using MOP (MD: 0.31, 95%CI: 0.20, 0.42, $P < 0.00001$, I2 = 76%). Subgroup analysis revealed that though experimental duration in both less than 4-week and more than 4-week, the TM were significant difference between MOP and controls. Besides, in both force subgroups including less than 100 g and more than 100g, the TM was a significant difference between MOP and controls.
Conclusion: This meta-analysis found that generally MOP has a positive effect on TM.

1. Introduction

The long passing time for tooth movement (TM) is one of the challenges in orthodontic. The long lasting treatment is accompanied by complications such as gingival recession, root resorption, and caries.[1] TM in orthodontic consists of three phases; the rapid TM occurs in the initial and last phases.[1] In the early phase of TM, inflammatory cytokines play a critical role, and in acute phase, cells such as fibroblasts, endothelial cells, alveolar cells were involved.[2] To address this, there is an increased tendency to find safe and effective methods to accelerating tooth movement. Different supplemental ways were introduced to accelerate tooth movement, including vitamin-D3, prostaglandins, parathyroid hormone, relaxin, laser therapy, vibrational stimulation, resonance vibration, and direct electrical current.[3–8]

Nevertheless, the surgical method has the faster effect in accelerating TM, one of them is micro-osteoperforations (MOP). MOP by activating alveolar bone remodeling accelerates the TM.[9] There is a large study in finding the best technique with the highest efficacy and lowest disadvantages. In the recent systematic reviews, the effect of MOP was evaluated in accelerating tooth movement in both animals and humans, but the analysis was done on specific surgical methods.[10,11] The current systematic review and meta-analysis aims to investigate the outcome of MOP in accelerating TM in animal studies.

2. Materials and methods

2.1. Search strategy

To evaluate the impact of MOP in Tm, we systematically searched the electronic database, including Scopus, Medline/PubMed, EMBASE, Web of sciences (WOS), and Cochrane library using Mesh-standardized keywords: (((MOP* OR micro-osteoperforations*) [Mesh] AND (("accelerating tooth movement " OR " tooth movement" [Mesh] AND " orthodontic tooth movement " OR " orthodontic ")) until May 2021. There is no restriction for time and language, and the citation lists of selected articles were hand-searched for additional papers.
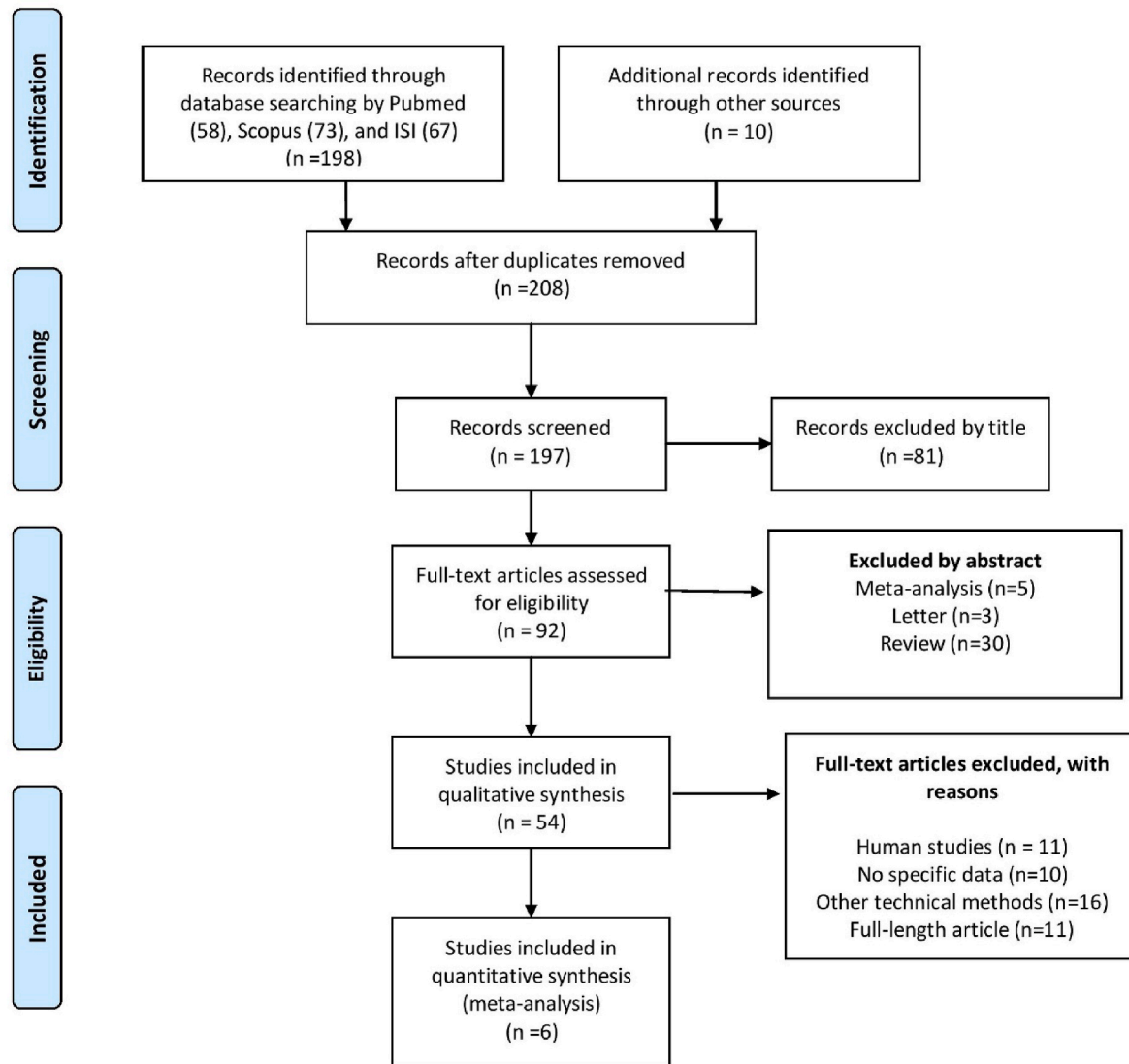
Fig. 1. PRISMA flow diagram of the literature search.

Table 1
Characteristics of Included animal Studies.

Authors, year Country	Species	Population	Average body weight	Age	Duration	Force (cN)	Outcome
Teixeira et al. 2010[20] USA	Adult male Sprague-Dawley rats	48	400 g	120 days	4-week	50	Increased rate of tooth movement
Cheung et al. 2016[23] USA	Adult male Sprague-Dawley rats	10	500 g	120 days	3-week	50	Accelerated tooth movement without increased risk for root resorption
Tsai et al. 2016[21] Taiwan	Adult male Sprague-Dawley rats	45	400–500 g	56 days	6-week	50	Induced faster orthodontic tooth movement
Cramer et al. 2019[24] USA	Skeletally mature male beagle dogs	14	9500–11350 g	24 months	7-week	50	Do not increase tooth movements
Kim et al. 2019[18] Korea	Female New Zealand white rabbits	24	3400–4300 g	14-week	3-week	100	Effective tool for enhancing tooth movement
Huang et al. 2021[22] China	Male New Zealand white rabbits	48	2200–2800 g	14-week	4-week	50 100 150	Fast tooth movement achieved

2.2. Data extraction

Two reviewers (ME and FR) independently screened titles and abstracts of all initially found articles. Information was extracted from selected studies, including the author's name, year of publication, country, sample size, species, average body weight, duration, force, and outcome. A third reviewer was consulted to resolve any disagreements between reviewers by discussion until consensus was reached.
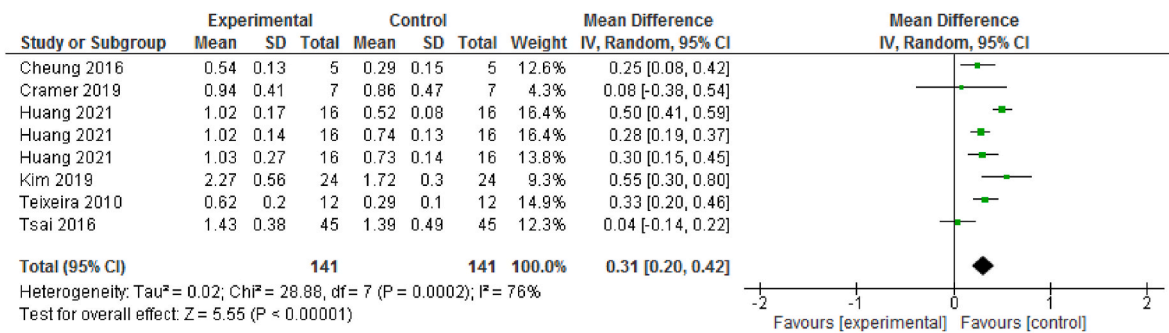
Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Cheung 2016	0.54	0.13	5	0.29	0.15	5	12.6%	0.25 [0.08, 0.42]
Cramer 2019	0.94	0.41	7	0.86	0.47	7	4.3%	0.08 [-0.38, 0.54]
Huang 2021	1.02	0.17	16	0.52	0.08	16	16.4%	0.50 [0.41, 0.59]
Huang 2021	1.02	0.14	16	0.74	0.13	16	16.4%	0.28 [0.19, 0.37]
Huang 2021	1.03	0.27	16	0.73	0.14	16	13.8%	0.30 [0.15, 0.45]
Kim 2019	2.27	0.56	24	1.72	0.3	24	9.3%	0.55 [0.30, 0.80]
Teixeira 2010	0.62	0.2	12	0.29	0.1	12	14.9%	0.33 [0.20, 0.46]
Tsai 2016	1.43	0.38	45	1.39	0.49	45	12.3%	0.04 [-0.14, 0.22]
Total (95% CI)			141			141	100.0%	0.31 [0.20, 0.42]

Heterogeneity: Tau² = 0.02; Chi² = 28.88, df = 7 (P = 0.0002); I² = 76%
Test for overall effect: Z = 5.55 (P < 0.00001)

Fig. 2. Forest plot for the mean difference of the mean difference of tooth movement comparing studies that used micro-osteoperforations (MOPs) system.
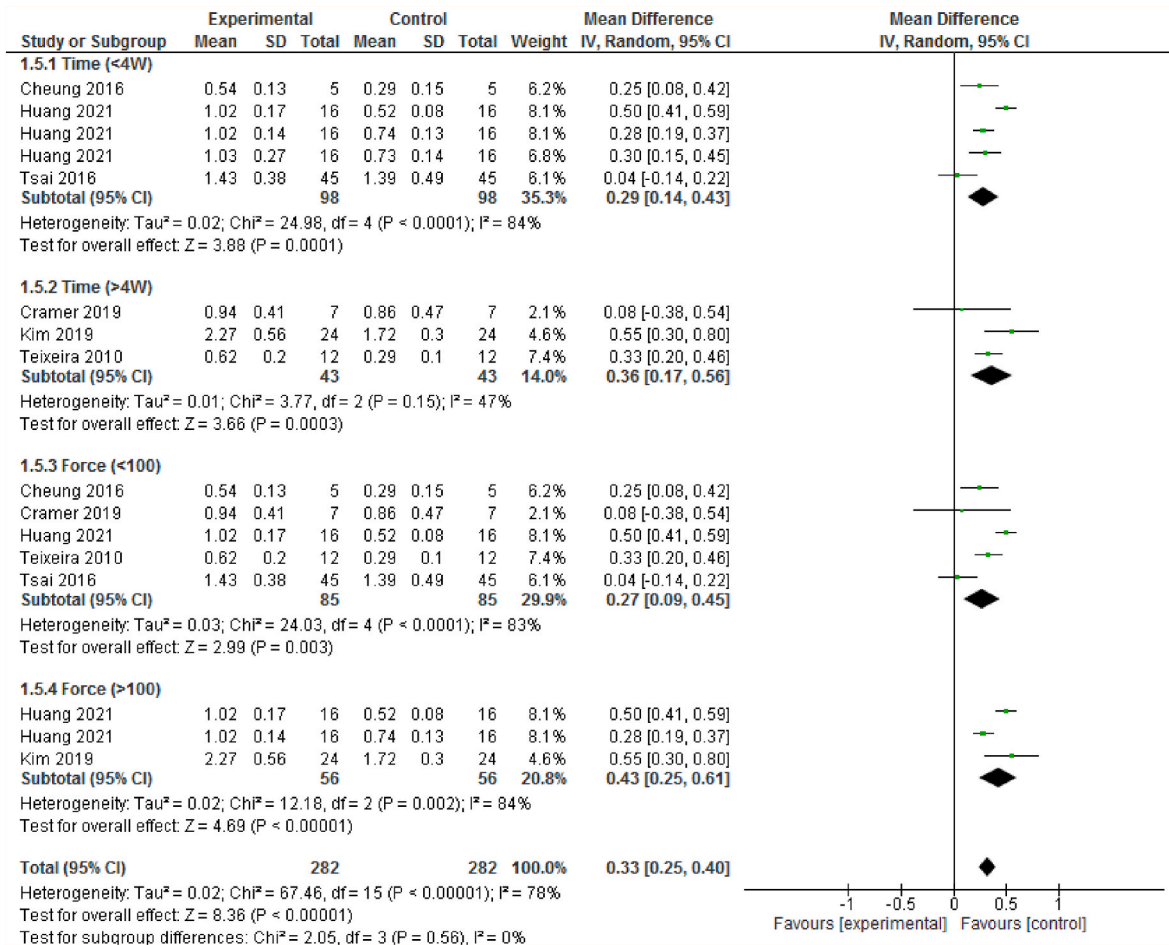
Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.5.1 Time (<4W)								
Cheung 2016	0.54	0.13	5	0.29	0.15	5	6.2%	0.25 [0.08, 0.42]
Huang 2021	1.02	0.17	16	0.52	0.08	16	8.1%	0.50 [0.41, 0.59]
Huang 2021	1.02	0.14	16	0.74	0.13	16	8.1%	0.28 [0.19, 0.37]
Huang 2021	1.03	0.27	16	0.73	0.14	16	6.8%	0.30 [0.15, 0.45]
Tsai 2016	1.43	0.38	45	1.39	0.49	45	6.1%	0.04 [-0.14, 0.22]
Subtotal (95% CI)			98			98	35.3%	0.29 [0.14, 0.43]

Heterogeneity: Tau² = 0.02; Chi² = 24.98, df = 4 (P < 0.0001); I² = 84%
Test for overall effect: Z = 3.88 (P = 0.0001)

1.5.2 Time (>4W)								
Cramer 2019	0.94	0.41	7	0.86	0.47	7	2.1%	0.08 [-0.38, 0.54]
Kim 2019	2.27	0.56	24	1.72	0.3	24	4.6%	0.55 [0.30, 0.80]
Teixeira 2010	0.62	0.2	12	0.29	0.1	12	7.4%	0.33 [0.20, 0.46]
Subtotal (95% CI)			43			43	14.0%	0.36 [0.17, 0.56]

Heterogeneity: Tau² = 0.01; Chi² = 3.77, df = 2 (P = 0.15); I² = 47%
Test for overall effect: Z = 3.66 (P = 0.0003)

1.5.3 Force (<100)								
Cheung 2016	0.54	0.13	5	0.29	0.15	5	6.2%	0.25 [0.08, 0.42]
Cramer 2019	0.94	0.41	7	0.86	0.47	7	2.1%	0.08 [-0.38, 0.54]
Huang 2021	1.02	0.17	16	0.52	0.08	16	8.1%	0.50 [0.41, 0.59]
Teixeira 2010	0.62	0.2	12	0.29	0.1	12	7.4%	0.33 [0.20, 0.46]
Tsai 2016	1.43	0.38	45	1.39	0.49	45	6.1%	0.04 [-0.14, 0.22]
Subtotal (95% CI)			85			85	29.9%	0.27 [0.09, 0.45]

Heterogeneity: Tau² = 0.03; Chi² = 24.03, df = 4 (P < 0.0001); I² = 83%
Test for overall effect: Z = 2.99 (P = 0.003)

1.5.4 Force (>100)								
Huang 2021	1.02	0.17	16	0.52	0.08	16	8.1%	0.50 [0.41, 0.59]
Huang 2021	1.02	0.14	16	0.74	0.13	16	8.1%	0.28 [0.19, 0.37]
Kim 2019	2.27	0.56	24	1.72	0.3	24	4.6%	0.55 [0.30, 0.80]
Subtotal (95% CI)			56			56	20.8%	0.43 [0.25, 0.61]

Heterogeneity: Tau² = 0.02; Chi² = 12.18, df = 2 (P = 0.002); I² = 84%
Test for overall effect: Z = 4.69 (P < 0.00001)

Total (95% CI)			282			282	100.0%	0.33 [0.25, 0.40]

Heterogeneity: Tau² = 0.02; Chi² = 67.46, df = 15 (P < 0.00001); I² = 78%
Test for overall effect: Z = 8.36 (P < 0.00001)
Test for subgroup differences: Chi² = 2.05, df = 3 (P = 0.56), I² = 0%

Fig. 3. Forest plot for the mean difference of the mean difference of tooth movement comparing studies that used micro-osteoperforations (MOPs) system.

2.3. Selecting studies

Inclusion criteria for selecting studies were considered as following: animal studies and evaluating the impact of MOP in accelerating TM. Exclusion studies were done based on the following criteria: studies evaluating the other methods in animal studies in accelerating TM, human studies, letter to editor, case report, and animal reviews.

2.4. Statistical analysis

Cochran Chi-square test and I^2 were used to assessing heterogeneity among studies. A fixed-effects model was used when $I^2 < 50\%$, while in the case of $I^2 > 50\%$, a random-effects model was selected. Fixed-model assumes that the population effect sizes are the same for all studies.[12] In contrast, the random-effects model attempted to generalize findings beyond the included studies by assuming that the selected studies are random samples from a larger population.[13] The 95% confidence intervals (CI) were calculated to investigating the differences TM between control sites and MOP. According to the heterogeneity test results, either Der Simonian's and Laird's random-effects method or Mantel-Haenszel's fixed-effects method were used to estimate the overall prevalence and 95% confidence intervals.[14] The Egger's test was used to investigate small study effects due to potential publication bias.[15,16] If there was statistical heterogeneity among the results, a further sensitivity analysis was conducted to determine the source of heterogeneity. After the significant clinical heterogeneity was excluded, the randomized effects model was used for meta-analysis. P < 0.05 was considered as statistical significance (2-sided). All data were analyzed using STAT
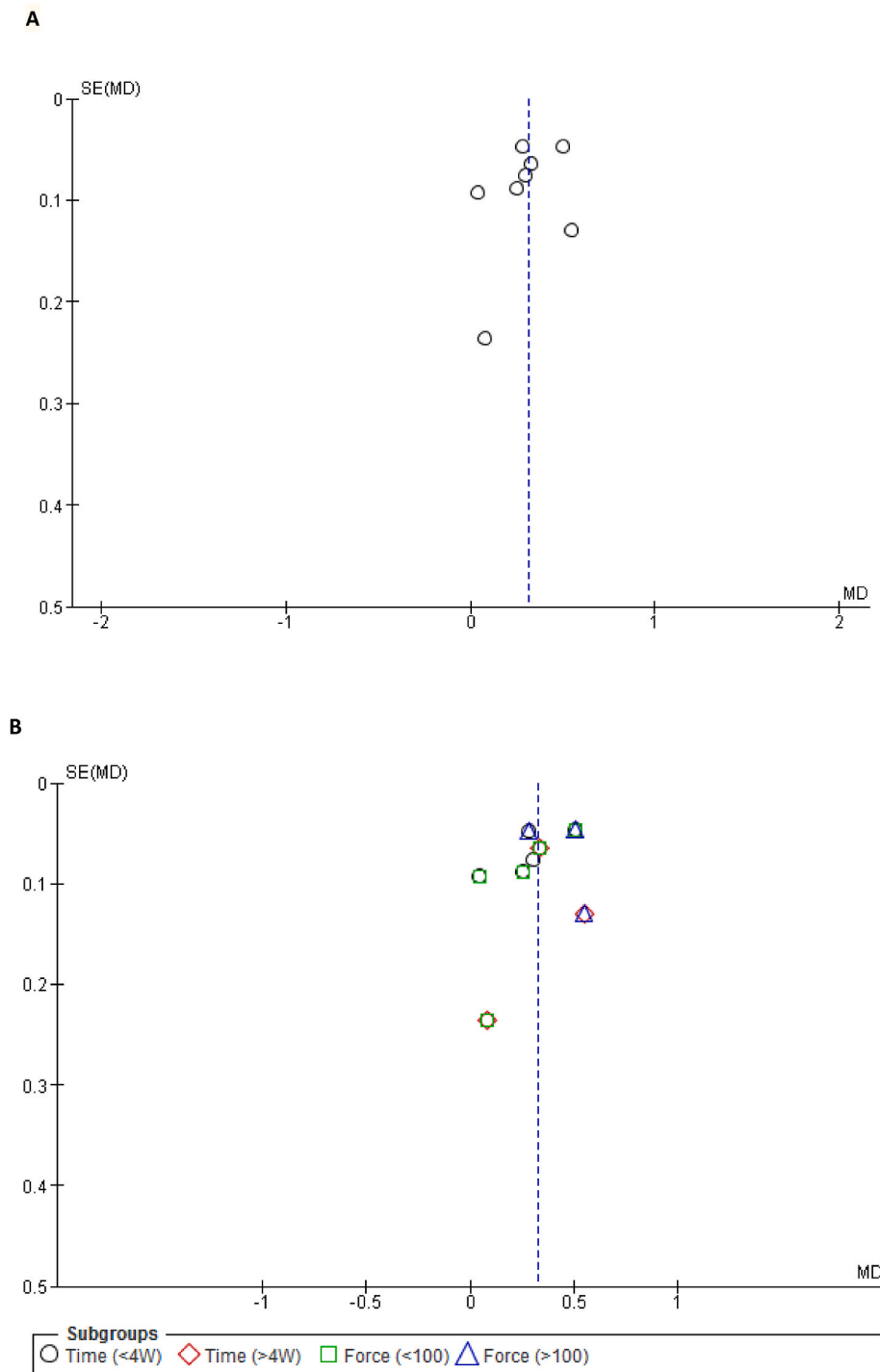
A

B

Fig. 4. Begg's funnel plot assessing overall and sub-group publication bias of the studies used micro-osteoperforations (MOPs) system.

16 (STATA Corporation, College Station, Texas).

3. Results

208 studies were included; after removing duplicates, 197 studies remained. 11 studies were excluded due to investigating in humans. Two studies were excluded due to reporting data in an unacceptable format.[9,17] Two studies used 100 g, two articles used 50 g for traction force, and just HUANG et al., evaluated 3 different traction forces including, 50, 100, and 150 g.[18–22] Additional assessment of TM, tartrate-resistant acid phosphatase (TRAP)-positive osteoclast count,

and bone volume fraction were evaluated in three studies.[18,19,21,23] Finally, the main properties of six articles on 210 animals included in this meta-analysis with a wide range of species such as rat (n = 3), beagle dog (n = 1), and rabbit (n = 2) (Fig. 1) (Table 1).

We found a statistically significant difference in TM between MOP and control (MD: 0.31, 95%CI: 0.20, 0.42, P < 0.00001, I^2 = 76%) (Fig. 2).

Subgroup analysis revealed that though experimental duration in both less than 4-week and more than 4-week, the TM were significantly difference between MOP and controls (Fig. 3). Besides, in both force subgroups including less 100 g and more than 100g, the TM were

significantly difference between MOP and controls (Fig. 3). The funnel plot seemed symmetrical for both overall and sub-group analyses, indicating the absence of publication bias (Fig. 4), of which these findings was quantitatively supported by Egger's test (overall: $t = -1.98$, $P = 0.375$ and subgroup: $t = -2.01$, $P = 0.286$).

4. Discussion

A considerable amount of literature has been published on the effect of MOP on accelerating TM. Additionally, several systematic reviews and meta-analyses were conducted to achieving the effectiveness of MOP on TM. For example, Shahabee et al., in a similar systematic review and meta-analysis, evaluated the effect of MOP on the rate of orthodontic TM, but they focused on surgical techniques; this causes high heterogeneity.[25] Furthermore, controversial findings were observed in randomized clinical trials; in this regard, Sivarajan et al., in a recent meta-analysis, investigated these inconsistent results. However, since they included homogeneity studies for a specific TM (canin retraction), they found just two low-risk bias studies and suggested further surveys with repeated MOPs to achieve conclusive results.[26] Hence, the current meta-analysis attempts to all aspects of MOP's effect on TM as a meta-analysis.

After evaluating with our Mesh terms, 6 studies were included for quantitative synthesis. Our data have shown that MOPs have hastened TM. Subgroup analyses without any publication bias revealed using MOPs, even with less than 4 weeks, the significant TM observe rather than without intervention site. From all selected studies, just Cramer et al. reported that even with a longer duration time of orthodontic, the MOP does not affect TM.[24] In comparison, Kim et al., with just one-week intervention, have shown a significant difference TM.[19] This can be explained by the fact that the intervention was conducted on beagle dogs, which is different from rabbits and rats.[24]

One of the main complications in orthodontic is external apical root resorption. Orthodontic by applying force causes root resorption.[27] By increasing applied force, the root resorption increases.[28–30] decreasing the period of orthodontic treatment time decreases the root resorption consequently. It was demonstrated that MOP by increasing TM does not increase root resorption.[31] This in line with our finding, that with a lower force than 100g during less than 4 weeks, the significant TM with the lowest risk of root resorption achieving.

5. Clinical implication

However, it contrasts with Chan et al. results; they have shown that in humans, after 28 days, the root resorption increases. It is worth noting that they used the 150 g buccal tipping.[32] Whereas, In two of included studies, the highest TM was seen with 50 g force after 2 weeks.[20,22] In this line, to evaluate the effect of increasing force on TM, Haung et al. assessed the rate of TM after 50, 100, and 150 g force; they found that by increasing applied force, the TM not changed significantly.[22] The evidence presented in this section suggested that there is very low supporting positive correlation between root resorption and applied force.[33] Secreting inflammatory cytokines due to forced applied causes TM by increasing osteoclasts. Osteoclasts with secreting osteopontin causes bone remodeling, which is crucial for TM.[34]

To determine the effect of MOP type on TM, Kim et al. compared the impact of single-vertical and multiple-horizontal MOPs with 100 g force on TM; the highest TM was observed in single-vertical MOP after 3 weeks. Also, as expected, the count of osteoclasts was significantly increased, especially after 3 weeks.[19] MOP by increasing bone resorption and canine retraction stimulates TM in orthodontic.[35] MOP decreases bone volume/tissue volume and bone mineral density, reduces the resistance to the movement, and accelerates the TM.[9,23]

6. Limitations

Some factors influence our analysis. In the current study, all studies which evaluated the effect of MOP in TM in animals were included. It was obvious that different animals affect technical methods and used materials. An issue that was not addressed in this study was side effects. since complications did not evaluate in all studies, this limited us to analyze the implications and discuss them.

7. Conclusion

The main goal of the current study was to determine the effect of MOP on TM as meta-analysis. This meta-analysis found that generally MOP has a positive effect on TM, and the reasons for this phenomenon have been discussed. What is now needed is a comparative study between animals and human studies to comparing the efficacy and complications to achieving the best protocol for increasing TM including applied force, MOP interval, and MOP type.

Authors' contributions

F.R conceived the manuscript and revised it. E.E, M.M, and R.Ch done the statistical analysis, wrote the manuscript, and prepared tables and figures. All authors have read and approved the manuscript.

Declaration of Competing Interest

The authors declare no conflict of interest. All procedure performs in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or compared ethical strand.

Acknowledgments

References

1 Nimeri G, Kau CH, Abou-Kheir NS, Corona R. Acceleration of tooth movement during orthodontic treatment - a frontier in Orthodontics. *Prog Orthod.* 2013;14:1–8.
2 Milošević-Jovčić N, et al. [The role of cytokines in orthodontic tooth movement]. *Srp Arh Celok Lek.* 2012;140:371–378.
3 Almoammar K. Vitamin D and orthodontics: an insight review. *Clin Cosmet Invest Dent.* 2018;10:165–170.
4 Kaklamanos EG, Makrygiannakis MA, Athanasiou AE. Does medication administration affect the rate of orthodontic tooth movement and root resorption development in humans? A systematic review. *EJO (Eur J Orthod).* 2020;42:407–414.
5 Jing D, Xiao J, Li X, Li Y, Zhao Z. The effectiveness of vibrational stimulus to accelerate orthodontic tooth movement: a systematic review. *BMC Oral Health.* 2017; 17.
6 Sant'Anna EF, et al. High-intensity laser application in orthodontics. *Dental Press J. Orthod.* 2017;22:99–109.
7 Shipley T, Farouk K, El-Bialy T. Effect of high-frequency vibration on orthodontic tooth movement and bone density. *J. Orthod. Sci.* 2019;8.
8 Kolahi J, Abrishami M, Davidovitch Z. Microfabricated biocatalytic fuel cells: a new approach to accelerating the orthodontic tooth movement. *Med Hypotheses.* 2009;73: 340–341.
9 Sugimori T, et al. Micro-osteoperforations accelerate orthodontic tooth movement by stimulating periodontal ligament cell cycles. *Am J Orthod Dentofacial Orthop.* 2018; 154:788–796.
10 Al-Khalifa KS, Baeshen HA. Micro-osteoperforations and its effect on the rate of tooth movement: a systematic review. *Eur J Dermatol.* 2021;15:158–167.
11 Sivarajan S, Ringgingon LP, Fayed MMS, Wey MC. The effect of micro-osteoperforations on the rate of orthodontic tooth movement: a systematic review and meta-analysis. *Am J Orthod Dentofacial Orthop.* 2020;157:290–304.
12 Cheung MWL, Ho RCM, Lim Y, Mak A. Conducting a meta-analysis: basics and good practices. *Int J Rheum Dis.* 2012. https://doi.org/10.1111/j.1756-185X.2012.01712. x.
13 Lim RBC, Zhang MWB, Ho RCM. Prevalence of all-cause mortality and suicide among bariatric surgery cohorts: a meta-analysis. *Int J Environ Res Publ Health.* 2018. https://doi.org/10.3390/ijerph15071519.

14 DerSimonian R, Laird N. Meta-analysis in clinical trials. Control. *Clin Trials*. 1986. https://doi.org/10.1016/0197-2456(86)90046-2.

15 Mantel N, Haenszel W. Statistical aspects of the analysis of data from retrospective studies of disease. *J Natl Cancer Inst*. 1959. https://doi.org/10.1093/jnci/22.4.719.

16 Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *Br Med J*. 2003. https://doi.org/10.1136/bmj.327.7414.557.

17 Suzuki SS, et al. Effects of corticopuncture (CP) and low-level laser therapy (LLLT) on the rate of tooth movement and root resorption in rats using micro-CT evaluation. *Laser Med Sci*. 2018;33:811–821.

18 Kim J, et al. Comparison of tooth movement and biological response in corticotomy and micro-osteoperforation in rabbits. *KOREAN J. Orthod*. 2019;49:205–213.

19 Kim S, et al. Comparison of horizontal and vertical osteoperforation on biological response and tooth movement in rabbits. *Korean J Orthod*. 2021.

20 Teixeira CC, et al. Cytokine expression and accelerated tooth movement. *J Dent Res*. 2010;89:1135–1141.

21 Tsai C-Y, Yang T-K, Hsieh H-Y, Yang L-Y. Comparison of the effects of micro-osteoperforation and corticision on the rate of orthodontic tooth movement in rats. *Angle Orthod*. 2016;86:558–564.

22 Huang C-Y, et al. Comparison of tooth movement and biological response resulting from different force magnitudes combined with osteoperforation in rabbits. *J Appl Oral Sci*. 2021;29:1–9.

23 Cheung T, et al. Ability of mini-implant-facilitated micro-osteoperforations to accelerate tooth movement in rats. *Am J Orthod Dentofacial Orthop*. 2016;150: 958–967.

24 Cramer CL, Campbell PM, Opperman LA, Tadlock LP, Buschang PH. Effects of micro-osteoperforations on tooth movement and bone in the beagle maxilla. *Am J Orthod Dentofacial Orthop*. 2019;155:681–692.

25 Shahabee M, Shafaee H, Abtahi M, Rangrazi A, Bardideh E. Effect of micro-osteoperforation on the rate of orthodontic tooth movement—a systematic review and a meta-analysis. *EJO (Eur J Orthod)*. 2020;42:211–221.

26 Sivarajan S, Ringgingon LP, Fayed MMS, Wey MC. The effect of micro-osteoperforations on the rate of orthodontic tooth movement: a systematic review and meta-analysis. *Am J Orthod Dentofacial Orthop*. 2020;157:290–304.

27 Kalra S, Gupta P, Tripathi T, Rai P. External apical root resorption in orthodontic patients: molecular and genetic basis. *J Fam Med Prim Care*. 2020;9:3872.

28 King AD, et al. Physical properties of root cementum: Part 21. Extent of root resorption after the application of 2.5° and 15° tips for 4 weeks: a microcomputed tomography study. *Am J Orthod Dentofacial Orthop*. 2011;140:e299–e305.

29 Wu ATJ, et al. Physical properties of root cementum: Part 18. The extent of root resorption after the application of light and heavy controlled rotational orthodontic forces for 4 weeks: a microcomputed tomography study. *Am J Orthod Dentofacial Orthop*. 2011;139:e495–e503.

30 Harris DA, Jones AS, Darendeliler MA. Physical properties of root cementum: Part 8. Volumetric analysis of root resorption craters after application of controlled intrusive light and heavy orthodontic forces: a microcomputed tomography scan study. *Am J Orthod Dentofacial Orthop*. 2006;130:639–647.

31 dos Santos CC, Mecenas P, de Castro Aragon ML, Normando D. Effects of micro-osteoperforations performed with Propel system on tooth movement, pain/quality of life, anchorage loss, and root resorption: a systematic review and meta-analysis. *Prog Orthod*. 2020;21.

32 Chan E, Dalci O, Petocz P, Papadopoulou AK, Darendeliler MA. Physical properties of root cementum: Part 26. Effects of micro-osteoperforations on orthodontic root resorption: a microcomputed tomography study. *Am J Orthod Dentofacial Orthop*. 2018;153:204–213.

33 Currell SD, Liaw A, Blackmore Grant PD, Esterman A, Nimmo A. Orthodontic mechanotherapies and their influence on external root resorption: a systematic review. *Am J Orthod Dentofacial Orthop*. 2019;155:313–329.

34 Singh A, Gill G, Kaur H, Amhmed M, Jakhu H. Role of osteopontin in bone remodeling and orthodontic tooth movement: a review. *Prog Orthod*. 2018;19.

35 Alikhani M, et al. Micro-osteoperforations: minimally invasive accelerated tooth movement. *Semin Orthod*. 2015;21:162–169.