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Scope of antimicrobial photodynamic therapy in Orthodontics and related research: A review

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ABSTRACT

Background: The aim of the present study was to comprehensively review indexed literature regarding the potential role of antimicrobial photodynamic therapy (aPDT) in Orthodontics.
Methods: Indexed databases were searched up to and including January 2019 using the following key words: (a) antimicrobial photodynamic therapy; (b) antimicrobial photodynamic chemotherapy; (c) orthodontic; and (d) orthodontics. Original (clinical and experimental) studies, case-reports, and case-series were included. Letters to the Editor, commentaries and review articles were excluded.
Results: Out of the 29 studies identified in the initial search, 4 studies were processed for data extraction. Three studies were randomized clinical trials performed in humans and 1 study was experimental. Results from 2 studies showed that aPDT is effective in the treatment of gingival inflammation in patients undergoing orthodontic therapy (OT). One study showed that oral decontamination can be successfully performed using aPDT among patients undergoing OT. Results of the experimental study showed that aPDT helps in surface decontamination of orthodontic instruments.
Conclusion: There is insufficient evidence in indexed literature to justify the potential role of aPDT in OT. Hence, further studies are required in this regard.

1. Introduction

Antimicrobial photodynamic therapy (aPDT) is a modern therapeutic strategy that involves interactions between a light source and a photosensitive dye (photosensitizer) in an aerobic domain. The photosensitizer [such as toluidine blue and methylene blue (MB)] is usually injected into the region of interest and then exposed to light of wavelength ranging between 630 and 700 nm. The resultant interaction produces reactive oxygen species (ROS) that damage the target cells (such as cancer cells) and exhibit an antimicrobial activity against broad-range of pathogenic microbes [1–3]. Studies [4–8] have shown that aPDT is a potential treatment strategy in the management of medical conditions such as cancers of the skin, breast and the colon, osteomyelitis and gastric infections. Moreover, aPDT has been used as an adjunct therapy in the management of oral inflammatory conditions such as periodontitis and peri-implant diseases [9–12]. Furthermore, aPDT has also been used for the treatment of denture stomatitis and disinfection of implant and acrylic-based denture surfaces [13–16].

Orthodontics is a specialty in dentistry that broadly involves the science and treatment of malocclusions of dental and skeletal origin. Brackets, wires, elastics and Stainless-Steel bands are often used in clinical orthodontic practice to rearrange teeth and improve the facial profile. Studies [17,18] have shown that periodontal or gingival inflammation (GI) is often manifested in patients with poor oral hygiene maintenance undergoing orthodontic treatment (OT). However, achievement of patient compliance towards regular oral hygiene maintenance is often challenging during OT [15,16]. In a recent clinical study, Gómez et al. [19] assessed the efficacy of aPDT for the prevention of GI in patients undergoing OT. The results showed that aPDT helps delay GI and formation of white spot lesions (that occur due to

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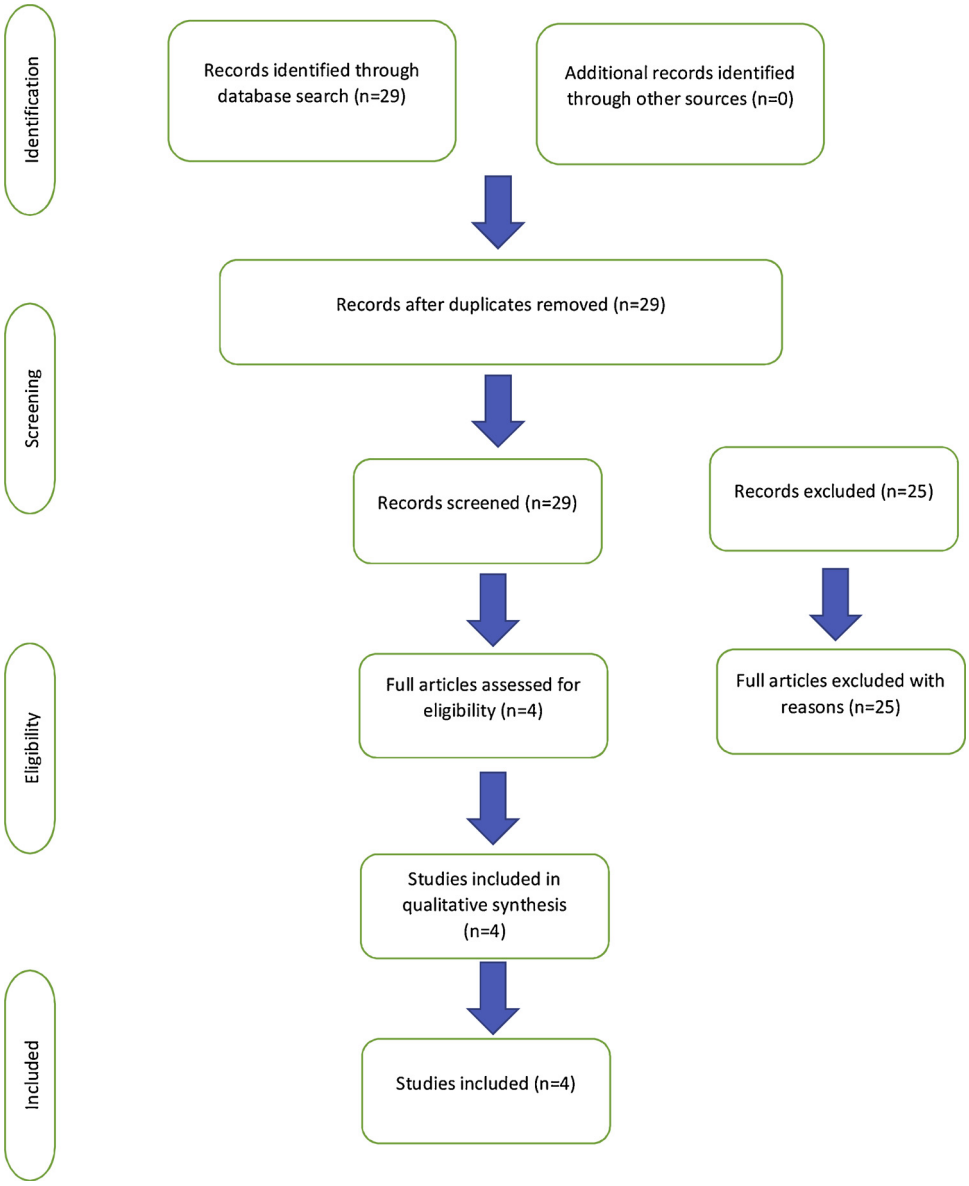

Fig. 1. PRISMA flow diagram.

enamel demineralization) in young patients undergoing fixed OT [19,20]. Moreover, aPDT has been shown to be an effective strategy for the decontamination of orthodontic instruments from microbes such as *Escherichia coli* (*E. coli*), *Staphylococcus aureus* (*S. aureus*) and *Streptococcus mutans* (*S. mutans*) [21]. Following a thorough review of indexed literature, it was observed that there are no studies, which comprehensively reviewed the potential role of aPDT in the dental specialty of Orthodontics.

With this background, the aim of the present study was to comprehensively review indexed literature regarding the potential role of aPDT in Orthodontics.

2. Materials and methods

2.1. Focused question

The Preferred Reporting Items for Systemic Reviews and Meta-Analysis (PRISMA) guidelines [22] were used to conduct the present literature review (Fig. 1). The addressed focused question was "Does aPDT have a potential role in the discipline of Orthodontics?"

2.2. Eligibility criteria

Original (clinical and experimental) studies, case-reports, and case-series were included. Letters to the Editor, historic reviews, and commentaries were excluded.

2.3. Literature search protocol

A structured literature search was used to identify the relevant papers that report the potential role of aPDT in the field of Orthodontics. Indexed databases (PubMed/Medline, OVID, EMBASE, ISI Web of knowledge and Google-Scholar) were searched up to and including January 2019 using the following key-words: (a) antimicrobial photodynamic therapy; (b) antimicrobial photodynamic chemotherapy; (c) orthodontic; and (d) orthodontics. Gray literature (unpublished studies) were identified by searching the Open-GRAY database; and reference list of the studies that fulfilled the eligibility criteria were also hand-searched to identify articles that could have been missed in the initial search. Disagreements regarding study selection were resolved via discussion.

Table 1
Characteristics of the included studies.

Authors et al.	Study design	Participants	Mean age (range)	Investigative parameter	Study groups	Main outcome	Conclusion
Gómez et al. [19]	RCT	21 patients undergoing OT	Group-1: 15 ± 1.8 years Group-2: 14.2 ± 1.3 years	GI	Group-1: aPDT Group-2: US	Significant reduction in GI in both groups	aPDT is useful in reducing GI in patients undergoing OT
Paschoal et al. [20]	RCT	45 patients undergoing OT	NA (13-18 years)	GI	Group-1: Placebo Group-2: CHX varnish Group-3: Curcumin mediated aPDT	Significant reduction in GI in Group-3 compared with other groups	aPDT is useful in reducing GI in patients undergoing OT
Foggiato et al. [21]	Experimental	NA	NA	Decontamination of orthodontic metal instruments	Group-1: Instruments immersed in MB Group-2: Instruments immersed in MB and irradiated with laser	Reduction in the CFUs of *S. aureus*, *S. mutans* and *E. Coli* in Group-2.	aPDT is effective in the decontamination of orthodontic metallic instruments
Panhóca et al. [23]	RCT	24 patients undergoing OT	NA (18-50 years)	Oral *Streptococcus mutans* count	Group-1: light alone Group-2: aPDT	Significant reduction in CFUs of *S. mutans* in Group-2 than Group-1.	aPDT and CHX promote oral decontamination in clinical orthodontic practice

aPDT: Antimicrobial photodynamic therapy, CFUS: Colony forming units, CHX: Chlorhexidine, *E. Coli*: *Escherichia coli*, GI: Gingival inflammation, OT: Orthodontic treatment, NA: Not applicable, MB: Methylene Blue, RCT: Randomized controlled trial, *S. aureus*: *Staphylococcus aureus*, *S. mutans*: *Streptococcus mutans*, US: Ultrasonic scaling.

3. Results

3.1. Study selection and general characteristics

Twenty-nine studies were identified through the initial search; out of which, 4 studies [19–21,23] fulfilled the eligibility criteria (as described earlier) and were processed for data extraction. Three studies [19,20,23] were randomized clinical trials performed in humans and 1 study [21] had an experimental design (Table 1). The excluded studies were either review articles or did not answer the focused question.

3.2. Summary of results from human studies

In the clinical studies [19,20,23], the number of participants ranged between 21 and 45. One study [19], reported the mean age of the participants. In this study [19], participants that underwent aPDT and ultrasonic scaling (US) were 15 ± 1.8 and 14.2 ± 1.3 years old, respectively. Results from 2 studies [19,20] showed that aPDT is an effective therapeutic strategy for the treatment of GI among patients undergoing OT; and Panhóca et al. [23] showed that aPDT is effective in the oral decontamination of patients undergoing OT.

3.3. Summary of results from the experimental study

In the experimental study [21], influence of aPDT on surface decontamination of orthodontic instruments was assessed. The results showed that placement of orthodontic instruments in 100 μmol/L of MB for 20 min followed by irradiation with 660 nm laser light (energy density of 026 J/cm^2) for another 20 min causes statistically significant reduction in the colony forming units of gram positive (*S. aureus* and *S. mutans*) and negative (*E. coli*) microbes.

4. Discussion

Following a comprehensive review of pertinent literature, a limited number of studies [19–21,23] with varying outcomes fulfilled the eligibility criteria. Due to this limitation, a systematic review and meta-analysis of the studies could not be performed. Though there is a scarcity of indexed literature regarding the significance of aPDT in Orthodontics, the available evidence [19–21,23] suggests that aPDT can be used in patients undergoing OT. For example, in the study by Gómez et al. [19], aPDT as well as US were effective in the treatment of GI in patients undergoing OT. Similarly, results by Foggiato et al. [21] showed that aPDT is an effective technique to disinfect metallic instruments used in clinical orthodontic practice. It is however emphasized that by no means should aPDT be a replacement for conventional mechanical debridement (MD) and sterilization techniques such as US and autoclaving, respectively. Studies [24–27] have shown that MD when performed with adjunct aPDT is more effective in the treatment of periodontal diseases (PD) (such as chronic periodontitis) compared with MD alone. Moreover, in the study by Foggiato et al. [21] efficacy of aPDT as a disinfectant was tested against a limited number of microbes (*S. aureus*, *S. mutans* and *E. Coli*). It is hypothesized that US and instrument sterilization when performed with adjunct aPDT are more effective compared with US and autoclaving alone. Further studies are needed to test these hypotheses.

Common side-effects associated with OT encompass dental caries, periodontal disease and white spot lesions [28,29]. According to Jurišić et al. [30] oral hygiene maintenance in patients undergoing OT helps reduce the incidence of white spot lesions (WSL) in adolescents. It is therefore crucial to reinforce routine oral hygiene instructions via routine follow-up in patients undergoing fixed and removable OT. It is speculated that aPDT-based full-mouth disinfection in conjunction with oral hygiene maintenance and routine dental check-ups is a reliable methodology to minimize the risk of PD and WSL in patients undergoing OT. However, to date, there are no studies in indexed literature

that have tested this hypothesis.

It has been reported that habitual use of nicotinic products, such as tobacco smoking jeopardize the outcomes of OT [31]. Moreover, psychological disorders and systemic diseases such as poorly controlled diabetes mellitus may also negatively influence the outcome of OT [32,33]. Furthermore, use of medications, such as corticosteroids and bisphosphonates have also been reported to affect OT [34,35]. To the authors knowledge, there are no studies in indexed literature that have assessed the outcome of OT with adjunct aPDT in smokers, patients systemic and/or psychological diseases, and individuals receiving medications, such as corticosteroids and bisphosphonates. It is hypothesized that the outcome of OT with or without aPDT are compromised in the patient groups referenced above. Further studies are needed to test these hypotheses.

5. Conclusion

There is insufficient evidence in indexed literature to justify the potential role of aPDT in OT. Hence, further studies are required in this regard.

References

[1] F. Vatansever, W.C. de Melo, P. Avci, D. Vecchio, M. Sadasivam, A. Gupta, R. Chandran, M. Karimi, N.A. Parizotto, R. Yin, G.P. Tegos, M.R. Hamblin, Antimicrobial strategies centered around reactive oxygen species–bactericidal antibiotics, photodynamic therapy, and beyond, FEMS Microbiol. Rev. 37 (6) (2013) 955–989.

[2] E.L. Belinello-Souza, L.H. Alvarenga, C. Lima-Leal, P. Almeida, C.G. Leite, T.R. Lima, B. Godoy-Miranda, J. Previati-Oliveira, L. de Pretto, A.Z. de Freitas, A.U. Fernandes, R. Labat Marcos, R.A. Prates, Antimicrobial photodynamic therapy combined to periodontal treatment: experimental model, Photodiagnosis Photodyn. Ther. 18 (2017) 275–278.

[3] Z. Zhou, J. Song, L. Nie, X. Chen, Reactive oxygen species generating systems meeting challenges of photodynamic cancer therapy, Chem. Soc. Rev. 45 (23) (2016) 6597–6626.

[4] N. Hodgkinson, C.A. Kruger, H. Abrahamse, Targeted photodynamic therapy as potential treatment modality for the eradication of colon cancer and colon cancer stem cells, Tumour Biol. 39 (10) (2017) 1010428317734691.

[5] S.M. Banerjee, A.J. MacRobert, C.A. Mosse, B. Periera, S.G. Bown, M.R.S. Keshtgar, Photodynamic therapy: inception to application in breast cancer, Breast 31 (2017) 105–113.

[6] S.R. Lucena, N. Salazar, T. Gracia-Cazana, A. Zamarron, S. Gonzalez, A. Juarranz, Y. Gilaberte, Combined treatments with photodynamic therapy for non-melanoma skin Cancer, Int. J. Mol. Sci. 16 (10) (2015) 25912–25933.

[7] J.A. Dos Reis Jr., J.N. Dos Santos, B.S. Barreto, P.N. de Assis, P.F. Almeida, A.L. Pinheiro, Photodynamic Antimicrobial Chemotherapy (PACT) in osteomyelitis induced by Staphylococcus aureus: microbiological and histological study, J. Photochem. Photobiol. B Biol. 149 (2015) 235–242.

[8] C.E. Millson, M. Wilson, A.J. MacRobert, S.G. Bown, Ex-vivo treatment of gastric Helicobacter infection by photodynamic therapy, J. Photochem. Photobiol. B Biol. 32 (1-2) (1996) 59–65.

[9] U.B. Cadore, M.B.L. Reis, S.H.L. Martins, M.I.M. de, A.B. Novaes Jr., M. Taba Jr., D.B. Palioto, M.R. Messora, S.L.S. Souza, Multiple sessions of antimicrobial photodynamic therapy associated with surgical periodontal treatment in patients with chronic periodontitis, J. Periodontol. (2018), https://doi.org/10.1002/JPER.18-0373 [Epub ahead of print].

[10] M.S. de Melo Soares, C. D'Almeida Borges, M. de Mendonca Invernici, F.G. Frantz, L.C. de Figueiredo, S.L.S. de Souza, M. Taba Jr., M.R. Messora, A.B. Novaes Jr., Antimicrobial photodynamic therapy as adjunct to non-surgical periodontal treatment in smokers: a randomized clinical trial, Clin. Oral Investig. (2018), https://doi.org/10.1007/s00784-018-2740-3 [Epub ahead of print].

[11] A.M. Albaker, A.S. ArRejaie, M. Alrabiah, K.A. Al-Aali, S. Mokeem, M.N. Alasqah, F. Vohra, T. Abduljabbar, Effect of antimicrobial photodynamic therapy in open flap debridement in the treatment of peri-implantitis: a randomized controlled trial, Photodiagnosis Photodyn. Ther. 23 (2018) 71–74.

[12] L. Chambrone, H.L. Wang, G.E. Romanos, Antimicrobial photodynamic therapy for the treatment of periodontitis and peri-implantitis: an American Academy of Periodontology best evidence review, J. Periodontol. 89 (7) (2018) 783–803.

[13] A. Davoudi, B. Ebadian, S. Nosouhian, Role of laser or photodynamic therapy in treatment of denture stomatitis: a systematic review, J. Prosthet. Dent. 120 (4) (2018) 498–505.

[14] A.M. de Senna, M.M.F. Vieira, R.M. Machado-de-Sena, A.O. Bertolin, S.C. Nunez, M.S. Ribeiro, Photodynamic inactivation of Candida ssp. On denture stomatitis. A clinical trial involving palatal mucosa and prosthesis disinfection, Photodiagn. Photodyn. Ther. 22 (2018) 212–216.

[15] B. Azizi, A. Budimir, I. Bago, B. Mehmeti, S. Jakovljevic, J. Kelmendi, A.P. Stanko, D. Gabric, Antimicrobial efficacy of photodynamic therapy and light-activated disinfection on contaminated zirconia implants: an in vitro study, Photodiagn. Photodyn. Ther. 21 (2018) 328–333.

[16] A. Saffarpour, R. Fekrazad, M.N. Heibati, A. Bahador, A. Saffarpour, A.R. Rokn, A. Iranparvar, M.J. KharaziFard, Bactericidal effect of erbium-doped yttrium aluminum garnet laser and photodynamic therapy on Aggregatibacter actinomycetemcomitans biofilm on implant surface, Int. J. Oral Maxillofac. Implants 31 (3) (2016) e71–8.

[17] P. Jose, B.K. Ramabhadran, R. Emmatty, T.P. Paul, Assessment of the effect of ozonated water irrigation on gingival inflammation in patients undergoing fixed orthodontic treatment, J. Indian Soc. Periodontol. 21 (6) (2017) 484–488.

[18] A.A. Folco, S.C. Benitez-Roge, M. Iglesias, D. Calabrese, C. Pelizardi, A. Rosa, M.I. Brusca, P. Hecht, M.E. Mateu, Gingival response in orthodontic patients: comparative study between self-ligating and conventional brackets, Acta Odontol. Latinoam. 27 (3) (2014) 120–124.

[19] C. Gomez, R. Abellan, J.C. Palma, Efficacy of photodynamic therapy vs ultrasonic scaler for preventing gingival inflammation and white spot lesions during orthodontic treatment, Photodiagnosis Photodyn. Ther. 24 (2018) 377–383.

[20] M.A. Paschoal, C.M. Moura, F. Jeremias, J.F. Souza, V.S. Bagnato, J.S. Giusti, L. Santos-Pinto, Longitudinal effect of curcumin-photodynamic antimicrobial chemotherapy in adolescents during fixed orthodontic treatment: a single-blind randomized clinical trial study, Lasers Med. Sci. 30 (8) (2015) 2059–2065.

[21] A.A. Foggiato, D.F. Silva, R. Castro, Effect of photodynamic therapy on surface decontamination in clinical orthodontic instruments, Photodiagnosis Photodyn. Ther. 24 (2018) 123–128.

[22] D. Moher, A. Liberati, J. Tetzlaff, D.G. Altman, Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement, Int. J. Surg. 8 (5) (2010) 336–341.

[23] V.H. Panhoca, F.L. Esteban Florez, T.Q. Correa, F.R. Paolillo, C.W. de Souza, V.S. Bagnato, Oral decontamination of orthodontic patients using photodynamic therapy mediated by blue-light irradiation and curcumin associated with sodium dodecyl sulfate, Photomed. Laser Surg. 34 (9) (2016) 411–417.

[24] P.D. Macedo, S.T. Corbi, G. de Oliveira, J.R. Perussi, A.O. Ribeiro, R.A.C. Marcantonio, Hypericin-glucamine antimicrobial photodynamic therapy in the progression of experimentally induced periodontal disease in rats, Photodiagn. Photodyn. Ther. (2018).

[25] V.G. Garcia, E.C.J. Gualberto, E. Ervolino, M.J.H. Nagata, J.M. de Almeida, L.H. Theodoro, aPDT for periodontitis treatment in ovariectomized rats under systemic nicotine, Photodiagn. Photodyn. Ther. 22 (2018) 70–78.

[26] P. Bundidpun, R. Srisuwantha, N. Laosrisin, Clinical effects of photodynamic therapy as an adjunct to full-mouth ultrasonic scaling and root planing in treatment of chronic periodontitis, Laser Ther. 27 (1) (2018) 33–39.

[27] L.H. Theodoro, N.Z. Assem, M. Longo, M.L.F. Alves, C. Duque, R.N. Stipp, N.L. Vizoto, V.G. Garcia, Treatment of periodontitis in smokers with multiple sessions of antimicrobial photodynamic therapy or systemic antibiotics: a randomized clinical trial, Photodiagn. Photodyn. Ther. 22 (2018) 217–222.

[28] M. Karkhanechi, D. Chow, J. Sipkin, D. Sherman, R.J. Boylan, R.G. Norman, R.G. Craig, G.J. Cisneros, Periodontal status of adult patients treated with fixed buccal appliances and removable aligners over one year of active orthodontic therapy, Angle Orthod. 83 (1) (2013) 146–151.

[29] M.K. Eltayeb, Y.E. Ibrahim, I.A. El Karim, N.M. Sanhouri, Distribution of white spot lesions among orthodontic patients attending teaching institutes in Khartoum, BMC Oral Health 17 (1) (2017) 88.

[30] S. Jurisic, D. Kozomara, H. Juric, Z. Verzak, G. Jurisic, The influence of different types of brackets and efficacy of two chlorhexidine mouthwashes on oral hygiene and the incidence of white spot lesions in adolescents during the orthodontic therapy, Psychiatr. Danub. 28 (Suppl. 2) (2016) 247–252.

[31] D. Michelogiannakis, P.E. Rossouw, D. Al-Shammery, Z. Akram, J. Khan, G.E. Romanos, F. Javed, Influence of nicotine on orthodontic tooth movement: a systematic review of experimental studies in rats, Arch. Oral Biol. 93 (2018) 66–73.

[32] S. Najeeb, F. Siddiqui, S.B. Qasim, Z. Khurshid, S. Zohaib, M.S. Zafar, Influence of uncontrolled diabetes mellitus on periodontal tissues during orthodontic tooth movement: a systematic review of animal studies, Prog. Orthod. 18 (1) (2017) 5.

[33] D. Al-Shammery, D. Michelogiannakis, E. Rossouw, G.E. Romanos, F. Javed, Influence of psychological stress exposure on orthodontic therapy: a comprehensive review, J. Investig. Clin. Dent. (2019) e12388.

[34] D. Michelogiannakis, D. Al-Shammery, P.E. Rossouw, H.B. Ahmed, Z. Akram, G.E. Romanos, F. Javed, Influence of corticosteroid therapy on orthodontic tooth movement: a narrative review of studies in animal-models, Orthod. Craniofac. Res. 21 (4) (2018) 216–224.

[35] B. Gupta, S. Singh, R.H. Tallents, E. Rossouw, Effects of bisphosphonates on orthodontic treatment and the TMJ: a systematic review, J. Clin. Orthod. 51 (8) (2017) 471–478.