Review Article

ORTHODONTIC CLEAR ALIGNER VS FIXED APPLIANCES' INFLUENCE ON ORAL MICROBIOTA AND SALIVARY PARAMETERS': A SYSTEMATIC REVIEW

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ABSTRACT

The goal of the present revision is to systematically investigate the background and statistically summarize the found evidence investigating the impact of thermoplastic clear aligners as well as fixed orthodontic appliances on oral microbiota and salivary parameters. The present systematic study was done according to PRISMA guidelines and the Cochrane Handbook. Five Electronic databases were used to search for relevant articles. A total of 5345 articles were relevant to this topic. Duplicates were removed which caused 4636 articles included in the initial screening after duplicates. 7 studies met the eligibility criteria. Out of 4 studies classified as low risk of bias, 2 of them were regarded as moderate bias hazard and only one research as high bias risk. All of them were included in the systematic review. Overall changes of oral microbiota are higher in patients with fixed appliances than removable appliances. No significant change was observed in salivary flow rate nor salivary buffering power for clear aligner, while there were variations in the results of the fixed orthodontic appliances group in previous studies. However, there were changes in other salivary parameters for fixed orthodontic groups.

Key words: Orthodontic appliance, Oral microbiota, Salivary parameters, Clear aligner.

Introduction

It is broadly believed that malocclusion hurts people's physical, social, and psychological welfare [1, 2]. Patients ask for orthodontic treatment to enhance their appearance, oral function, psychosocial well-being, and quality of life, hence the major motivation for adult patients is mainly to improve their appearance. Current orthodontic appliances include fixed and removable orthodontic appliances. The primary elements of stable devices (brackets, band, ligature, and orthodontic wire) are capable to decrease the physiologic function of self-cleaning by the tongue or cheeks, also establish various plaque cumulation areas interfering with oral hygiene measures, and hence may lead to form white spot lesions, caries, gingival inflammation and/or periodontal diseases [3]. Moreover, brackets may cause an unpleasant appearance, functional restrictions, and some discomforts. As the need for esthetic dentistry has enlarged in the last few decades, more patients are selecting invisible aligners, lingual brackets, and/or tooth-colored brackets over conventional ones [4]. On the other hand, the application of portable orthodontic appliances is capable to grant a sufficient oral hygiene measure so it can be easily removed for cleaning hence it decreases the risk for such adverse dental and periodontal complications in addition to more esthetic manifestation [5].

Periodontal diagnosis before orthodontic treatment is highly recommended as well as giving instructions to maintain good oral hygiene [6]. The significant key to periodontitis is the taxonomic composition of the microbiome while mutants streptococci are mainly significant in caries stimulation [7, 8]. S. mutans is a powerful acid producer and it is present in early carious lesions [9]. The biologic factors within saliva contribute to protecting the tooth from caries, includes salivary flow rate, antimicrobial activity, microorganism aggregation, and clearance from the oral cavity [10]. PH 6.7 is the average range of saliva but it ranges from 6.2-7.6 [11]. The evidence shows that the pathologically decreased salivary flow rate is regarded as a risk parameter for caries formation [12].

Many studies represent that conventional orthodontic appliances affect oral microbiota [13, 14].

Although various studies have evaluated the oral environment from different perspectives during orthodontic treatment using different protocols, for example, oral microorganism evaluation during active orthodontic phase using clear aligners, fixed appliances also, have assessed the nonmicrobial salivary parameters. However, there are deficient supporting literature in the form of systematic review nor meta-analysis combined all these factors in one study.

Hence, the goal of the present review is to consistently evaluate the literature and statistically summarize the found evidence evaluating the impact of thermoplastic clear

aligners as well as fixed orthodontic appliances on oral microbiota and salivary parameters.

Materials and Methods

Search strategy and data sources

The review was registered with registration number FIRP/2020/66/252, and ethical approval has been obtained from the institutional review board IRP of Riyadh Elm (IRB) committee of Riyadh Elm University FIRP/2020/66/252/247.

Focused question

In orthodontic conventional fixed appliances and clear therapeutic aligners, were there a systematic change in oral microbial type and/or concentrations of salivary parameters among non-grower patients?

Data source

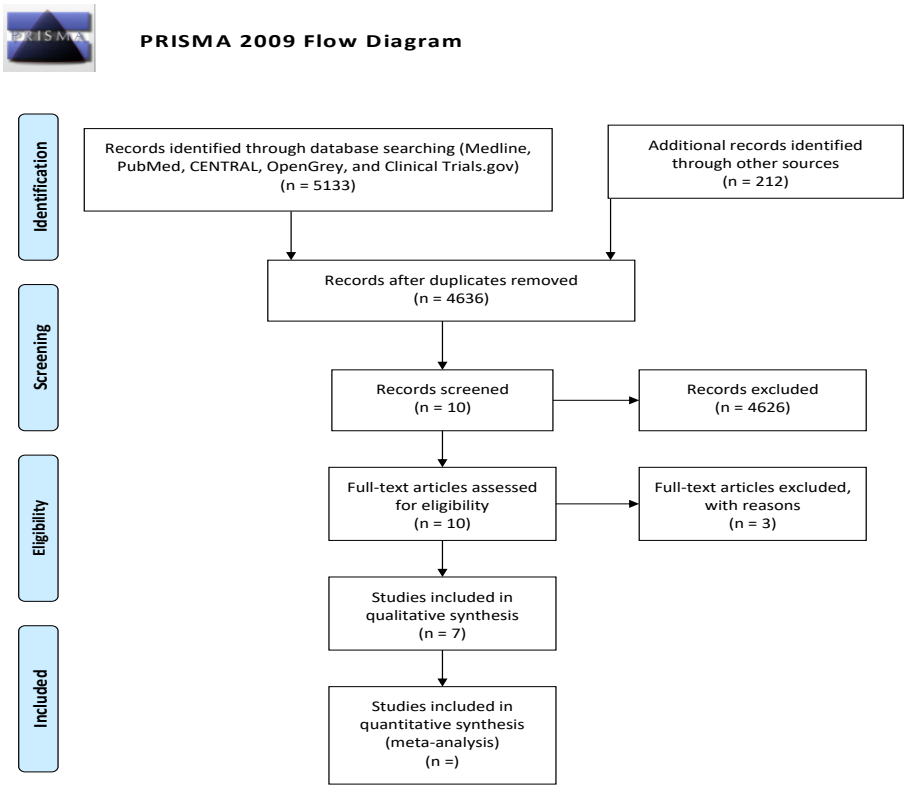
This systematic review was done according to PRISMA guideline [15]. and the Cochrane handbook [16]. A search was conducted in PubMed, Google Scholar, The Cochrane library, Saudi digital library, And Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS).

The following keywords were used "((salivary parameter) OR (oral microbiota)) AND (periodontopathic bacteria)) OR (cariogenic bacteria)) AND (fixed orthodontic appliances)) OR (clear aligner)." The search was limited to the last five years from 2015 until 24/6/2020.

Duplicates were removed and articles were screened initially by title and abstract.

Studies were done during the retentive phase for orthodontic patients; articles measured oral health by PI, GI, and PSR only, and the study was done for growing patients, and articles uncorrelated to the aim of the present organized review were excluded. The collected articles were individually strictly applied to clear inclusion and exclusion criteria as shown in **Table 1**. The procedure of article choosing is shown in **Figure 1**.

Articles were screened using the Problem, Intervention, Comparator, and Outcome (PICO) approach. Population/Problem was defined as non-grower patients' orthodontic treatment needs. The intervention was defined as orthodontic treatment during the active phase. Comparator defined as two types of orthodontic appliances (Fixed appliances and clear aligner). The outcome was defined as oral microflora and salivary parameters.



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

Figure 1. PRISMA Chart Shows Selection Process of the Articles

Table 1. Eligibility Criteria

Criteria	Inclusion criteria	Exclusion criteria
Language	English language	Any other language
Population/Age group	Non-growers (18 years old patients or older) of both genders	Grower (patients younger than 18 years old)
Publication date	Articles from 2015 up to 2020	Studies published before 2015
Type of study	In human, randomized and non-randomized clinical trials -Retrospective and/or prospective cohort studies	-Animal studies -Low quality of evidence -Case report, review studies, as well as cross-sectional studies (questionnaires based). -Unsupported opinion of expert or replies to the author/editor. Books'/ conferences' abstract.
Intervention	Studies are done during the active phase of orthodontic treatment	Studies are done during the retentive phase among patients with retainer
Subjects	-Medically fit patient. -Patient with good oral hygiene.	-Medically compromised patients and patient with medication that causes side effect in the oral cavity environment -Patient with active periodontal disease. -Patient with poor oral hygiene.
Treatment protocol/ comparison	-Conventional fixed orthodontic appliances -clear therapeutic appliances	-Functional appliances. -Orthognathic surgical involvement.
Study duration	Studies were done for 1 month or more	Studies were done for less than 1 month.
Outcome	Studies evaluate the change of oral microflora and salivary parameters	Studies that evaluate candida only

Quality synthesis

One particular reviewer (First Author) assessed the methodological quality of the studies after the final assessment of the full text (n=10) independently. Accordingly, 7 final articles were individually applied for qualitative and quantitative assessments. Quality assessment of the 7 final articles were appraised for risk of bias using a well-formulated quality assessment tool [15, 16]. Sampling bias was appraised by assessing and evaluating the sample selection, performance, detection of outcome assessors, attrition, and reporting. The overall assessment provided ranges from low to moderate risk of bias for the 7 articles; the main methodological points of these studies are summarized in **(Table 2)**.

Table 2. Risk of Bias Assessment

Bias Type	**Selection**		**Performance**	**Detection**	**Attrition**	**Reporting**	**Overall Assessment**
Bias	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding Outcome Assessment	Incomplete Resulted Data	Selective Reporting	
Levrini L. *et al*. 2015 [5].	Low	Unclear	Low	Unclear	Low	Low	Low
Runzhi Guo. *et al*. 2018 [17].	Low	Unclear	Low	Unclear	Low	Low	Low
A. Marda *et al*. 2018 [18].	Low	Unclear	Low	Unclear	Low	Low	Low
Alshahrani I. *et al*. 2019 [19].	Unclear	Unclear	Low	Unclear	Low	Low	Moderate
Al-Melh M *et al*. 2020 [20].	Unclear	Unclear	Low	Unclear	Low	High	High
Mummolo S. *et al*. (2020) [14].	High	Unclear	Low	Low	Low	Low	Moderate
Mummolo, S. *et al*. (2020) [21].	Unclear	Unclear	Low	Low	Low	Low	Low

Criteria for judging the risk of bias in the 'Risk of bias assessment tool – reproduced from The Cochrane Tool [16]. Criteria of judgment following low, high, or unclear risk was judge based on the following: 1- Random succession creation: election bias (prejudiced allocation to interventions) because of insufficient formation of a randomized succession. 2- Allotment hiding: election bias (biased allotment to interventions) as a result of insufficient hiding of allotments before assignment. 3-Blinding of participants and employees: function bias because of knowledge of the allotted interventions by participants and employees within the research. 4-Blinding of result evaluation: recognition of bias as a result of knowledge of the allotted interventions by result assessors. 5-Defected result data: attrition bias because of amount, nature, or handling of defected result data. 6-Elective reporting: reporting bias as a result of selective result reporting.

Results and Discussion

A total of 4636 were related to this topic. A total of 4626 were excluded by initial screening. There were 10 studies screened for eligibility criteria 7 of them included in qualitative synthesis, while 3 of them were excluded **(Table 3)**.

Table 3. Summary of Excluded Studies

Authors	Reason for exclusion
Turssi CP. *et al*. 2015 [22]	Full-text article can't be found
Ioannis P. Zogakis. *et al.* 2018 [23]	mean age of 15.8 +- 4.4 years.
DIAN JING. *et al.* 2019 [24]	patient age between 14 and 20 years

Overall, the bias risk for intended studies ranged from weak to high **(Table 2)**.

Oral microbiota

6 studies evaluated oral microbiota for orthodontic patients during the active phase. Their results were summarized in **Table 4**.

Table 4. Summary of changing the oral microbiota during orthodontic treatment

Author (Year)	n	Type of Study	Type of orthodontic appliance	measures	Method/test	Duration	Results
Levrini L. *et al*. 2015 [5].	77	prospective study	-Invisalign -fixed appliance.	Total biofilm mass and periodontal pathogens	real-time polymerase chain reaction (PCR)	3 months	-There was no periodontal pathogenic bacteria in the Invisalign treatment group while the fixed orthodontic treatment group show A.actinomycetemcomitans only in one patient. -fixed orthodontic treatment group indicated a higher extent of bacteria condensation"
A. Marda *et al.* 2018 [18].	18	Prospective study	Fixed Orthodontic Appliances	oral microbial flora changes	The plaque was collected by gauze from the surface of the teeth - Rapid ID32 STREP galleries biochemical and enzymatic experiments (Bio-Merieux, SA) for Streptococci and API-20A (BioMerieux, SA) for anaerobic bacteria. -To make sure the bacterial recognition: automaton Phoenix.	3 months	This study shows an increase in cariogenic bacteria especially Streptococcus mitis, Streptococcus sobrinus, and Lactobacillus.
Runzhi Guo. *et al.* 2018 [17].	10	prospective study	Clear aligners	Subgingival Plaque - plaque index (PI) and gingival bleeding index (GBI) evaluations	DNA was taken from plaque specimens and analyzed by 16S rRNA gene sequencing.	3 months	- Less microbial variety with a remarkable alteration of microbial structure within the first three months of clear aligner treatment (CAT). - This study states that clear aligners cause nonpathogenic alterations of the subgingival microbiome during the first three-month therapy.
Mummolo S, Nota A, Albani F, Marchetti E, Gatto R, Marzo G, *et al.* (2020) [14].	80	prospective controlled study	-Clear aligners (CA) -Multibrackets appliance (MB)	S. mutans and Lactobacilli count	Bacteria CRT	6 months	- the increase of S. mutans and Lactobacilli colonies were progressive in MB group it showed a risky value at t2 for 37.5% of participants while in the clear aligners group only 8% of participants show the risky value at t2

Mummolo, S, Tieri, M, Nota, A, *et al.* 2020 [21].	90	Prospective study	clear aligners (CA) removable positions (RP) -multibrackets fixed orthodontic appliance (MB)	S. mutans and Lactobacilli count in saliva	CRT® bacteria (Ivoclar Vivadent Clinical, Schaan, Liechtenstein).	6 months	"CA group, the number of patients with CFU/ml >105 somewhat enhanced after 6 months, without statistic relationship. The same trend was seen in patients using RP appliances. In the MB group, it enhanced progressively over time, with a statistically significant difference from beginning to 3 months, and from beginning to 6 months. The diversities among the groups were statistically significant at 3 months and 6 months
Al-Melh M. *et al.* 2020 [20].	80	Cross-Sectional study	Patients with orthodontic brackets and healthy controls without brackets.	streptococci and a Lactobacillus species were diagnosed and assessed	polymerase chain reaction (PCR) and real-time quantitative PCR.	involved patients with fixed orthodontic appliances for at least 12 months.	Orthodontic patients with brackets for 12 months show higher quantities of S. mutans and S. salivarius than control participants

Salivary parameters

There were two studies that evaluated salivary parameters for orthodontic patients during the active phase. Their result summarized in **Table 5**.

Table 5. Summary of salivary parameters assessment during orthodontic treatment

Author (Year)	n	Type of Study	Type of orthodontic appliance	measures	Method/test	Duration	Results
Alshahrani I. et al.2019 [19].	60	Prospective Study	fixed orthodontic treatment.	Salivary parameter change: glucose, total proteins, amylase, and calcium levels in the saliva samples. Salivary PH Flowrate	enzyme-linked immunosorbent assay (ELISA)	before and 2 months after treatment	-Salivary pH and flow the rate decreased while glucose and amylase levels significantly increased 2 months after commencing treatment. -Salivary buffering capacity, total protein concentration, and calcium levels were showed significant reductions in all three parameters after commencing treatment. -Increase in the number of patients with low and medium buffering capacity after commencing treatment; however, a significant decrease was noted in the percentage of patients in the high buffering category.
Mummolo S, Nota A, Albani F, Marchetti E, Gatto R, Marzo G, *et al.* (2020) [14]	80	Prospective Study	Clear aligners -fixed orthodontic appliance (Multibrackets appliance)	Salivary flow Buffering power	CRT buffer system	6 months	No significant changes in salivary flow nor salivary buffering during orthodontic treatment for both groups

There were 7 studies included in this review, 6 of the studies were about the oral microbiota while the other 2 studies were about evaluating the change of salivary parameters during orthodontic treatment. Furthermore, the majority of the studies were prospective studies however, there was one cross-sectional study.

There were changes in oral microbiota in orthodontic conventional fixed appliances and clear aligners reported by Levrini L. *et al.* (2015) [5], Mummolo S., Tieri M, *et al.* (2020) [21], Runzhi Guo. *et al.* (2018) [17], A. Marda. *et al.* (2018) [18], Mummolo, Nota, A, *et al.* (2020) [14], and Al-Melh M. *et al.* (2020) [20]. A prospective study done by

Levrini L. *et al*. (2015) [5] includes 77 participants classified into 3 groups (Invisalign group, fixed orthodontic appliances group, and control group). The authors reported fixed orthodontic treatment group showed a higher level of bacterial concentrations and only one patient in this group show *A. actinomycetemcomitans.* while there were no periodontal pathogenic bacteria in the clear aligner treatment group. However, another prospective controlled study done by Mummolo S. *et al.* (2020) [14] include 80 participants 40 subjects were treated with clear aligners (CA), and 40 were treated with fixed multi brackets (MB). The result showed an increase of S. mutans and Lactobacilli colonies were progressive in MB group it showed a risky value at 6 months for 37.5% of participants while the clear aligners group only 8% of participants show the risky value at 6 months. In addition, A. Marda *et al.* (2018) [18] reported with another prospective study included 18 participants, which showed an increase in cariogenic bacteria especially Streptococcus mitis, Streptococcus sobrinus, and Lactobacillus with fixed orthodontic appliances. Another prospective study including 10 participants done by Runzhi Guo. *et al.* (2018) [17] states that clear aligners cause nonpathogenic changes of the subgingival microbiome in the first three-month therapy. A prospective study done by Mummolo, S, Tieri, M, Nota, A, *et al.* (2020) [21] including 90 patients divided into 3 groups 30 participants in each group: removable clear aligners (CA), fixed multi brackets group (MB) appliance and removable positioner (RP) reported that just nearly 10% of CA patients and 13.3% of RP patients achieved microbial colonization after six months of therapy, in comparison to MB patients, for which about 40%- and 20% after 3 months - of cases are very sensitive to forming caries. A cross-sectional study reported by Al-Melh M. *et al.* (2020) [20] including 40 patients with orthodontic brackets and 40 healthy controls without brackets, stated that orthodontic patients with brackets for 12 months showed higher quantities of S. mutans and S. salivarius than control participants.

Regarding the evaluation of salivary parameters for orthodontic patients, two prospective studies reported it. One of them including 60 participants with fixed orthodontic appliances only conducted by Alshahrani, I. *et al.* 2019 [19] to assess the alterations in necessary salivary parameters in patients undergoing fixed orthodontic therapy. The measure was done before treatment and 2 months after. These measures include salivary flow rate, pH, buffering capacity, and extents of amylase, total protein, and glucose.

The rate of salivary flow was measured until 2 ml of unstimulated saliva was collected. A small handheld pH meter was used to measure salivary PH. compact pH meter was used to detect buffering capacity, promptly after the collection of the samples. While glucose, total proteins, amylase, and calcium levels in the saliva samples were evaluated by Enzyme-linked Immunosorbent Assay (ELISA). Treatment showed Salivary pH and flow rate decreased while glucose and amylase levels significantly increased 2 months after commencing treatment. Salivary buffering capacity, total protein concentration, and calcium levels were compared before and after commencing treatment using Wilcoxon matched pairs t-test, showed a significant reduction in all three parameters after commencing treatment ($P < 0.001$)

The Total salivary protein concentration significantly correlated with the buffering capacity after commencing orthodontic treatment ($r = 0.34$; $P < 0.05$). Moreover, significant relationships ($P < 0.05$) were seen between salivary calcium and total protein levels, as well as salivary amylase and glucose levels.
An increase in the number of patients with low and medium buffering capacity after commencing treatment; however, a significant decrease was noted in the percentage of patients in the high buffering category

The other study was conducted by Mummolo S. *et al.* 2020 [14]. This study compared 2 groups (Orthodontic patients with clear aligner and Orthodontic patients Multibrackets orthodontic appliance), a total of 40 participants for each group. The salivary parameters included in this study are salivary flow and buffering power. Measurement was done before orthodontic therapy, after 3 months, and after 6 months. Authors report that No significant changes in salivary flow nor salivary buffering during orthodontic treatment for both groups. Which is the opposite of the evidence of previous articles.

Conclusion

- Overall changes of oral microbiota are higher in patients with fixed appliances comparing to patients with removable appliances.
- A significant reduction was seen in salivary PH, total protein concentration, and calcium level in saliva of fixed orthodontic appliances group whereas glucose and amylase significantly increased.
- No significant change was observed in salivary flow rate nor salivary buffering power for clear aligner, while there were variations in the results of the fixed orthodontic appliances group in previous studies.

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Conflict of interest: None

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