Clinical Evidence for Treatment of Class II Periodontal Furcation Defects. Systematic Review and Meta-analysis

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ABSTRACT

Background: This systematic review evaluated the most effective therapeutic approach to treat periodontal furcation defects with a minimum follow-up of 12 months. The primary outcome was clinical attachment level (CAL). Secondary outcomes were probing pocket depth, gingival margin level, gingival index and plaque index.

Methods: A comprehensive search of studies published up to December 2019 and listed in PubMed/MEDLINE, Scopus, and Cochrane Library databases was performed in accordance with the Preferred Reporting Items for Systematic Reviews (PRISMA) statement. Two reviewers independently searched eligible studies, made a final article selection, and extracted the data of the selected studies to evaluate qualitatively and quantitatively (meta-analysis).

Results: Overall, 19 studies were selected for the analysis. Six hundred and eighteen patients (mean age, 45.3) were treated. More commonly used treatment was polytetrafluoroethylene barrier (ePTFE), followed by enamel matrix derivative (EMD) and open-flap debridement (OFD). Only one study evaluated maxillary arch and remaining evaluated mandibular arch. All treatments provided CAL gain, but meta-analysis did not show significant difference among more commonly used treatments and controls (P=0.91; P=0.47; P=0.08, respectively).

Conclusion: There is no difference on effectiveness of main therapeutic approaches evaluated for treatment of Class II periodontal furcation defects.

Keywords: Periodontics; guided tissue regeneration; furcation defects; systematic review; review

Introduction

The furcation area represents a challenge for dental treatment due to its specific anatomy that has important therapeutic and pathologic implications (Sanz *et al.*, 2015). Periodontal disease can invade furcation areas resulting in irreversible marginal alveolar bone resorption and attachment loss in the interradicular area. This can result in destruction of the periodontium progressing apically and the furcation of multirooted teeth becomes exposed (Siddiqui *et al.*, 2016).

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Predictable closure of furcation defects with different types of treatments aimed at regeneration of bone, cementum and periodontal ligament has been a major objective of periodontal regenerative therapy (Lohi *et al.*, 2017). Various types of treatments have been used for areas with furcation exposure, including non-surgical scaling and root planning with manual and power-driven scalers, open flap debridement (OFD), resective surgery, and regenerative approaches (Cattabriga *et al.*, 2000; Queiroz *et al.*, 2016).

Many different types of regenerative treatments that have been used effectively for the treatment of furcation defects, such as guided tissue regeneration (GTR) using polytetrafluoroethylene barrier (ePTFE) (Leite *et al.*, 2013; Eickholz *et al.*, 2006); enamel matrix

derivatives (EMD) (Queiroz *et al*., 2016; Jaiswal and Deo, 2013; Casarin *et al*., 2010); β-tricalcium phosphate (Siddiqui *et al*., 2016); hydroxyapatite (Queiroz *et al*., 2016); bioresorbable collagen membranes (Deo *et al*., 2014). However, complete closure of furcation defects is still considered unpredictable, and it is still unclear if definitive clinical regenerative procedures compare favorably with conservative treatments (Troiano *et al*., 2016; Sanz *et al*., 2015).

The ultimate goal of these treatments is furcation closure via periodontal regeneration that encourages new formation of root cementum, periodontal ligament (PDL), and alveolar bone encompassing the entire furcation area (Laugisch *et al*., 2019). Evidence from randomized clinical trials indicates that currently available treatments improve clinical parameters (Ipshita *et al*., 2018; Queiroz *et al*., 2016; Jaiswal *et al*., 2013; Pradeep *et al*., 2013; Casarin *et al*., 2010; Santana *et al*., 2009; Eickholz *et al*., 2006; Hoffmann *et al*., 2006; Jepsen *et al*., 2004; Meyle *et al*., 2004; Cury *et al*., 2003; Machtei *et al*., 2003; Couri *et al*., 2002; Eickholz and Hausmann, 2002; Maragos *et al*., 2002; Pruthi *et al*., 2002; Eickholz *et al*., 2001; Eickholz *et al*., 2000). However, human histologic evidence of periodontal regeneration is limited to case reports involving only some biomaterials (Laugisch *et al*., 2019).

Even though there are several types of regenerative treatments available the greatest challenge for periodontal regeneration is to reestablish of a good tooth contour to facilitate self-performed microbial plaque control (Asimuddin *et al*., 2017). There is always a risk that the treatment will not be effective, due to systemic or patient-related factors (Asimuddin *et al*., 2017). Alternative treatments in these cases can include tooth extraction and placement of dental implants t.

A Consensus Report from the American Academy of Periodontology (AAP) Regeneration Workshop concluded that regenerative therapy is a viable option to achieve predictable outcomes for the treatment of furcation defects in certain clinical scenarios (Reddy *et al*., 2015). Furthermore, a recent systematic review concluded that future studies should have long-term follow-up and place more emphasis on patient-reported outcomes (Avila-Ortiz *et al*., 2015). This new information will provide critical information to better understand the influence that periodontal regenerative therapies could have on the quality of life of patients, which will be of great value to develop cost-effective and predictable clinical protocols (Ávila-Ortiz *et al*., 2015).

This systematic review evaluated most effective therapeutic approach to treat periodontal furcation defects with minimum follow-up of 12 months. The primary outcome was clinical attachment level (CAL). Secondary outcomes were probing pocket depth, gingival margin level, gingival index and plaque index.

Materials and Methods

This systematic review is based on the Preferred Reporting Items for Systematic Reviews (PRISMA) checklist structure and in accordance with a model proposed in previously published reports. The study was registered on the international prospective register of systematic reviews (PROSPERO CRD42018083767).

Two independent investigators (H.F.F.O. and C.S.S.) conducted an electronic search of PubMed/MEDLINE, Scopus, and Cochrane Library for articles published up to December 2019, using the following search terms: "furcation defects". Other researcher (C.A.A.L) manually searched for articles published in the following journals: Journal of Clinical Periodontology, Journal of Periodontology (1970), Journal of Periodontal Research, The International Journal of Periodontics & Restorative Dentistry and Periodontology 2000. He also conducted a search of the non-peer reviewed reports and currently unpublished registered trials. All differences in choices between the investigators were analyzed by a third investigator (F.R.V.), and consensus was reached through discussion.

Studies were independently selected and classified as included or excluded by the two investigators (C.S.S. and H.F.F.O.), based on the title and abstract of the articles. Eligible studies included randomized controlled trials (RCTs), studies that compared different furcation defects treatments to promote CAL gain, studies that had at least 10 participants, and studies published in English. Exclusion criteria were non randomized retrospective or prospective studies, *in vitro* or animal studies, computer simulations, case reports, studies that evaluated only one type of treatment without a comparison group, published report reviews and studies with less than 12 months follow-up. A specific question was formulated based on the population, intervention, control, and outcome (PICO) criteria. The focused question was: "What is the most effective treatment to treat Class II periodontal furcation defects?" Based on these criteria, the population was the participants who were treated patients treated with biomaterials to promote periodontal regeneration in Class II furcation defects, the intervention was regenerative therapy, and the comparison was control groups. The primary outcome was clinical attachment level, and secondary outcomes were gingival margin level, probing pocket depth, gingival index and plaque index.

Data extracted from the articles were sorted as quantitative or qualitative by one of the researchers (C.A.A.L.) and then checked by two others (F.R.V. and V.E.S.B.). Any disagreements were resolved through discussion until consensus was reached. The quantitative and qualitative data were tabulated for ease of comparison (Tables 1 and 2).

Table 1. Qualitative characteristics of the studies related to patients

Author	*Study Design*	*Gender*	*Systemic conditions*	*Sample size*	*Mean age (years)*	*Study site*
Ipshita *et al.* 2018	Groups evaluated isolated	F/M	Health	90	-	Government Dental College and Research Institute (GDCRI), Bangalore, Karnataka, India
Queiroz *et al*. 2016	Groups evaluated isolated	F/M	Health	41	35	UNIMCAP, Piracicaba Dental School
Pradeep *et al.* 2013	Groups evaluated isolated	F/M	Health	69	40	Department of Periodontics, Government Dental College and Research Institute, Bangalore, India
Leite *et al*. 2013	Split mouth	F/M	Health	20	46.01	Clinic of Ribeirão Preto School of Dentistry, University of São Paulo, Brazil
Jaiswal *et al.* 2013	Groups evaluated isolated	F/M	Health	30	36.6	Department of Periodontics, S.P. Dental College, Wardha, India
Casarin *et al*. 2010	Split mouth	F/M	Health	12	35	UNIMCAP, Piracicaba Dental School
Santana *et al*. 2009	Groups evaluated isolated	F/M	Health	60	48.3	Periodontology clinic of Federal Fluminense University
Hoffmann *et al.* 2006	Split mouth	F/M	Smoking, age, gender, hypertension, oral hygiene were not excluded	51	54	Department of Conservative Dentistry University of Technology, Dresden, Germany
Eickholz *et al.* 2006	Split mouth	F/M	Health and smokers were not excluded	9	46.9	Department of Conservative Dentistry, University Hospital Heidelberg
Jepsen *et al*. 2004	Split mouth	F/M	Health and smokers were not excluded	45	54	Department of Periodontology, University of Bonn, Bonn, Germany
Meyle *et al.* 2004	Split mouth	F/M	Health and smokers were not excluded	48	54	Department of Periodontology, University of Giessen, Giessen, Germany
Cury *et al*. 2003	Split mouth	F/M	Health	9	45	UNIMCAP, Piracicaba Dental School
Machtei *et al.* 2003	Groups evaluated isolated	F/M	Smoker pacients with good health	38	47.1	Periodontal Unit, Rambam Medical Center, Haifa, Israel
Couri *et al*. 2002	Split mouth	F/M	Health	13	53.2	University of Nebraska Medical Center College of Dentistry
Eickholz *et al.* 2002	Groups evaluated isolated	F	Not reported	19	47.8	Department of Operative Dentistry and Periodontology, University of Heidelberg
Maragos *et al.* 2002	Groups evaluated isolated	F/M	Health	17	55.8	Case Western Reserve University, School of Dentistry
Pththi *et al.* 2002	Split mouth	F/M	Health	17	56.5	University of Manitoba, Winnipeg
Eickolz *et al*. 2001	Split mouth	F/M	Smoker pacients with good health	9	46.9	Department of Operative Dentistry and Periodontology, University of Heidelberg
Eickholz *et al.* 2000	Split mouth	F/M	Health	21	43.5	Department of Operative Dentistry and Periodontology, University of Heidelberg

Table 2. Qualitative characteristics of the studies related to the treatment, methods and results

Author	*Area*	*Comparative groups*	*Primary Outcome (Clinical attachment level)*	*Secondary Outcomes (probing pocket depth, gingival margin level, gingival index and plaque index)*	*Follow up (months)*	*Results (positive or negative)*
Ipshita *et al*. 2018	Mandibular Arch	Group 1: scaling and root planing (SRP), followed by placebo gel local drug delivery (LDD). Group 2: (SRP) followed by 1% Alendronate gel LDD. Group 3: with SRP followed by Aloe Vera gel LDD	CAL	PPD, PI	6 and 12	Positive
Queiroz *et al*. 2016	Mandibular arch	Enamel matrix derivative and β-tricalcium phosphate/ hydroxyapatite (test) or β tricalcium phosphate/ hydroxyapatite (control)	CAL	PPD	12	Positive
Pradeep *et al*. 2013	Mandibular arch	Scaling and root planning (control) combined or not to 1% alendronate gel (test)	CAL	GI, PI, PPD	12	Positive
Leite *et al*. 2013	Mandibular arch	Removal of ePTFE membrane with 2 (test) or 4 weeks postoperative (control)	CAL	GI, PI, PPD, GML	12	No difference
Jaiswal *et al*. 2013	Mandibular arch	Enamel matrix derivative proteins in combination with demineralized freeze-dried bone allograft and bioresorbable membrane (test) or demineralized freeze-dried bone allograft and bioresorbable membrane (control)	CAL	PPD, GML	12	Positive
Casarin *et al*. 2010	Maxillar arch	Open flap debridement and EDTA plus enamel matrix derivative proteins (test) or open flap debridement and EDTA (control)	CAL	PPD, GML	24	Positive
Santana *et al*. 2009	Mandibular arch	Bioabsorbable hydroxyapatite and tetracycline combined with guided tissue regeneration barrier and a coronally advanced flap (test) or open flap debridement (control)	CAL	GI, PI, GML, PPD	12	Positive

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Hoffmann *et al.* 2006	Mandibular arch	Enamel matrix protein derivative (test) and guided tissue regeneration (control)	CAL	PPD	14	Positive
Eickholz *et al.* 2006	Mandibular arch	Non-resorbable expanded polytetrafluoroethylene barrier (test) or bioabsorbable polyglactin 910 barrier (control)	CAL	GI, PI, PPD	120	Positive
Jepsen *et al.* 2004	Mandibular arch	Enamel matrix derivative (test) or membrane (control)	CAL	GML, PPD, GI	14	Positive
Meyle *et al.* 2004	Mandibular arch	Enamel matrix derivative (test) or guided tissue regeneration with bioabsorbable membrane (control)	CAL	GI, PI, GML, PPD	14	Positive
Cury *et al.* 2003	Mandibular arch	Guided tissue regeneration (test) or O=open flap debridement (control)	CAL	GI, PI, GML, PPD	24	Positive
Machtei *et al.* 2003	Mandibular arch	Membrane with 25% metronidazole gel (test) or membrane only or open flap debridement (control)	CAL	GI, PI, PPD	12	Positive
Couri *et al.* 2002	Mandibular arch	Barrier of medical grade calcium sulfate hemihydrate (test) or demineralized freeze-dried bone allograft and polytetrafluoroethylene barrier (control)	CAL	PPD, GML	12	Positive
Eickholz *et al.* 2002	Mandibular arch	Polytetrafluoroethylene membrane (test) and polyglactin 910 barrier (control)	CAL	GI, PI, PPD	60	Positive
Maragos *et al.* 2002	Mandibular arch	Calcium sulfate plus doxycycline (test) and barrier of calcium sulfate (control)	CAL	GI, PI, PPD, GML	12	Positive
Ptthi *et al.* 2002	Mandibular arch	Bioabsorbable collagen membrane (test) or polytetrafluoroethylene membrane (control)	CAL	PPD, GML	12	Positive
Eickolz *et al.* 2001	Mandibular arch	Polyglactin 910 barrier (test) or polytetrafluoroethylene barrier (control)	CAL	GI, PI, PPD	60	Positive
Eickholz *et al.* 2000	Mandibular arch	Polidyoxanon barrier (test) or bioabsorbibles polylactide acetyltributyl citrate barrier (control)	CAL	GI, PI, PPD	12	Positive

Two investigators (C.A.A.L. and R.S.C.) assessed the methodological quality of the studies included in the review according to the Cochrane collaboration criteria for judging risk of bias (Figure 1).

The meta-analysis was based on continuous outcome (mean ± standard deviation) evaluated by mean difference (MD) in millimeters of clinical attachment level (CAL), through the inverse variance (IV) method. The MD values were considered significant when $p<0.05$, both with corresponding 95% confidence intervals (CI). Subgroup analysis were performed between biomaterials versus ePTFE, EMD and OFD. The I2 statistic was used to express the percentage of total variation across studies due to heterogeneity (25% corresponding to low heterogeneity, 50% indicating moderate heterogeneity, and 75% indicating high heterogeneity). The software Reviewer Manager 5 (Cochrane Group) was used for the meta-analysis.

The kappa coefficient value was calculated to determine inter-reader agreement in the study selection process for publications in the PubMed/MEDLINE, Scopus, and Cochrane Library databases.

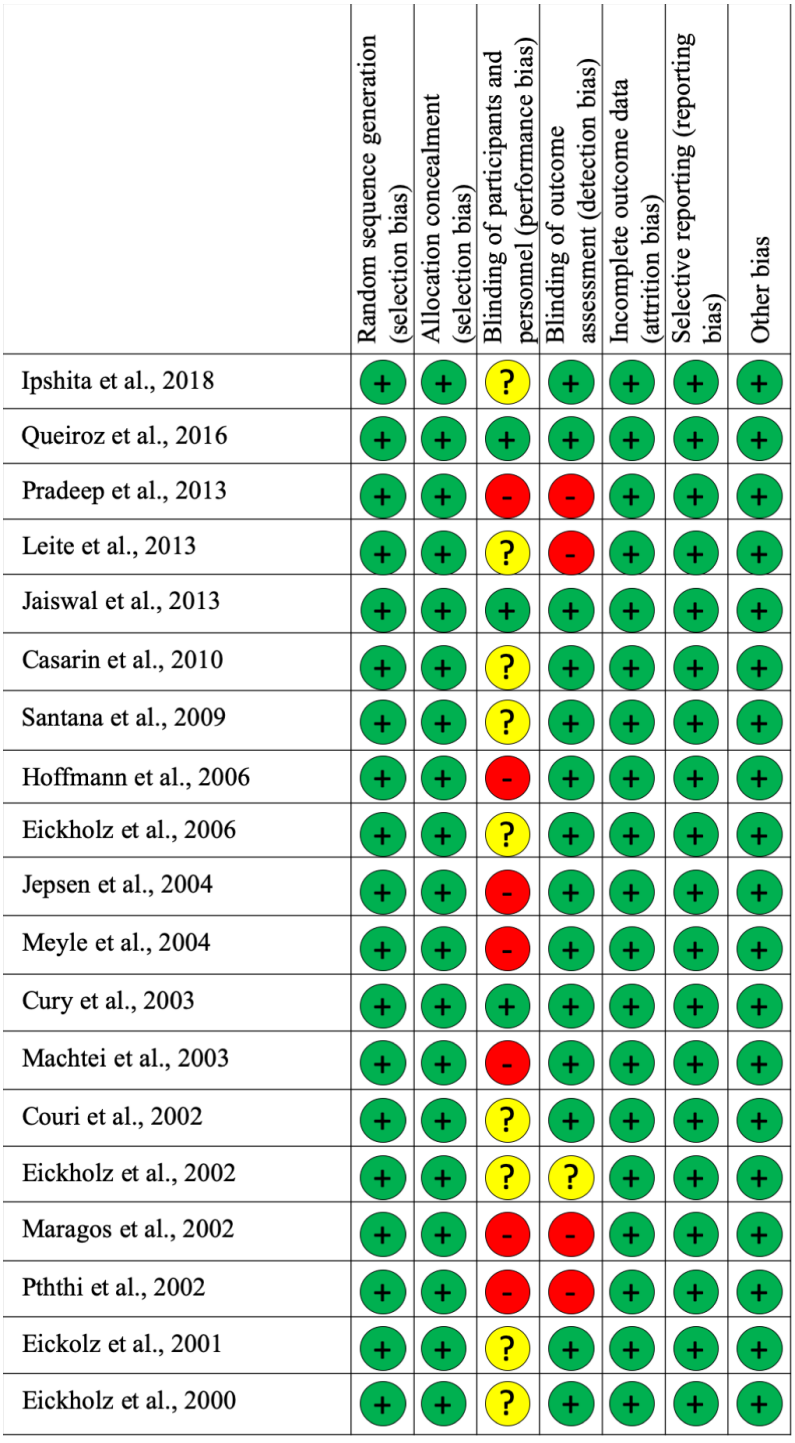

Figure 1. Cochrane risk of bias evaluation of the included studies.

Results

Literature search

The database search retrieved 454 references, including PubMed/Medline, Scopus, and the Cochrane Library. After applying the inclusion/exclusion criteria to the titles and abstracts of the selected comparative studies, 70 studies remained. Four articles had restricted access in journals and were excluded. Reading these study texts resulted in exclusion of other 48 studies because they were involved other types of intrabony defects (non-Class II), another tooth (non-molar), applied non-surgical treatment of furcation defects or the follow up was less than 1 year. A manual search for articles identified one more study. Overall, 19 studies were selected for the analysis (Ipshita *et al*., 2018; Queiroz *et al*., 2016; Leite *et al*., 2013; Jaiswal *et al*., 2013; Pradeep *et al*., 2013; Casarin *et al*., 2010; Santana *et al*., 2009; Eickholz *et al*., 2006; Hoffmann *et al*., 2006; Jepsen *et al*., 2004; Meyle *et al*., 2004; Cury *et al*., 2003; Machtei *et al*., 2003; Couri *et al*., 2002; Eickholz and Hausmann, 2002; Maragos *et al*., 2002; Pruthi *et al*., 2002; Eickholz *et al*., 2001; Eickholz *et al*., 2000).

The kappa inter-investigator agreement for articles that were selected (kappa value=0.72) showed an acceptable level of agreement (Landis and Koch, 1977).

Characteristics of the included studies related to patients

A total of 618 patients were treated for furcation defects, and they had a mean age of 45.3 years. All included studies were conducted at universities. One study included only female patients (Eickholz *et al*., 2002), and other studies included patients of both sexes. Twelve studies applied the "split mouth" model as an experimental design (Leite *et al*., 2013; Casarin *et al*., 2010; Eickholz *et al*., 2006; Hoffmann *et al*., 2006; Jepsen *et al*., 2004; Meyle *et al*., 2004; Cury *et al*., 2003; Couri *et al*., 2002; Pruthi *et al*., 2002; Eickholz *et al*., 2001; Eickholz *et al*., 2000) and in the others, researchers evaluated experimental groups in different subjects. Most of the studies indicated that they enrolled healthy patients with no systemic conditions, and six studies included smoking patients with no systemic conditions (Eickholz *et al*., 2006; Hoffmann *et al*., 2006; Jepsen *et al*., 2004; Meyle *et al*., 2004; Machtei *et al*., 2003; Eickholz *et al*., 2001). Table 1 summarises this information.

Characteristics of the included studies related to treatment, methods, and results

The most commonly used treatment was polytetrafluoroethylene barrier membranes which were used in seven studies (Leite *et al*., 2013; Eickholz *et al*., 2006; Couri *et al*., 2002; Pruthi *et al*., 2002; Eickholz *et al*., 2001), followed by enamel matrix derivative (Queiroz *et al*., 2016; Jaiswal *et al*., 2013; Casarin *et al*., 2010). Other types of treatments described included bioresorbable collagen membrane, alendronate gel, open-flap debridement, others absorbable synthetic materials used has barrier for GTR or phytotherapy.

Follow-up times varied from 3–60 months. Only one study evaluated the maxillary teeth (Casarin *et al*., 2010) and the remaining studies evaluated teeth in the mandibular arch. The experimental model evaluated was Class II furcation defects. All selected studies evaluated clinical attachment level that is the subject (primary outcome) of the present systematic review (Table 2). Of these, only one study did not show improvement directly related to periodontal regeneration (primary outcomes) in the groups treated with polytetrafluoroethylene barrier (ePTFE) (Leite *et al*., 2013). All studies evaluated the secondary outcomes, but the parameters were different among studies.

Meta-analysis

Four studies (Eickholz *et al*., 2006; Couri *et al*., 2002; Pruthi *et al*., 2002; Eickholz *et al*., 2001) evaluated the influence of different biomaterials versus ePTFE. The results found no difference between biomaterials compared to ePTFE (P = 0.91; MD: -0.04; 95% CI: -0.69 to 0.62; heterogeneity: I2 = 22%).

Three studies compared different biomaterials versus EMD (Queiroz *et al*., 2016; Jaiswal *et al*., 2013; Casarin *et al*., 2010) and also found no difference between biomaterials versus EMD (P = 0.47; MD: -0.37; 95% CI: -1.35 to 0.62; heterogeneity: I2 = 80%).

In addition, two studies compared different biomaterials and OFD (Casarin *et al*., 2010; Santana *et al*., 2009). The authors showed no significant difference between treatments (P = 0.08; MD: 1.56; 95% CI: -0.20 to 3.32; heterogeneity: I2 = 92%).

Table 3 shows the mean differences ± standard deviation of CAL for control and test groups per study included in the meta-analysis. Meta-analysis results are presented in Figure 2.

Discussion

Periodontal disease is a very common condition with the main clinical features being bone loss and clinical attachment level reduction. After treatment, residual periodontal pockets of >5 mm are associated with increased risk for disease progression (Sculean *et al*., 2015). Ideal periodontal treatment includes elimination of infection and reduction of probing pocket depths. Several periodontal surgical techniques to induce periodontal regeneration have been evaluated.

This systematic review evaluated the most effective therapeutic approach to treat periodontal furcation defects. Molar teeth with furcation involvement are the

Table 3 - Mean difference (MD) ± standard deviation (SD) of vertical clinical attachment level (CAL) for control and test groups per study included in the meta-analysis

		Groups	*Follow up*	*Vertical CAL (mm)*	
				Control MD ± SD	*Test* MD ± SD
ePFT x Biomaterials	Eickholz *et al.*, 2006	Bioabsorbable polyglactin 910 barrier (control) / Non-resorbable expanded polytetrafluoroethylene barrier (test)	12 months	1.5 ± 1.2	1.0 ± 1.6
	Couri *et al.*, 2002	Demineralized freeze-dried bone allograft and polytetrafluoroethylene barrier (control) / Barrier of medical grade calcium sulfate hemihydrate (test)	12 months	1.0 ± 1.08	0.38 ± 1.12
	Pthithi *et al.*, 2002	Bioabsorbable collagen membrane (test) / Polytetrafluoroethylene membrane (control)	12 months	0.47 ± 1.81	1.00 ± 1.22
	Eickholz *et al.*, 2001	Polytetrafluoroethylene barrier (control) / Polyglactin 910 barrier (test)	60 months	0.7 ± 1.0	0.2 ± 2.7
EMD x Biomaterials	Queiroz *et al.*, 2016	β tricalcium phosphate/hydroxyapatite (control) / Enamel matrix derivative and β-tricalcium phosphate/ hydroxyapatite (test)	12 months	2.64 ± 0.93	2.93 ± 0.83
	Jaiswal *et al.*, 2013	Demineralized freeze-dried bone allograft and bioresorbable membrane (control) / Enamel matrix derivative proteins in combination with demineralized freeze-dried bone allograft and bioresorbable membrane (test)	12 months	0.85 ± 0.31	2.12 ± 1.07
	Casarin *et al.*, 2010	Open flap debridement and EDTA (control) / Open flap debridement and EDTA plus enamel matrix derivative proteins (test)	12 months	0.2 ± 1.0	0.8 ± 1.4
Open flap debridement x Biomaterials	Casarin *et al.*, 2010	Open flap debridement and EDTA (control) / Open flap debridement and EDTA plus enamel matrix derivative proteins (test)	12 months	0.2 ± 1.0	0.8 ± 1.4
	Santana *et al.*, 2009	Open flap debridement (control) / Bioabsorbable hydroxyapatite and tetracycline combined with guided tissue regeneration barrier and a coronally advanced flap (test)	12 months	0.65 ± 0.6	3.05 ± 0.6

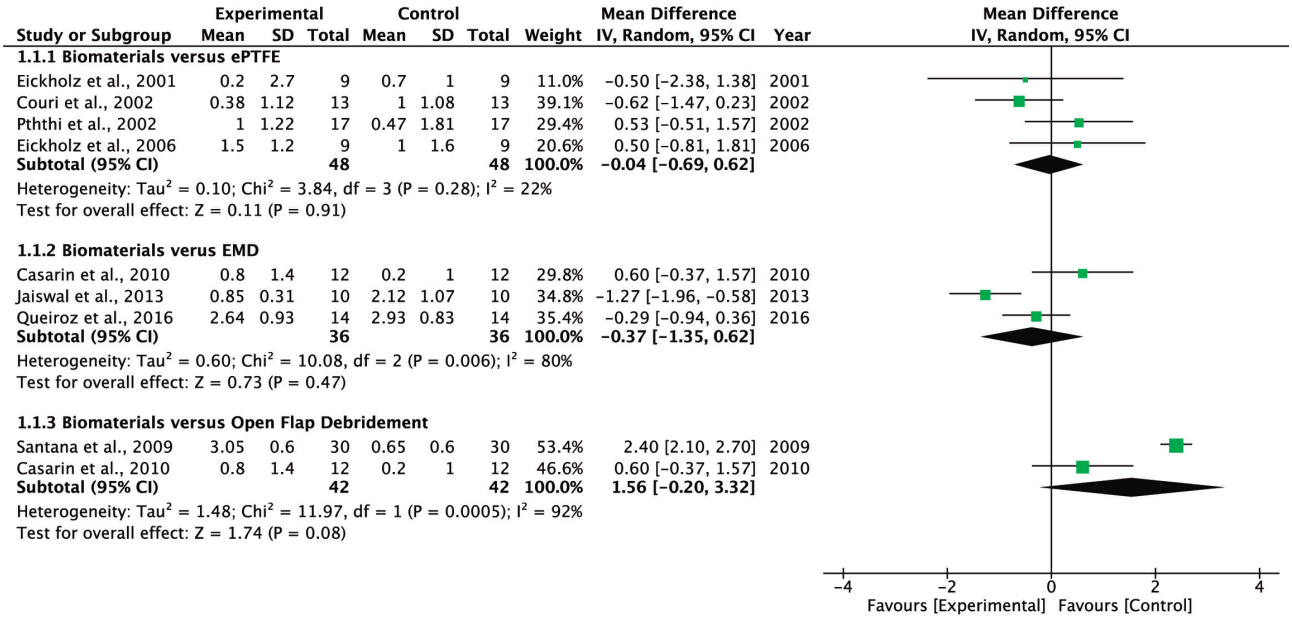

Figure 1. Meta-analysis results.

most common teeth to be lost (Chace and Low, 1993; Ramfjord *et al*., 1987; McFall, 1982; Hirschfeld and Wasserman, 1978). Tsao *et al.* (2006) identified factors that can affect the outcome of furcation therapy as shallow initial probing depth (PD), poor oral hygiene, gingivitis, *Actinobacillus actinomycetemcomitans* infection, and absence of connective tissue cells on retrieved membranes.

The methodological quality of the studies included in this review was assured not only according to results of the Cochrane collaboration criteria for judging risk of bias but also by the fact that the included studies evaluated (primary or secondary outcomes) the above mentioned factors contributing to successful treatment of the Class II furcation defects. All included studies evaluated CAL and, in a general way, assessed probing pocket depth, gingival margin level, gingival index and plaque index.

A recent systematic review evaluated available histologic evidence for periodontal regeneration for treated Class II and III furcations in animals and humans (Laugisch *et al*., 2019). Fifty-seven studies reported animal outcomes and six studies reported human outcomes from cases series or case report. Reports results in humans showed important but weak scientific evidence of the results based on case series and case report (Laugisch *et al*.,2019).

Periodontal regeneration can be assessed by different methods, i.e., histology, probing, radiographs, and direct measurement of bone (Caton, 1997). The primary outcome of this review was CAL that is considered a standard clinical method to evaluate regenerative technologies (Bansal and Singh, 2016; Reddy and Jeffcoat, 1999). Qualitative analysis of the results showed that all treatments evaluated resulted in beneficial results on periodontal healing. In this context, other factors related to the treatments can be consider by clinicians such as price (which may vary around the world) and need of a second surgical procedure for non-resorbable barriers removal.

Regarding the sites where the treatments were performed, only one study evaluated maxillary teeth (Casarin *et al*., 2010) while the other 18 remaining studies evaluated mandibular teeth. We included both maxillary and mandibular teeth in this study because the consensus report from the AAP about regeneration of furcation defects states that both maxillary and mandibular Class II furcation defects show histologic evidence f periodontal regeneration after the application of various regenerative therapies (Reddy *et al*., 2015).

Is important to consider that the studies included in this review evaluated different surgical techniques and biomaterials either alone or in different combinations. Previous systematic reviews of pre-clinical (Ivanovic *et al*., 2014) or clinical studies (Sculean *et al*., 2015) have observed that there is substantial heterogeneity with respect to the materials utilized (i.e. resorbable and nonresorbable membranes, types of biomaterials and various combinations thereof). Furthermore, as observed in this review, there is wide variety among the studies due to differences in study design (split mouth or groups evaluated separately). It is important to note that the study by Sculean *et al.* (2015) evaluated biomaterials for promoting periodontal regeneration in human intrabony defects while the present study evaluated only Class II furcation defects.

Because of the heterogeneity of the included studies in the present review, the meta-analysis necessitated the authors to consider more commonly used treatments as the controls to other biomaterials. Data were divided in subgroups comparing ePTFE (Eickholz *et al.*, 2006; Couri *et al.*, 2002; Pruthi *et al*, 2002; Eickholz *et al.*, 2001), EMD (Queiroz *et al.*, 2016; Jaiswal *et al.*, 2013; Casarin *et al.*, 2010) and OFD (Casarin *et al.*, 2010; Santana *et al.*, 2009) to other types of treatment (connective tissue graft, bioresorbable collagen membrane, alendronate gel, and others absorbable synthetic materials used has barrier for guided tissue regeneration).

In this review, inclusion criteria included a minimal follow up period of 12 months. The aim of this was to consider treatment that had good long-term follow-up (Avila-Ortiz *et al.*,2015). In a study evaluating clinical, radiographic, histologic and microbiologic outcomes of periodontal regeneration in Class I, II or III furcation it was concluded that future studies should have long term follow ups, ideally >5 years after baseline (Avila-Ortiz *et al.*,2015). In the present review, except for the study by Casarin *et al.* (2010) which presented 24 month follow up, Eickholz *et al.* (2002; 2001) which presented 60 and 120 (Eickholz *et al.* 2006) months follow up, most studies evaluated clinical results for up to 12 months. Therefore, the present study reinforced that further studies should have longer follow-up periods to ensure that periodontal regenerative therapy is stable and effective.

Today, dental implants must be considered as an alternative treatment in cases where periodontally compromised teeth have a poor or uncertain prognosis. Nonetheless, implants suffer from complicatios as well including peri-implantitis and also require careful peri-implant maintenance therapy (Monje *et al.*, 2016);. The high reported implant survival rates of 92.8-97.1% over a follow up period of 10 years indicate that the implants are a good treatment option (Srinivasan *et al.*, 2014; Albrektsson *et al.*, 2012).

In conclusion, from this review it can be concluded that there is no difference ineffectiveness of the therapeutic approaches evaluated for treatment of Class II periodontal furcation defects. The professional choice of an effective and predictable treatment to promote periodontal regeneration depends on the availability of regenerative agents, need for a second surgical procedure for non-resorbable barriers removal and cost of these treatments.

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