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Use of platelet-rich fibrin versus connective tissue graft in treatment of gingival recessions: Literature review

Aušra Balčiūnaitė[1], Henrikas Rusilas[2], Juozas Žilinskas[3]

SUMMARY

Aim. To compare and evaluate the effects of two different approaches on treating gingival recessions: coronally advanced flap (CAF) with platelet rich-fibrin (PRF) membrane and coronally advanced flap (CAF) with connective tissue graft (CTG).

Material and methods. A systematic literature review was performed of randomized control trials in English identified in MEDLINE (PubMed), Cochrane Central Register of Controlled Trials (Cochrane Library), Springer Link, Science Direct and Google Scholar databases, published between 2015 and 2020. Studies had to be performed in vivo with follow-up periods of ≥6 months.

Results. 153 publications were found, out of which 8 were identified as relevant to the theme. Six of these studies evaluated periodontal parameters such as probing depth (PD), clinical attachment level (CAL), recession depth (RD), keratinized tissue width (KTW) and gingival thickness (GT). In 3 studies discomfort and aesthetic scores were analyzed as subjective parameters. 1 study histologically evaluated different techniques of gingival recession treatment.

Conclusion. Both techniques are effective in the treatment of Miller's class I and II gingival recessions. Although the CTG technique may provide better results in KTW and GT, PRF avoids a donor site, which means a major decrease in postoperative discomfort.

Key words: gingival recession, platelet-rich fibrin, connective tissue graft, systematic review.

INTRODUCTION

Gingival recession (GR) is the apical migration of the marginal soft tissue beyond the cementoenamel junction (CEJ) (1). There is a variety of etiological and predisposing factors related to GR, including trauma from brushing, malposition of teeth, excessive frenulum and muscle attachments (2). Apart from compromised esthetics, GR also results in a variety of other problems such as root hypersensitivity, a higher incidence of root caries and diminished plaque control, thus necessitating treatment (3).

The goal of periodontal plastic surgery is not only full and predictable coverage of exposed root surface but also to develop less invasive techniques that favor rapid healing, less postoperative discomfort and bigger patient satisfaction (4, 5). In the last 30 years, various surgical procedures have been used to treat gingival recession, including laterally positioned flap (LPF), free gingival graft (FGG), coronally advanced flap (CAF), connective tissue graft (CTG), and guided tissue regeneration with membranes, acellular dermal matrix, platelet-rich plasma (PRP), and platelet-rich fibrin (PRF) in combination with CAF (6-8).

A CTG combined with CAF is considered the gold standard for Miller I and II recession defects (9-10). The advantage of this technique is the enhancement of keratinized tissue width, which is determined by CTG surface epithelium characteristics (9). Moreover, there are many disadvantages, such as postoperative pain or bleeding, second surgical site is required, which prompted researchers to investigate alternative materials and methods to CTG (11).

A recent innovation is the use of second-generation platelet concentrate which is an autologous PRF for tissue regeneration in dental plastic surgery (12, 13). PRF includes a leukocyte aggregate, high-density fibrin network, vascular endothelial growth factor (VEGF), insulin-like growth factor, platelet-derived growth factor (PDGF), transforming growth factor

[1]*Faculty of Odontology, Medical Academy, Lithuanian University of Health Sciences, Kaunas Lithuania*
[2]*Department of Oral and Maxillofacial surgery, Lithuanian University of Health Sciences, Kaunas, Lithuania*
[3]*Department of Dental and Maxillofacial Orthopedics, Lithuanian University of Health Sciences, Kaunas, Lithuania*

Address correspondence to Aušra Balčiūnaitė, Faculty of Odontology, Medical Academy, Lithuanian University of Health Sciences, Taikos pr. 65-23, 50436 Kaunas, Lithuania.
E-mail: abalciunaite96@gmail.com

(TGF), epidermal growth factor, and basic fibroblast growth factor (14). Recent studies have demonstrated that PRF has a significant slow, sustainable release of key growth factors for at least 1 week (15) and up to 28 days, which means that PRF could stimulate its environment for a significant time during wound healing (16). Because of these characteristics, PRF accelerates hemostasis, wound healing and has a supportive effect on the immune system, cell migration and proliferation (14).

The purpose of this review is to compare and evaluate the effects of two different approaches on treating gingival recessions: CAF with PRF membrane and CAF with CTG.

MATERIALS AND METHODS

A systematic literature search was performed according to PRISMA guidelines in search of clinical trials published between 2015 and 2020. Electronic and manual literature searches were conducted independently by all authors in several databases, including MEDLINE (PubMed), Cochrane Central Register of Controlled Trials (Cochrane Library), Springer Link, Science Direct and Google Scholar. Databases were searched using different combinations of the following key words: gingival recession, platelet rich fibrin, clinical trial. The titles and abstracts first were analyzed, followed by the selection of complete articles for careful reviewing and analysis according to the eligibility criteria.

According to PRISMA guidelines a specific question was constructed according to the PICO (participants, intervention, comparison, outcomes) principle.

- P (participants) – it was essential for participants to have at least two Miller Class I and / or Miller Class II gingival recession;
- I (intervention) – gingival recession treatment with CAF and PRF membrane;
- C (comparison) – control intervention was gingival recession treatment with CAF and CTG;
- O (outcome) – PD, CAL, RD, KTW, GT changes after GR treatment.

Selected studies were published in English and no older than 5 years, describing in vivo studies evaluating the comparative effects of PRF with CAF and CTG with CAF, follow-up period ≥6 months. All case reports or case series, animal and in vitro studies were excluded. Publications that met inclusion criteria were drawn to the qualitative analysis study pool. From this, publications that met qualitative assessment criteria were selected into this literature review.

The quality of selected randomized clinical trials (RCT) was assessed using the Cochrane Risk of Bias Tool (Table 1).

RESULTS

Search outcomes

In total, the initial search strategies generated 153 articles. After the first evaluation duplicates were identified and excluded. After screening 14 potential

Table 1. Quality assessment using Cochrane Risk of Bias Tool of included RCT in systematic review

Study	Selection bias		Performance bias	Detection bias	Attrition bias	Reporting bias	Overall judgement
	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	
Eren G. *et al.* (2016) (4)	?	+	?	?	+	+	?
Uraz A. *et al.* (2015) (5)	+	+	?	?	+	+	?
Mufti S. *et al.* (2017) (17)	+	+	+	+	+	+	+
Oncu E. (2017) (18)	+	+	?	?	+	+	?
Culhaoglu R. *et al.* (2018) (19)	+	+	+	+	+	+	+
Chenchev I. *et al.* (2016) (20)	+	+	+	+	+	+	+
Al-Quershi M. *et al.* (2019) (21)	+	+	?	?	+	+	?
Kumar A. *et al.*. (2017) (22)	+	+	+	+	+	+	+

+ – low risk; ? – unclear risk.

articles were selected for full article review and 6 were excluded because they lacked at least one of the required inclusion criteria. The article search and selection process is presented in Figure.

Table 2. Evaluated studies

Studies	Study design	Evaluation parameters	No. of participants	Age (years)	No. of treated recessions	Site of recession	Single (S) / Multiple (M) recession
Eren G. *et al.* (2016) (4)	RCT	Histological	14	18-45	28	Both jaws	M
Uraz A. *et al.* (2015) (5)	RCT (split-mouth)	Periodontal	15	23-48	106	Both jaws	M
Mufti S. *et al.* (2017) (17)	RCT	Periodontal, subjective	32	≥18	32	Both jaws	S
Oncu E. (2017) (18)	RCT (split-mouth)	Periodontal, subjective	20	20-60	60	Maxillary	M
Culhaoglu R. *et al.* (2018) (19)	RCT	Periodontal, subjective	22	21-52	63	Both jaws	M
Chenchev I. *et al.* (2016) (20)	RCT (split-mouth)	Periodontal, subjective	30	23-70	118	Both jaws	M
Al-Quershi M. *et al.* (2019) (21)*	RCT (split-mouth)	Periodontal	20	20-45	40	Both jaws	M
Kumar A. *et al.* (2017) (22)	RCT	Periodontal, subjective	36	≥18	45	Maxillary	S&M

Table 3. Periodontal parameters among PRF groups

Studies	Miller Class	Procedure	Periodontal parameters at baseline and after 6 months					Methods for PRF preparation	
			PD	CAL	RD	KTW	GT	Volume of blood drawn (ml)	Centrifugation parameters Speed (rpm)× Time (minutes)
Eren G. *et al.* (2016) (4)	I & II	CAF+PRF (split thickness flap)	-	-	-	-	-	10	2.700×12
Uraz A. *et al.* (2015) (5)	I & II	CAF+PRF (split-full thickness flap)	1.53±0.17 1.31±0.14 (p>0.05)	6.27±1.27 2.48±1.41 (p<0.05)	4.73±1.30 1.17±1.47 (p<0.05)	3.45±1.05 4.63±0.86 (p<0.05)	-	10	2.700×12
Mufti S. *et al.* (2017) (17)	I	CAF+PRF (split-full thickness flap)	-	4.06±1.18 2.81±0.83 (p=0.001)	2.19±0.98 1.12±0.81 (p=0.001)	4.06±1.61 4.44±2.25 (p=0.15)	1.02±0.20 1.21±0.25 (p=0.001)	10	3.000×10
Oncu E. (2017) (18)	I & II	CAF+PRF (split-full thickness flap)	1.47±0.51 1.17±0.38 (p=0.004)	5.37±1.07 2.07±1.17 (p<0.001)	3.93±0.91 0.90±1.03 (p<0.001)	2.70±0.70 3.80±0.93 (p<0.001)	0.69±0.21 0.99±0.20 (p<0.001)	9	2.700×12
Culhaoglu R. *et al.* (2018) (19)	I	CAF+2PRF (split thickness flap)	1.45±0.25 1.25±0.18 (p>0.05)	4.10±1.03 2.86±0.74 (p<0.05)	2.71±0.70 1.67±0.64 (p<0.05)	4.43±1.21 4.86±0.96 (p<0.05)	1.75±0.35 1.86±0.449 (p<0.05)	10×2	2.700×12
Culhaoglu R. *et al.* (2018) (19)	I	CAF+4PRF (split thickness flap)	1.37±0.30 1.21±0.24 (p>0.05)	3.86±0.69 1.93±0.69 (p<0.05)	2.48±0.60 0.81±0.56 (p<0.05)	3.95±1.02 4.14±1.24 (p>0.05)	1.60±0.34 1.78±0.42 (p<0.05)	10 x 4	2.700×12
Chenchev I. *et al.* (2016) (20)	I & II	CAF+PRF	-	-	-	-	-	10	1.500×8
Al-Quershi M. *et al.* (2019) (21)*	I & II	CAF+PRF	0.95±0.42 1.27±0.34 (p<0.05)	3.95±1.09 1.15±0.81 (p<0.05)	3.05±0.71 0.20±0.50 (p<0.05)	2.23±0.69 3.54±0.70 (p<0.05)	-	10	2.700×12
Kumar A. *et al.* (2017) (22)	I & II	CAF+PRF (split-full-spilt thickness flap)	1.87±0.74 1.53±0.64 (p=0.29)	3.73±0.70 2.00±1.00 (p=0.0001)	1.80±0.56 0.53±0.74 (p=0.0001)	3.53±1.18 4.67±1.21 (p=0.0001)	0.73±0.07 0.70±0.07 (p=0.005)	10	2.700×12

* – follow-up 12 months.

Study characteristics

8 randomized clinical trials (RCT) (4, 5, 17-22) were included in this systematic review, 4 of them were split-mouth studies (5, 18, 20, 21). 6 articles analyzed periodontal parameters (5, 17-22) in 3 of them subjective parameters were also evaluated (17-20, 22) and in 1 included study only histological parameters were analyzed (4). The number of participants in the studies ranged from 14 (4) to 36 (22) with their ages ranging from 18 (4, 17, 22) to 70 (20) years. 7 studies dealt with multiple gingival recessions (4, 5, 18-22) , 2 included single recessions (17, 22). Recessions were treated either in mandible and maxilla (4, 5, 17, 19-21) or only in maxilla (18, 22). A total of 492 recessions were treated (4, 5, 17-22). The follow-up period was ranging from 6 months (4, 5, 17-20, 22) to 12 months (21) (Tables 2-4).

Surgical procedures

All studies included CAF combined with PRF in the test group and CTG in the control group. CAF was performed by elevating a full thickness (21) , split thickness (4,19), split-full thickness (5, 17, 18) or split-full-split thickness flap (22), only Chenchev *et al.* (20) did not explain surgical protocol.

The PRF membrane production protocols varied. In most of the studies intravenous blood was collected in 10-mL glass-coated plastic tubes without anticoagulants and immediately centrifuged before the surgery (Table 3).

In all studies control groups palatal tissues were selected as the donor area (4, 5, 17-22). The thickness of the CTG ranged from 1 mm (17, 19) to 2 mm (17) (Table 4).

Periodontal parameters

Kumar *et al.* in their study did not find statistically significant difference in probing depth (PD) between baseline and 6 months after surgery in both groups (22), similar results were reported in Uraz *et al.* (5) and Culhaoglu *et al.* (19) studies. Oncu *et al.* also have not noticed statistically significant difference in PD in CTG group, however he reported statistically significant PD decrease in PRF group from 1.47±0.51 mm to 1.17±0.38 mm (P<0.05) (18). Al-Quershi *et al.*, however, reported statistically significant increase in PD in both, PRF and CTG groups from 0.95±0.42 mm to 1.27±0.34 mm and from 0.85±0.36 mm to 1.27±0.30 mm, respectively (21).

Table 4. Periodontal parameters among CTG groups

Studies	Miller Class	Procedure	Periodontal parameters at baseline and after 6 months					Surgical technique	
			PD	CAL	RD	KTW	GT	CTG thickness (mm)	Donor site place
Eren G. *et al.* (2016) (4)	I & II	CAF+CTG (split thickness flap)	-	-	-	-	-	1.5	Palate
Uraz A. *et al.* (2015) (5)	I & II	CAF+CTG (split-full thickness flap)	1.38±0.58 1.13±0.35 (p>0.05)	4.40±0.86 1.18±0.35 (p<0.05)	3.11±0.80 0.11±0.27 (p<0.05)	3.93±0.72 5.11±0.76 (p<0.05)	-	-	Palate between the premolar and the molar
Mufti S. *et al.* (2017) (17)	I	CAF+CTG (split-full thickness flap)	-	4.12±1.258 4.44±1.031 (p=0.166)	2.13±0.806 1.38±0.806 (p=0.001)	4.31±0.793 4.63±0.806 (p=0.025)	1.03±0.21 1.43±0.31 (p=0.001)	1-2	Palate between the second premolar and the second molar
Oncu E. (2017) (18)	I & II	CAF+CTG (split-full thickness flap)	1.33±0.66 1.17±0.38 (p=0.244)	5.53±1.07 1.77±0.97 (p<0.001)	4.17±0.83 0.68±0.92 (p<0.001)	2.60±0.77 4.33±0.88 (p<0.001)	0.69±0.23 0.85±0.21 (p<0.001)	1.5	Palate between the canine and the first molar
Culhaoglu R. *et al.* (2018) (19)	I	CAF+CTG (split thickness flap)	1.31±0.28 1.17±0.20 (p>0.05)	3.88±0.80 1.57±0.71 (p<0.05)	2.64±0.57 0.52±0.51 (p<0.05)	3.05±0.86 5.29±1.01 (p<0.05)	1.61±0.49 2.35±1.02 (p<0.05)	1	Palate
Chenchev I. *et al.* (2016) (20)	I & II	CAF+CTG	-	-	-	-	-	-	Palate
Al-Quershi M. *et al.* (2019) (21)*	I & II	CAF+CTG (full thickness flap)	0.85±0.36 1.27±0.30 (p<0.05)	3.76±0.89 1.27±0.34 (p<0.05)	2.91±0.70 0.05±0.15 (p<0.05)	2.25±0.70 4.10±0.71 (p<0.05)	-	-	Palate
Kumar A. *et al.* (2017) (22)	I & II	CAF+CTG (split-full-spilt thickness flap)	2.33±0.61 2.33±0.97 (p>0.05)	4.53±1.24 3.33±1.17 (p=0.0001)	2.20±0.41 0.93±0.70 (p=0.0001)	3.80±1.32 5.00±1.46 (p=0.0001)	0.78±0.72 0.84±0.07 (p=0.0001)	-	Palate

* – follow-up 12 months.

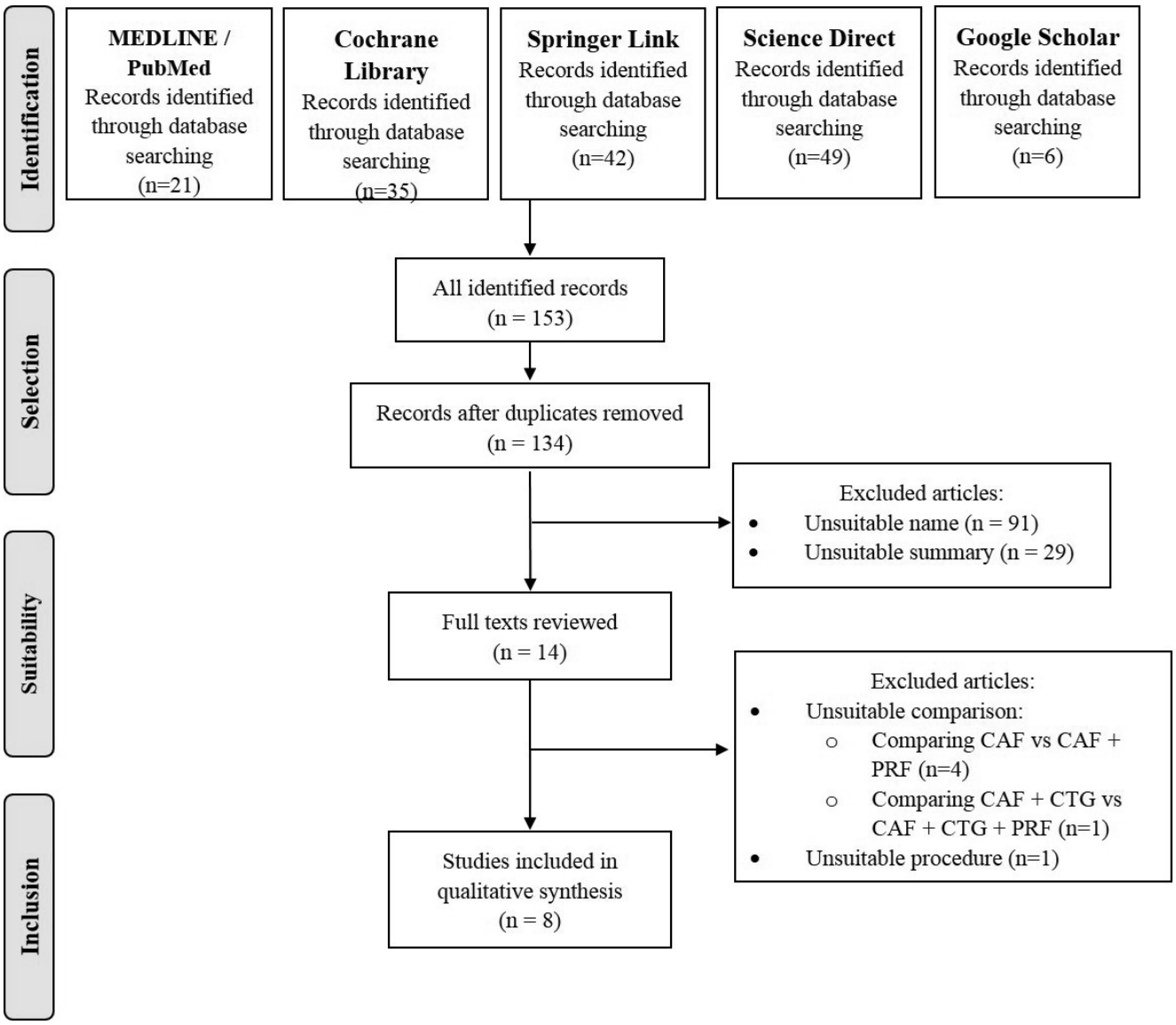

Fig. PRISMA flowchart

Kumar *et al.* reported significant (P<0.05) change in clinical attachment level (CAL) from baseline to 6 months in both, PRF and CTG groups from 3.73±0.70 mm to 2.00±1.00 mm and from 4.53±1.24 to 3.33±1.17, respectively (22), similar results were reported by Uraz *et al.* (5), Oncu *et al.* (18), Culhaoglu *et al.* (19) and Al-Quershi *et al.* (21). In contract to these studies Mufti *et al.* have reported significant difference only in PRF group from 4.06±1.18 mm to 2.81±0.83 mm (17).

Recession depth (RD) significantly (P<0.05) decreased in both groups from 1.80±0.56 mm to

Table 5. Subjective parameters evaluation

Studies	Discomfort PRF / CTG				Aesthetic PRF / CTG		
	Baseline	7th-10th day	3rd month	6th month	10th day	3rd month	6th month
Culhaoglu R. *et al.* (2018) (19)	2.333±1.528 6.619±1.884 P<0.05	0.00±0.00 0.619±1.203 P<0.05	-	-	-	-	-
Chenchev I. *et al.* (2016) (20)	1.50±0.63 4.53±1.50 P<0.05	-	-	-	-	-	9.03±1.0 8.37±1.19 P<0.05
Kumar A. *et al.* (2017) (22)	5.07±1.33 4.07±1.28 P=0.07	4.2±0.56 4.47±1.55 P=0.77	3.07±1.16 4.2±1.26 P=0.02	2.2±1.08 3.53±1.72 P=0.02	4.40±1.40 4.33±0.72 P=0.98	6.13±1.76 5.20±1.01 P=0.13	7.00±1.19 5.20±1.01 P=0.001

0.53±0.74 mm in PRF group and from 2.20±0.41 to 0.93±0.70 in CTG group and no statistically significant difference was noticed between the groups in Kumar *et al.* study (22). Mufti *et al.* (17), Oncu *et al.* (18) and Al-Quershi *et al.* (21) also published similar results to the study before. However, Uraz *et al.* reported that the RD measurments at initial and final examinations were statistically significant not only within but also between the groups favoring experimental (PRF) group (5). Culhaoglu *et al.* in their study also reported that RD values significantly reduced in all groups after recession treatment, however, the reduction was significantly higher in 4 membranes of PRF and CTG groups compared with the group with 2 membranes of PRF (19).

Statistically significant increase was noticed in keratinized tissue width (KTW) from baseline to 6 months in both groups in most of the studies (5, 18, 19, 21, 22). However, significant ($P<0.05$) difference between the groups was noticed only in two studies: Oncu *et al.* (18) and Culhaoglu *et al.* (19) studies. In contrast to these studies, Mufti *et al.* reported KTW increase only in CTG group from 4.31±0.793 mm to 4.63±0.806 mm ($P<0.05$) (17).

Significant increase in gingival thickness (GT) in both groups was reported by Mufti *et al.* (17), Oncu *et al.* (18) and Culhaoglu *et al.* (19). Moreover, Mufti *et al.*, Culhaoglu *et al.* and Kumar *et al.* (17, 19, 22) in their studies reported significantly ($P<0.05$) higher increase in CTG group than in PRF group. Oncu *et al.*, reported significant difference in favor of PRF group ($P<0.05$) from 0.69±0.21 mm to 0.99±0.20 mm of GT (18).

Subjective parameters

As the subjective parameters patients discomfort score (DS) and aesthetic score (AS) were evaluated (Table 5). For the evaluation the standard visual analog scale (VAS) was used. Patients had to put mark based on their opinion on a scale from 0 to 10. Kumar *et al.* in their study reported no significant ($P>0.05$) difference in DS among the groups at baseline and 10 days, however there was a significantly lower DS at 3 and 6 months in PRF treated group (22). Culhaoglu *et al.* (19) and Chenchev *et al.* (20) reported significantly lower DS in PRF group immediately after procedure.

Chenchev *et al.* reported significantly ($P<0.05$) higher AS in the CTG group (20), while Kumar *et al.* reported significantly ($P < 0.05$) higher AS in the PRF group (22).

Histological parameters

Eren *et al.* in their study reported that rete peg formation was significantly ($P < 0.05$) increased in the sites treated with PRF compared to CTG group after 6 months. However, the number of vessels was significantly higher in CTG group. No statistically significant differences were observed in the collagen density. Higher staining intensity of CD31 and CD34 molecules was observed in the submucosal area of PRF group after 1 and 6 months, respectively, showing higher migration of leukocytes (4).

DISCUSSION

The limitation of this study was a low number of randomized clinical trials and different surgical protocols or evaluations among the studies. None of the trials analyzed the histological parameters of PRF membranes. Moreover, different CTG thickness was used in the included studies, which limits data comparison.

Even though, discomfort, pain and aesthetic view are subjective and hard to evaluate they are one of the most important parameters for the patient. Our results showed that in all clinical trials PRF seemed to perform better in terms of discomfort, pain and aesthetic view, while only 1 study showed better results while using connective tissue graft (19, 20, 22).

Regarding histological parameters the results suggested that use of PRF results in earlier blood vessel formation and tissue maturation compared to CTG because of the biological compounds within it (4). However, more histological evaluations are required for a better comparison.

Although, CTG technique is accepted as the golden standard, this review found that PRF has similar outcomes in treatment of Miller class I and II GR defects. After treatment improved periodontal parameters in the analyzed studies either did not have a significant difference between groups (5,19,21-22) or even PRF group performed better (18). Keeping in mind that CTG requires additional surgery, second donor site and the healing is compromised, it is quite clear that PRF can and should be used to treat Miller I and II class defects.

Use of platelet rich fibrin membrane seems to be a reliable method for gingival recession treatment. It has a strong histological justification, the production of it is relatively fast and easy performed within a few minutes. A randomized clinical trial with standardized surgical protocol, selection of patients, PRF centrifugation protocol, higher number of participants and multidisciplinary analysis would be required in order to evaluate the use of PRF membrane as option for a reliable treatment option instead of connective tissue grafting.

CONCLUSION

The review inferred that both techniques (CAF + PRF and CAF + CTG) are effective procedures in the treatment of Miller's class I and II gingival recessions. Although the CTG technique may provide better results in keratinized tissue width and gingival thickness, PRF avoids a donor site, which provides a major decrease in postoperative discomfort. As a result, though CTG is the golden standard material, PRF can be successfully used as an alternative for keeping patient comfortable and painless during the procedure and postoperative period.

CONFLICT OF INTERESTS

All authors declare no conflict of interests.

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