Effectiveness of Amniotic Membrane with Coronally Advanced Flap in the Treatment of Gingival Recession in Adult Patients: A Systematic Review

Ankita A Katkurwar¹, Swapna A Mahale²

ABSTRACT

Aim and objective: To evaluate the effectiveness of amnion membrane on the clinical parameters when used in the treatment of Millers Class I and Class II gingival recession in chronic periodontitis patients along with coronally advanced flap (CAF).

Data resources: Four databases MEDLINE (by PubMed), Cochrane database, EBSCO, and Google Scholar were explored to identify the studies in English up to April 2020. An additional hand search of relevant journals was also done. Two independent reviewers screened the retrieved articles using the particular inclusion criteria. Randomized control trials (RCTs) evaluating the effectiveness of amnion membrane with CAF in treatment of Millers Class I and Class II gingival recession in chronic periodontitis patients were included in the study. Outcome variables examined were recession width (RW), recession depth (RD), clinical attachment level (CAL), keratinized width of gingiva (KWG), probing pocket depth (PD), and gingival thickness (GT). Data were analyzed using Revman5.3 software. The mean differences and 95% confidence interval were used to illustrate the estimate of effect size.

Study selection: Seven relevant articles were recognized for data procurement. One hundred and twenty patients with 244 gingival recession sites in total with an age range between 18 years and 55 years of participants were selected. There is an equal effect in both the groups for the RD reduction. For RW reduction, the result was in the favor of amnion membrane with CAF group, whereas for CAL gain, PD reduction, KWG gain, and GT gain results favored the different biomaterial other than amnion membrane but no statistical significant difference was found.

Conclusion: Within the limitation of the study, it seems that the amnion membrane can be used successfully along with CAF to treat the gingival recession.

Keywords: Amnion membrane, Chronic periodontitis, Coronally advanced flap, Gingival recession, Placental membrane, Root coverage, Systematic review.

International Journal of Experimental Dental Science (2021): 10.5005/jp-journals-10029-1223

INTRODUCTION

"Gingival recession (GR) is the change in the position of the marginal part of the gums apically to the cemento-enamel junction (CEJ) with denudation of the root surface". It is induced due to pathological, anatomical, and traumatic factors.¹ It is responsible for esthetic concern, difficulty in oral hygiene maintenance, loss of the tooth, root sensitivity, and root caries.² Gingival recession is seen in subjects with periodontal disease as well as with good oral hygiene.³ The gingival recession of 1 mm or more in one or more sites is seen in 50% of the population.⁴

For the root coverage of single or multiple recessions, several newer and advanced techniques of periodontal plastic surgery have been propounded. Coronally advanced flap (CAF) is a commonly used mucogingival procedure where the gingival flap is shifted coronally over the exposed root surface. Evidence suggests that CAF is a predictable as well as an effective technique since the results of root coverage are favorable with good color blending, restores the original morphology of the treated gingival site postoperatively.⁵ The procedure is convenient and less invasive since no graft is harvested when treated with CAF alone. However, it was reported that the result of root coverage is not stable in a long-term follow-up. The root coverage was 89% at 1 month and declined to 58.8% at a 6-month postoperative follow-up.⁶ In CAF, healing occurs by repair (forming long junctional epithelium) and not by regeneration. Thus, it is often combined with many biological factors or regenerative materials following the technique based on the GTR principle.

^{1,2}Department of Periodontology, MGVS KBH Dental College and Hospital, Nashik, Maharashtra, India

Corresponding Author: Ankita A Katkurwar, Department of Periodontology, MGVS KBH Dental College and Hospital, Nashik, Maharashtra, India, Phone: +91 9309199790, e-mail: katkurwarankita@gmail.com

How to cite this article: Katkurwar AA, Mahale SA. Effectiveness of Amniotic Membrane with Coronally Advanced Flap in the Treatment of Gingival Recession in Adult Patients: A Systematic Review. *Int J Experiment Dent Sci* 2021;10(1):25–35.

Source of support: Nil

Conflict of interest: None

The gold standard technique for the treatment of gingival recession is coronally advanced flap (CAF) along with connective tissue graft (CTG).⁷ But the need for donor tissue that results in a second surgical site is the main disadvantage of the CTG technique. It also causes patient discomfort, postoperative pain, and a large amount of tissue is needed to treat multiple recessions.⁸ Thus, alternative grafts and biomaterials recommended are autologous plasma,³ enamel matrix derivatives (EMDs),⁹ acellular dermal matrices,¹⁰ chorion membrane,¹¹ amnion membrane,¹² and collagen membrane.¹³

Amnion membrane was first used by Davis in 1910.¹⁴ It is a tough, thin, transparent, avascular composite allograft membrane

of different layers such as thin epithelium, a thick basement membrane, and an avascular mesenchyme pieced of collagen mainly.¹⁵ Owing to the presence of various growth factors like epidermal growth factor (EGF), fibroblast growth factor (FGF), hepatocyte growth factor (HGF), transforming growth factor- α (TGF- α), transforming growth factor- β (TGF- β), and keratinocyte growth factor (KGF), it induces angiogenesis, reduces the pain, and promotes epithelialization and extracellular matrix deposition. It has a variety of specialized proteins like proteoglycan, fibronectin, laminin, and collagen type I, IV, V, and VII. It also possess various biological properties such as anti-inflammatory, antiviral, antimicrobial, anti-scarring, and immunomodulatory.¹⁶ Thus, a third generation bioresorbable amniotic membrane provides the structural as well as anatomical arrangement of regenerated tissues, boost the gingival wound healing and augments a rich source of stem cell thus advocated in various periodontal plastic surgical procedures.¹⁷

Thus, this systematic review aimed to evaluate the effectiveness of amnion membrane in comparison with different biomaterials when used with CAF for root coverage in chronic periodontitis patients.

MATERIALS AND METHODS

Protocol and Registration

To avoid any unintentional reiteration of the review on this topic, registration of the review protocol was done at an international database of prospectively registered systematic reviews PROSPERO (CRD42020175541). We composed the review as per Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guidelines^{18,19} and also ensued PRISMA statement and Cochrane Handbook for Systematic Reviews of Interventions.^{20,21} Our review question was: "What is the effectiveness of amnion membrane with Coronally Advanced Flap in the treatment of gingival recession in adult patients".

Focused PICOS Question

The following PICOS model was employed for this review:

P—Chronic periodontitis patients with Millers Class I or Class II localized gingival recession.

I—Interventions being evaluated was the surgical technique of CAF in combination with amnion membrane.

C—Comparison was done with the surgical technique of CAF in combination with different biomaterials other than amnion membrane.

O—Different type of outcome being measured were

- Primary outcome:
 - Gingival recession depth (RD)
 - Gingival recession width (RW)
 - Width of keratinized gingiva (KWD)
- Secondary outcomes:
 - Probing pocket depth (PD)
 - Gingival biotype (GT)
 - Clinical attachment level (CAL)

In the included studies, all these clinical parameters were evaluated for a period of a minimum 6-month postoperatively.

S—Studies searched were randomized control clinical trials (RCTs), published only in the English language and restricted to human gingival recession defect.

Search Strategy

We executed a comprehensive literature search up to April 2020. All randomized control clinical trials done on the human gingival tissues were scouted in four databases MEDLINE (by PubMed), EBSCO, Cochrane Database, and Google Scholar. Journals like Journal of Periodontology, Journal of Clinical Periodontology, Journal of Periodontal Research, and International Journal of Periodontics and Restorative Dentistry were hand searched to recover additional articles. Even the references list of relevant articles were appraised.

The electronic search included the following terms: ("amnion membrane" OR "placental membrane" OR "amnion") AND ("coronally advanced flap") AND ("Class I" OR "Class II") AND ("gingival recessions" OR "root coverage") AND ("randomized controlled trial").

Inclusion and Exclusion Criteria

Inclusion Criteria

- Subjects who are systemically healthy having age >18 years
- Patients diagnosed with chronic periodontitis having a defect of Miller's Class I or Class II gingival recessions.
- Patients who can maintain good oral hygiene.
- Both males and females subjects were included.
- Patients who are willing to take part in the study and report for regular follow-up.

Exclusion Criteria

- Subjects having a habit of smoking.
- Female patients who are lactating or pregnant during the study period.
- Patients treated for periodontal disease in the last 6 months
- Subjects who fail to maintain good oral hygiene.

Screening and Data Extraction

Two reviewers independently screened the title and abstract of the initially identified studies. Any duplication or articles that do not meet inclusion criteria were exempted. Full-text copy for all eligible articles was obtained and two reviewers assessed them separately to determine whether they qualify the inclusion norms. Any disagreement was resolved by discussion. Articles were excluded if they were not as per the inclusion norms. The reasons for exclusion were recited. In a Microsoft excel sheet, the data of the included studies were extracted.

For the meta-analysis, the clinical parameters (i.e., RD, RW, KTW, PD, CAL, and GT) were collected from the included studies. If the included studies did not disclose the mean difference and standard deviation of the clinical parameters assessed (difference between follow-up and baseline), a further calculation of the mean difference would be requested. For each comparison, the initial step was to calculate the intragroup mean difference between baseline and follow-up.

Intragroup mean difference:²²

$\delta \text{ Mean}_{\text{ctrl}} = (\text{Follow-up data of control group}) - (\text{Baseline data of control group})$

$\delta \text{ Mean}_{\text{test}} = (\text{Follow-up data of test group}) - (\text{Baseline data of test group})$

The second step was to calculate the intergroup difference by:

$\Delta \text{ Mean} = \delta \text{ Mean}_{\text{ctrl}} - \delta \text{ Mean}_{\text{test}}$

Outcome Measurements

Primary Outcome

- Change in RD was reported as a reduction in recession at the 6-month follow-up evaluation (RD was measured at the mid-buccal from CEJ to the gingival margin).
- Change in RW was reported as a reduction in RW at the 6-month follow-up evaluation (RW was measured at the buccal surface at the level of the CEJ from the mesial most to the distal-most of the gingiva).
- Change in KTW was reported as gain in KTW at the 6-month follow-up evaluation (KTW was measured as the distance from the mucogingival junction to the free gingival margin).

Secondary Outcome

- Change in PD was reported as a reduction in PD at the 6-month follow-up evaluation (PD was measured from margin of free gingiva to periodontal pocket).
- Change in CAL was reported as a reduction in CAL at the 6-month follow-up evaluation (CAL was referred to as the distance from the CEJ to the most apical part of the sulcus).
- Change in GT was reported as gain in GT at the 6-month follow-up evaluation (GT was measured 3 mm below the gingival margin at the level of attached gingiva).

Risk of Bias

Two investigators appraised the quality of selected studies separately using the risk of bias assessment tool (The Cochrane collaboration's tool).²⁰ If any debate over a review, then it was settled by conversation. By using the risk of bias assessment tool, the studies were categorized as a high, low, or unclear risk of bias. After the quality assessment, the included studies were graded into (1) low risk: when all criteria were met or one criterion was unclear/not met; (2) moderate risk: when two criteria were unclear/not met; (3) high risk: when more than two criteria were not met. As per the Cochrane handbook, Chi-square and Higgins index (I^2) were used to decide the heterogeneity.²⁰

Statistical Analysis

For the meta-analysis, Revman5.3 (Review Manager Version 5.3; The Cochrane Collaboration, Copenhagen, Denmark) software²¹ was employed for the included studies. The continuous data (including RD, RW, KTW, PD, CAL, and GT) were estimated as mean difference (MD) and 95% confidence interval (CI), with $p < 0.05$ being statistically significant. The fixed-effect model was applied when the heterogeneity between the studies was low ($p \geq 0.10$, $I^2 \leq 50\%$) and when heterogeneity was high ($p < 0.10$, $I^2 > 50\%$), the random effect models were applied for meta-analysis. The heterogeneity across studies in RD, RW, WKG, CAL, PD, and GT were correlated through subgroup analysis. The results of meta-analysis were represented in the forest plot.

RESULTS

Study Selection

Two hundred and ninety studies were identified after the initial electronic search and only two studies were obtained by hand search. After duplicate removal, 121 records were screened for title and abstract, 111 articles were eliminated, and remaining 10 articles were scrutinized for full text.^{5,23-31} Three articles were excluded after the full text evaluation²⁹⁻³¹ because one study reported insufficient follow-up period and even bone graft (DFDBA) was used along with amnion membrane²⁹ and in other two studies no biomaterials were utilized along with CAF for control group.^{30,31} Finally seven studies were selected for data extraction.^{5,23-28} The selection process was outlined in the PRISMA flowchart (Flowchart 1).

Study Characteristic

Total 120 patients with 244 sites with either Millers Class I or Class II gingival recession were included except in Rehan et al.'s⁵ study where only Millers Class I gingival recession sites were enrolled. A maximum of 30 patients participated in Jain et al.'s²⁷ study, whereas a minimum of 10 patients participated in Rehan et al.'s⁵ study. Ghahroudi et al.'s²³ study included a maximum of 71 sites, whereas Rehan et al.'s⁵ study included a minimum of 10 sites. Three articles^{24,25,28} were according to a split-mouth study design and four articles^{5,23,26,27} followed a parallel study design. The age

Flowchart 1: Literature search PRISMA flow diagram

range of the participants was between 18 years and 55 years in all the studies except in the study of Agarwal et al.²⁶ age was not mentioned. The mean age of participants was intimated in the study of Chakraborty et al.²⁴ and Lafzi et al.²⁵ Five studies^{5,23,26–28} described gender distribution of patients and in one study only male patients were included.⁵ In all the included studies minimum follow-up was of 6 months. Maximum of 18-month follow-up was mentioned in Rehan et al.'s study.⁵ Two out of seven included studies were conducted in Iran^{23,25} and the other five studies in India. In Table 1, the characteristics of the included articles were illustrated and the extracted data were outlined in Table 2.

Quality of Studies

All the seven articles mentioned sequence generation: two articles used a flip a coin method,^{23,25} one used chit method,²⁶ one lottery method,²⁷ and the remaining three articles^{23,24,28} did not explain the method of random sequence generation. Out of seven included articles, six articles^{5,23–27} did not account allocation concealment, whereas one article²⁸ intimated it. Since it is a surgical procedure, it was not possible to be blind to the patients. In Rehan et al.'s⁵ study, only patients were blinded whereas in Lafzi et al.'s²⁵ study only assessors were blind. In one article,²³ the patients and the assessors were both were blind while in the remaining four^{24,26–28} articles it was unclear. All the studies had complete follow-up reports. None of the study stated selective reporting and other biases. On evaluation, one article²³ was claimed as low risk, two articles^{5,25} as moderate risk (when two criteria were not met or unclear), and four articles^{24,26–28} as high risk (when three or four criteria were not met or unclear). Figure 1 summarizes the quality assessment of the included studies.

Outcome

RD Reduction

Seven studies^{5,23–28} were included in the meta-analysis. A model employed was a fixed-effects model ($I^2 = 41\%$). According to the result obtained the use of amnion membrane and other biomaterials

along with CAF caused an equal reduction in RD in the treatment of gingival recessions (Fig. 2A). No significant difference was found for CTG, PRF, collagen, and chorion group as per subgroup analysis.

RW Reduction

The meta-analysis for RW reduction was performed on five studies. Two studies^{27,28} were excluded for their incomplete data. A model employed was a random-effects model ($I^2 = 55\%$). The results manifested that the use of amnion membrane along with CAF causes a reduction in RW in the treatment of gingival recessions (Fig. 2B). No significant difference was found for CTG, PRF, and chorion group according to the subgroup analysis.

Keratinized Width of Gingiva Gain

The meta-analysis was performed on five studies for keratinized width of gingiva (KWG) gain. Two articles^{23,28} did not provide specific data thus were excluded from the meta-analysis. A model employed ($I^2 = 39\%$) was a fixed-effects model. The results manifested that the use of different biomaterial groups (other than amnion membrane) caused a reduction in KWG when combined with CAF in the treatment of gingival recessions (Fig. 2C). As per the results of the subgroup analysis, only chorion membrane could significantly improve the KTW, with an MD of 0.09 mm (95% CI: 0.07–0.26 mm; $p = 0.04$). A significant difference was not found in the subgroup of CTG and PRF groups.

PD Reduction

The meta-analysis for PD reduction was performed on four studies. Three studies^{23,24,27} were excluded for its incomplete data. A model employed was fixed-effects model ($I^2 = 0\%$). The results revealed that in the treatment of gingival recessions the use of different biomaterial group (other than amnion membrane) caused a reduction in PD when added to CAF (Fig. 2D). No significant difference was found for CTG, PRF, and collagen group as per subgroup analysis.

Table 1: General information of included studies

Author	Publication year/place	Journal	Age range	Gender	Follow-up	Intervention	
						Test	Control
Ghahroudi et al. ²³	2014/Iran	International Academy of Periodontology	Above 18 years	Male-30 Female-41	3, 6 months	CAF+ amnion membrane	CAF+ CTG
Chakraborty et al. ²⁴	2015/India	Journal of Clinical and Diagnostic Research	33.5 ± 6.89 years	Not specified	1, 3, 6 months	CAF+ amnion membrane	CAF+ chorion membrane
Lafzi et al. ²⁵	2016/Iran	Journal of Dental Restorative, Dental Clinics, Dental Prospects	34 ± 12 years	Not specified	1,3,6 months	CAF+ amnion membrane	CAF+ CTG
Agarwal et al. ²⁶	2016/India	European Journal of Dentistry	Not specified	Males-18, Females-5	3, 6 months	CAF+ amnion membrane	CAF+ PRF and CAF alone
Jain et al. ²⁷	2017/India	Journal of Clinical and Diagnostic Research	18–55	Males-15, Females-15	3, 6 months	CAF+ dehydrated amnion membrane	CAF+ PRF
Mahajan et al. ²⁸	2018/India	Journal of Indian society of periodontology	18–40	Males-5, Females-7	3, 6 months	CAF+ amnion membrane	CAF+ collagen membrane
Rehan et al. ⁵	2018/India	Contemporary Clinical Dentistry	20–45 years	Males-10	6, 18 months	CAF+ amnion membrane	CAF+ PRF

Table 2: Data of included studies

Reference (year)	MD in RD between baseline and 6 months follow-up (mm)	MD in RW between baseline and 6 months follow-up (mm)	MD in WKG between baseline and 6 months follow-up (mm)	MD in PD between baseline and 6 months follow-up (mm)	MD in CAL between baseline and 6 months follow-up (mm)	MD in gingival biotype between baseline and 6 months follow-up (mm)	Other outcome
Ghahroudi et al. (2014)	2.4 ± 1.654	1.5 ± 1.739	NR	NR	2.4 ± 1.40	0.8 ± 1.57	Papilla dimension
Chakraborty et al. (2015)	2.3 ± 1.594	2.7 ± 1.561	NR	NR	2.2 ± 1.892	1 ± 1.39	PI, GI, RAL, % root coverage
Lafzi et al. (2016)	1.56 ± 0.68	2.17 ± 0.58	1.42 ± 0.51	NR	NR	NR	% root coverage
Agarwal et al. (2016)	2.00 ± 0.85	2.50 ± 1.17	1.00 ± 0.51	NR	NR	NR	PI, GI, AG, PCS, PES, HS
Jain et al. (2017)	2.1 ± 1.12	2.7 ± 1.45	0.11 ± 0.3	0.15 ± 0.35	2.14 ± 1.29	NR	PI, GI, AG, PCS, PES, HS
Mahajan et al. (2018)	2.1 ± 1.13	2.7 ± 1.46	0.11 ± 0.4	0.15 ± 0.36	2.14 ± 1.30	NR	PI
Rehan et al. (2018)	0.7 ± 1.23	1.5 ± 1.28	0.99 ± 1.56	0.1 ± 0.98	1.2 ± 1.39	-0.01 ± 0.15	PI, GI
	1.5 ± 0.99	1.8 ± 1.79	1.4 ± 1.56	0.3 ± 0.79	1.52 ± 1.73	-0.07 ± 0.13	
	1.81 ± 0.97	NR	0.69 ± 0.60	NR	NR	NR	
	1.34 ± 0.77	NR	0.55 ± 0.72	NR	NR	NR	
	2.33 ± 0.86	NR	NR	0.2 ± 0.33	2.45 ± 0.89	-0.63 ± 0.13	
	1.83 ± 0.91	NR	NR	0.25 ± 0.54	2.20 ± 1.19	-1.49 ± 0.14	
	1.80 ± 0.92	0.30 ± 0.48	1.10 ± 1.10	0.20 ± 0.63	1.50 ± 1.35	-0.20 ± 0.42	
	1.50 ± 1.53	0.20 ± 0.42	0.80 ± 1.03	0.30 ± 1.34	1.00 ± 1.05	-0.20 ± 0.42	

CAL Reduction

The meta-analysis was performed in five studies. Two studies^{24,27} were excluded as they provided incomplete data. A fixed-effects model was employed ($I^2 = 0\%$) since there was no reported heterogeneity. The results exhibited that in the treatment of gingival recessions the use of different biomaterial groups (other than amnion membrane) caused a gain of CAL when added to CAF (Fig. 2E). No significant difference was found for CTG, PRF, and collagen group as per subgroup analysis.

GT Gain

Three studies^{24,25,27} out of seven were excluded from meta-analysis as there was incomplete data. As the heterogeneity was high ($I^2 = 98.4\%$) a random-effect model was employed. According to the results of our meta-analysis different biomaterial groups other than amnion (Fig. 2F) achieved a greater GT gain. Subgroup analysis exhibited significant difference for collagen membrane group, with an MD of 0.86 mm (95% CI: 0.75–0.97 mm; $p < 0.00001$) but for the CTG and PRF groups, no significant difference was intimated.

DISCUSSION

Ever since CAF was introduced by Norberg in 1926 researchers have done enormous work to achieve predictable, less invasive, and effective outcomes from this surgical procedure. But in the case of CAF, many surgical defects regenerate incompletely since the formation of long junctional epithelium occurs by an invasion of the epithelial cell into the defect which plays a vital role in repair and not regeneration.³² So, the technique based on the GTR principle is used where CAF is combined with different biomaterials like PRF, amnion, chorion, collagen, and ADM which act as a barrier membrane so as to improve the result.³³

Amnion membrane has shown exceptional biocompatibility, good healing capacity with easy availability at an affordable cost having a good shelf life. Moreover, to a great extent, it resembles the basement membrane of human oral mucosa,^{34,35} so this membrane have been suited for the treatment of different periodontal conditions like furcation defects,³⁶ intrabony defects,³⁷ and gingival recession. The clinical evidence was insufficient to conform reconfil the effect of amnion membrane, so this review was intended to compare the effectiveness of amnion membrane with CAF in the treatment of gingival recession in adult patients.

Only RCTs were scrutinized for this systematic review; to avoid serious methodological flaws and to get stronger evidence for the systematic review. Miller's Class I and II gingival recession shows the highest success rates for root coverage procedures.³⁸ So, the studies with the patients diagnosed with chronic periodontitis and having Miller's Class I and II recession were only included. Smokers were eliminated in all studies as they negatively influence CAL gain and gingival recession reduction.³⁹

Regarding the outcome, there is an equal effect by both the groups for the RD reduction. But in the case of RW reduction, the results were in favor of amnion membrane with CAF group but the difference was not statistically significant. Heterogeneity of RW seems to be linked to the different surgical techniques like in Agarwal et al.'s²⁶ study microsurgical protocol was used, in Lafzi et al.'s²⁵ study, only partial-thickness flap was elevated, in Chakraborty et al.'s²⁴ study root biomodification with EDTA was performed whereas in Ghahroudi et al.'s²³ study tetracycline was applied for 2 minutes over the exposed root surface. In terms of PD reduction, CAL gain, KWT, and GT gain different biomaterial (CTG, PRF, and collagen) exhibited effective results along with CAF but the difference was not statistically significant. Heterogeneity in GT seems to be because of different technique employed for

Fig. 1: Risk of bias summary of the included studies

measurement of GT in different studies. Gain in CAL suggests periodontal regeneration, new attachment or reattachment but due to the lack of histological evidence in all of the included study the actual phenomenon behind gain in clinical attachment level cannot be explained.²⁸

For KWT gain, statistically significant difference was found in the study where chorion membrane was used along with CAF which was similar to the result found in Sharma et al.'s¹⁷ study.

GT gain in the collagen membrane group demonstrated a statistically significant difference which is attributed due to the thickness of the amnion membrane is around 300 nm in cross-section, unlike collagen membrane which averages around

750 nm.⁴⁰ Degradation of collagen membrane is slow it takes around 6–8 weeks. Space created by the barrier membranes with clot formation leads to cellular proliferation and migration which may be responsible to increase the thickness of the gingival biotype. Later as the barrier membrane is degraded by the host enzymes secondary space is created which further increases the thickness of the gingival tissue.²⁸ The results observed were similar to the findings of Cardaropoli and Cardaropoli.⁴¹

It is important to consider that the results may be affected significantly by other factors also such as flap tension, soft tissue thickness, and experience of the operator.

CONCLUSION

Thus, within the limitation of the study, it seems that the amnion membrane can be used successfully along with CAF for the treatment of gingival recession.

But only a tentative conclusion can be drawn from this study since there is a limited number of studies with restricted data, a follow-up period of short duration, and having a comparatively high risk of bias. Hence, higher quality RCTs with longer follow-up and substantial sample size are needed to draw a definitive conclusion.

Contd...

Contd...

Figs 2A and F: (A) Forest plot for RD reduction; (B) RW reduction; (C) Forest plot for WKG gain; (D) PD reduction; (E) Forest plot for CAL reduction; (F) GT gain

REFERENCES

- Zucchelli G, Mounssifi I. Periodontal plastic surgery. *Periodontol* 2000;68(1):333–368. DOI: 10.1111/prd.12059.
- Dapirle G, Gatto MR, Checchi L. The evolution of buccal gingival recessions in a student population: a 5-year follow-up. *J Periodontol* 2007;78(4):611–614. DOI: 10.1902/jop.2007.060277.
- Serino G, Wennström JL, Lindhe J, et al. The prevalence and distribution of gingival recession in subjects with a high standard of oral hygiene. *J Clin Periodontol* 1994;21(1):57–63. DOI: 10.1111/j.1600-051x.1994.tb00278.x.
- Kassab MM, Cohen RE. The etiology and prevalence of gingival recession. *J Am Dent Assoc* 2003;134(2):220–225. DOI: 10.14219/jada.archive.2003.0137.
- Rehan M, Khatri M, Bansal M, et al. Comparative evaluation of coronally advanced flap using amniotic membrane and platelet-rich fibrin membrane in gingival recession: an 18-month clinical study. *Contemp Clin Dent* 2018;9(2):188–194. DOI: 10.4103/ccd.ccd_799_17.
- McGuire MK, Cochran DL. Evaluation of human recession defects treated with coronally advanced flaps and either enamel matrix derivative or connective tissue. Part 2: histological evaluation. *J Periodontol* 2003;74(8):1126–1135. DOI: 10.1902/jop.2003.74.8.1126.
- Aroca S, Keglervich T, Barbieri B, et al. Clinical evaluation of a modified coronally advanced flap alone or in combination with a platelet-rich fibrin membrane for the treatment of adjacent multiple gingival recessions: a 6-month study. *J Periodontol* 2009;80(2):244–252. DOI: 10.1902/jop.2009.080253.
- Zuhr O, Bäumer D, Hürzeler M. The addition of soft tissue replacement grafts in plastic periodontal and implant surgery: critical elements in design and execution. *J Clin Periodontol* 2014;41(Suppl. 15):S123–S142. DOI: 10.1111/jcpe.12185.
- Aroca S, Keglervich T, Nikolidakis D, et al. Treatment of class III multiple gingival recessions: a randomized clinical trial. *J Clin Periodontol* 2010;37(1):88–97. DOI: 10.1111/j.1600-051X.2009.01492.x.
- Modaressi M, Wang HL. Tunneling procedure for root coverage using acellular dermal matrix: a case series. *Int J Periodont Restorat Dent* 2009;29(4):395–403.
- Esteves J, Bhat KM, Thomas B, et al. Efficacy of human chorion membrane allograft for recession coverage: a case series. *J Periodontol* 2015;86(8):941–944. DOI: 10.1902/jop.2014.140025c.
- Shieh AT, Wang HL, O'Neal R, et al. Development and clinical evaluation of a root coverage procedure using a collagen barrier membrane. *J Periodontol* 1997;68(8):770–778. DOI: 10.1902/jop.1997.68.8.770.
- Singh H, Singh H. Bioactive amnion as a guided tissue regeneration (GTR) membrane for treatment of isolated gingival recession. A case report. *Indian J Dent* 2013;4(2):110–113. DOI: 10.1016/j.ijid.2012.12.007.
- Niknejad H, Peirovi H, Jorjani M, et al. Properties of the amniotic membrane for potential use in tissue engineering. *Eur Cell Mater* 2008;15:88–99. DOI: 10.22203/ecm.v015a07.
- Rana MP, Mehrotra N. Human amniotic membrane: hope in periodontal regeneration. *Int J Sci Res (JSR)* 2016;5(4):564–569. DOI: 10.21275/v5i4.NOV162635.
- Mishra S, Singh S. Human amniotic membrane: can it be a ray of hope in periodontal regeneration? *Indian J Res* 2014;3(9):118–121.
- Sharma A, Komal Y. Amniotic membrane—a novel material for the root coverage: a case series. *J Indian Soc Periodontol* 2015;19(4):444–448. DOI: 10.4103/0972-124X.154166.
- Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *J Clin Epidemiol* 2009;62(10):e1–e34. DOI: 10.1016/j.jclinepi.2009.06.006.
- Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015;4(1):1. DOI: 10.1186/2046-4053-4-1.
- Higgins J, Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1. 0. The Cochrane Collaboration; 2011. Available from: <http://www.cochrane-handbook.org>.
- Manager RR, The Nordic Cochrane Centre, the Cochrane Collaboration. Version 5.3. Copenhagen: Computer Program; 2014.
- Cheng GL, Fu E, Tu YK, et al. Root coverage by coronally advanced flap with connective tissue graft and/or enamel matrix derivative: a meta-analysis. *J Period Res* 2015;50(2):220–230. DOI: 10.1111/jre.12199.
- Ghahroudi AA, Khorsand A, Rokn AR, et al. Comparison of amnion allograft with connective tissue graft for root coverage procedures: a double-blind, randomized, controlled clinical trial. *J Int Acad Periodontol* 2013;15(4):101.
- Chakraborty S, Sambashivaiah S, Kulal R, et al. Amnion and chorion allografts in combination with coronally advanced flap in the treatment of gingival recession: a clinical study. *J Clin Diagn Res* 2015;9(9):ZC98. DOI: 10.7860/JCDR/2015/12971.6572.
- Lafzi A, Abolfazli N, Faramarzi M, et al. Clinical comparison of coronally-advanced flap plus amniotic membrane or subepithelial connective tissue in the treatment of Miller's class I and II gingival recessions: a split-mouth study. *J Dent Res, Dent Clin, Dent Prosp* 2016;10(3):162. DOI: 10.15171/joddd.2016.026.
- Agarwal SK, Jhingran R, Bains VK, et al. Patient-centered evaluation of microsurgical management of gingival recession using coronally advanced flap with platelet-rich fibrin or amnion membrane: a comparative analysis. *Eur J Dent* 2016;10(1):121. DOI: 10.4103/1305-7456.175686.
- Jain A, Jaiswal GR, Kumathalli K, et al. Comparative evaluation of platelet rich fibrin and dehydrated amniotic membrane for the treatment of gingival recession—a clinical study. *J Clin Diagn Res* 2017;11(8):ZC24. DOI: 10.7860/JCDR/2017/29599.10362.
- Mahajan R, Khinda P, Shewale A, et al. Comparative efficacy of placental membrane and Healiguide™ in treatment of gingival recession using guided tissue regeneration. *J Indian Soc Periodontol* 2018;22(6):513. DOI: 10.4103/jisp.jisp_88_18.
- Chopra P, Kassal J, Masamatti SS, et al. Comparative evaluation of clinical efficacy of coronally advanced flap alone and in combination with placental membrane and demineralized freeze-dried bone allograft in the treatment of gingival recession. *J Indian Soc Periodontol* 2019;23(2):13. DOI: 10.4103/jisp.jisp_308_18.
- Irfan M, Mehta T, Kumar S, et al. Comparative clinical study of coronally positioned flap with and without dehydrated amnion allograft in the treatment of gingival recession. *J Dent Health Oral Disord Ther* 2017;8(3):00281. DOI: 10.15406/jdhodt.2017.08.00281.
- George SG, Kanakamedala AK, Mahendra J, et al. Treatment of gingival recession using a coronally-advanced flap procedure with or without placental membrane. *J Investig Clin Dent* 2018;9(3):e12340. DOI: 10.1111/jicd.12340.
- Blumenthal NM. The use of collagen membranes to guide regeneration of new connective tissue attachment in dogs. *J Periodontol* 1988;59(12):830–836. DOI: 10.1902/jop.1988.59.12.830.
- Wang HL, Al-Shammari KF. Guided tissue regeneration--based root coverage utilizing collagen membranes: technique and case reports. *Quintessence Int* 2002;33(10):715–721.
- Pakkala T, Virtanen I, Oksanen J, et al. Function of laminins and laminin-binding integrins in gingival epithelial cell adhesion. *J Periodontol* 2002;40(7):709–719. DOI: 10.1902/jop.2002.73.7.709.
- Takashima S, Yasuo M, Sanzen N, et al. Characterization of laminin isoforms in human amnion. *Tissue and Cell* 2008;40(2):75–81. DOI: 10.1016/j.tice.2007.09.001.
- Kaur J, Bathla SC. Regenerative potential of autologous platelet-rich fibrin with and without amnion membrane in the treatment of grade-II furcation defects: a clinicoradiographic study. *J Indian Soc Periodontol* 2018;22(3):235. DOI: 10.4103/jisp.jisp_119_18.
- Kiani YF, Moloudi F, Nozari HB. Comparison of amnion membrane with Bio-Gide in conjunction with Bio-Oss in treatment of intrabony periodontal defects. *Sadra Medical Sciences Journal* 2013;1(4):215–232.

38. Alghamdi H, Babay N, Sukumaran A. Surgical management of gingival recession: a clinical update. *Saudi Dent J* 2009;21(2):83–94. DOI: 10.1016/j.sdentj.2009.07.006.
39. Chambrone L, Chambrone D, Pustiglioni FE, et al. The influence of tobacco smoking on the outcomes achieved by root-coverage procedures: a systematic review. *J Am Dent Associat* 2009;140(3):294–306. DOI: 10.14219/jada.archive.2009.0158.
40. Chopra A, Thomas BS. Amniotic membrane: a novel material for regeneration and repair. *J Biomim Biomater Tissue Eng* 2013; 18:106.
41. Cardaropoli D, Cardaropoli G. Healing of gingival recessions using a collagen membrane with a hemineralized xenograft: a randomized controlled clinical trial. *Int J Periodontics Restorative Dent* 2009;29(1):59–67.