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·临床研究·

釉基质蛋白衍生物辅助治疗牙龈退缩临床效果的系统评价

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【摘要】 目的　对釉基质蛋白衍生物(enamel matrix derivative，EMD)辅助结缔组织瓣(connective tissue graft，CTG)治疗牙龈退缩的临床效果进行评价。**方法**　通过检索The Cochrane Library、PubMed、EMbase、Web of Science、万方公共数据库、VIP数据库和中国知网数据库，搜索有关EMD辅助CTG治疗牙龈退缩的随机对照试验(randomized controlled trial，RCT)，检索时间由建库至2022年9月23日，试验组为EMD+CTG，对照组为单纯采用CTG。应用Review Manager 5.4.1及Stata12.0软件进行Meta分析。**结果**　Meta分析结果显示，试验组仅在治疗后12个月在探诊深度(probing depth，PD)及临床附着丧失(clinical attachment loss，CAL)这两个结局指标上优于对照组，差异有统计学意义[MD_{PD}=−0.10，95%*CI*(−0.19，−0.01)，*P* = 0.03]，[MD_{CAL}=−0.38，95%*CI*(−0.71，−0.04)，*P* = 0.03]；其余指标试验组和对照组均无显著差异。**结论**　EMD辅助CTG治疗牙龈退缩对PD及CAL的减少存在益处。

【关键词】 釉基质蛋白衍生物；　结缔组织瓣；　牙龈退缩；　角化组织宽度；　探诊深度；　临床附着丧失；　随机对照试验；　Meta分析；　系统评价
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Systematic review of clinical effects of enamel matrix derivative as adjunctive therapy for gingival recession

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【Abstract】 Objective　To evaluate the clinical effect of enamel matrix derivative(EMD) assisted with connective tissue graft(CTG) in the treatment of gingival recession. **Methods**　Search The Cochrane Library, PubMed, EMbase, Web of Science, Wanfang Public Database,VIP database and CNKI to search for randomized controlled trials of EMD in the treatment of gingival recession. The search period is from the establishment of the databases to October 3, 2022. The test group was treated with EMD+CTG, while the control group was treated with CTG alone. Meta-analyses were performed using Review Manager 5.4.1 and Stat12.0. **Results**　Meta analysis results showed that only 12 months after treatment, there was a statistically significant difference in the PD and CAL outcome indicators between the EMD assisted treatment group and the control group [MD_{PD}=−0.10, 95% *CI* (−0.19, −0.01), *P* = 0.03], [MD_{CAL}=−0.38, 95% *CI* (−0.71, −0.04), *P* = 0.03]. There was no significant difference between the test group and the control group in other indicators. **Conclusion**　EMD assisted CTG in the treatment of gingival recession may be beneficial to the reduction of PD and CAL.

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【Key words】 enamel matrix derivative; connective tissue graft; gingival recession; keratinized tissue width; probing depth; clinical attachment loss; randomized controlled trial; meta analysis; systematic review
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釉基质蛋白衍生物(enamel matrix derivative, EMD)主要由釉原蛋白组成,是牙周病治疗中最为常见的生物制剂之一,其可以通过模拟牙周组织生长过程从而诱导牙周附着来促进再生[1]。有研究显示使用EMD有利于血管的生成和局部细胞生长因子的表达[2],同时其还可以刺激结缔组织中胶原纤维的生成从而加速黏膜的愈合[3],除此之外有学者认为EMD还具有一定的抗炎、抗氧化作用[4-5],故常用于根面覆盖相关术式的辅助治疗[6]。

牙龈退缩不仅会影响美观,同样会带来牙本质敏感、根面龋及牙体硬组织非龋性疾病等一系列问题[7],临床上通常会采用根面覆盖的方法进行治疗。其中结缔组织瓣(connective tissue graft, CTG)和冠向复位瓣(coronally advanced flap, CAF)的联合应用一直以来都是“金标准”,对于单发和多发的Miller Ⅰ类及Ⅱ类牙龈退缩均表现出良好的治疗效果[8]。EMD虽在临床已较为广泛地用于这项术式,但关于其辅助作用目前仍存在争议。本研究旨在通过循证医学的方法系统评价EMD辅助治疗牙龈退缩的临床效果,以期为临床实践提供一定的理论依据。

1　资料和方法

1.1　文献检索策略

使用The Cochrane Library、PubMed、EMbase、Web of Science、万方、VIP和CNKI数据库进行文献检索。英文检索词包括:amelogenins, enamel matrix derivative, enamel matrix proteins, connective tissue graft, coronally advanced flap, gingival recession。中文检索词包括:釉基质蛋白衍生物、结缔组织移植物、结缔组织瓣、冠向复位瓣。检索时间由建库至2022年9月23日。检索策略如下:(amelogenins OR enamel matrix derivative OR enamel matrix proteins) AND (coronally advanced flap OR tunnel) AND connective tissue graft AND gingival recession。

1.2　纳入和排除标准

文献的纳入标准:①研究对象:天然牙存在Miller Ⅰ~Ⅲ类的牙龈退缩者,年龄、性别、种族不限;②研究类型:随机对照试验(randomized controlled trial, RCT),随访时间≥6个月;③试验组:EMD+CTG,对照组单纯采用CTG;④包含全部或部分结局指标:牙龈退缩高度(gingival recession height, GRH)、牙龈退缩宽度(gingival recession width, GRW)、角化组织宽度(Keratinized tissue width, KTW)、探诊深度(probing depth, PD)及临床附着丧失(clinical attachment loss, CAL)。排除标准:①动物实验、综述、系统评价、病例报告及非随机对照试验;②非中文及英文文献;③原始数据不完整,并且难以通过其他途径获得。

1.3　文献筛选与内容提取

文献检索由两名成员独立完成,首先阅读文题排除不相关的研究,之后通读全文明确纳入文献并核对结果,若两名成员意见不一则由第三方介入协商裁定。主要提取内容分为以下几点:①文题、发表时间、第一作者和发表期刊;②研究对象的基线信息、干预措施和结局指标;③评估偏倚风险所需要素等。

1.4　偏倚风险评价

质量评价采用Cochrane手册5.1.0中推荐使用的RCT偏倚风险评估工具[9],两名成员分别评估纳入研究的偏倚风险,并对二者结果进行交叉核对。

1.5　统计学分析

通过Review Manager 5.4.1软件分析纳入的相关研究,均数差为计量资料效应分析统计量。纳入研究间的异质性采用卡方检验进行分析,同时I^2可对异质性大小进行定量的判断。Meta分析的检验水准为$\alpha = 0.05$。固定效应模型在各研究间不存在统计学异质性时使用,否则需了解异质性的来源,排除临床相关影响后使用随机效应模型。若异质性无法排除,则选择进行描述性分析。采

用Stata12.0对纳入研究进行发表偏倚分析。

2　结　果

2.1　检索结果

初检共检索到162篇相关研究，经过逐层的筛选最终确定纳入9篇文献[10-18]。文献的筛选流程及纳入研究的基本情况如下（图1、表1）。

2.2　质量评价

本次研究一共纳入9篇文献，2篇未描述随机方法，4篇研究进行了分配隐藏，4篇研究使用了盲法，还有2篇研究存在失访。偏倚风险详见图2。

2.3　Meta分析结果

2.3.1　GRH　治疗后6个月纳入6篇RCT[10-12, 14, 15, 18]，包括213名受试对象。$I^2=0$，固定效应模型Meta分析结果显示EMD的使用针对GRH这一指标两组差异无统计学意义[MD=−0.04，95%CI（−0.28，0.20），$P=0.76$]（图3）；治疗后12个月与6个月结果一致[MD=−0.14，95%CI（−0.34，0.07），$P=0.19$]。

2.3.2　GRW　治疗后6个月纳入3篇RCT[10, 14, 18]，包括112名受试对象。Meta分析结果显示两组差异无统计学意义[MD=−0.23，95%CI（−0.85，0.40），$P=0.48$]；治疗后12个月同样纳入3篇RCT[16-18]，包括114名受试对象；研究结果与治疗后6个月一致[MD=−0.02，95%CI（−0.61，0.56），$P=0.94$]。

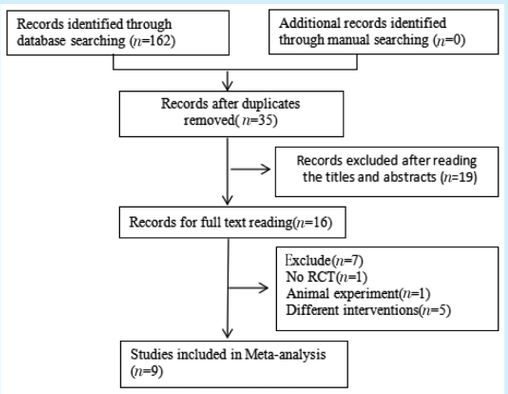

Figure 1　Literature screening process

图1　文献筛选过程

2.3.3　KTW　治疗后6个月纳入6篇RCT[10-12, 14, 15, 18]，包括213名受试对象，治疗后12个月纳入5篇RCT[10-13, 16, 18]，共194名受试对象。分析结果均显示两组差异均无统计学意义[MD_6=−0.04，95%CI（−0.34，0.27），$P=0.81$]、[MD_{12}=−0.01，95%CI（−0.59，0.57），$P=0.97$]。

2.3.4　PD　治疗后6个月纳入4篇RCT[11-12, 14, 18]，包括142名受试对象。Meta分析结果显示试验组和

表1　纳入研究的基本特征

Table 1　Basic characteristics of included studies　　$\bar{x}\pm s$

Studies	Sample size		Age/year	Classification	Interventions	Follow-up time/month	Outcome indicators
	T	C					
Dias AT 2022[10]	16	16	42.7*	Miller Ⅰ-Ⅱ	T: EMD+CAF+CTG C: CAF+CTG	6	GRH、GRW、KTW
Roman A 2013[11]	21	21	T: 34.09 ± 8.65 C: 30.18 ± 7.61	Miller Ⅰ-Ⅱ	T: EMD+CAF+CTG C: CAF+CTG	12	GRH、GRW、PD
Henriques PS 2010[12]	12	12	42.7 ± 5.8	Miller Ⅰ-Ⅲ	T: EMD+CAF+CTG C:CAF+CTG	12	GRH、KTW、PD、CAL
Rasperini G 2011[13]	26	30	T: 35.7 ± 8.4 C: 35.3 ± 10.0	Miller Ⅰ-Ⅱ	T: EMD+CAF+CTG C: CAF+CTG	12	GRH、KTW、PD、CAL
Górski B 2020 [14]	20	20	T: 35.7 ± 8.4 C: 35.3 ± 10.0	Miller Ⅰ-Ⅲ	T: EMD+MCAT+CTG C: MCAT+CTG	6	GRH、GRW、KTW、PD、CAL
Stähli A 2020[15]	20	20	T: 32.8 ± 11.1 C: 30.8 ± 9.9	Miller Ⅰ-Ⅲ	T: EMD+MCAT+CTG C: MCAT+CTG	6	GRH、KTW
Górsk 2022[16]	20	20	28.35 ± 4.51	Miller Ⅰ-Ⅱ	T: EMD+MCAT+CTG C: MCAT+CTG	12	GRH、GRW、KTW、PD、CAL
Aydinyurt HS 2019[17]	19	19	32.18 ± 8.91	Miller Ⅰ-Ⅱ	T: EMD+CAF+CTG C: CAF+CTG	12	GRH、KTW
Aroca S 2010[18]	20	20	31.7*	Miller Ⅲ	T: EMD+MCAT+CTG C: MCAT+CTG	12	GRH、GRW、KTW、PD、CAL

T: treatment group; C: control group; *: average age; GRH: gingival recession height; GRW: gingival recession width; KTW: keratinized tissue width; PD: probing depth; CAL: clinical attachment loss; MCAT: modified coronally advanced tunnel; CAF: coronally advanced flap; EMD: enamel matrix derivative; CTG: connective tissue graft

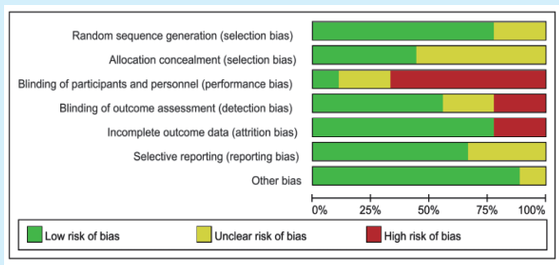

Figure 2　Bias assessment chart

图2　偏倚风险评估图

对照组间无统计学差异[*MD*=−0.08，95%*CI*(−0.25，0.10)，*P* = 0.39]；治疗后12个月纳入5篇RCT[11-13,16,18]，结果显示EMD的使用有助于降低PD[*MD*=−0.10，95%*CI*(−0.19，−0.01)，*P* = 0.03]（图4）。

2.3.5　CAL　治疗后6个月纳入4篇RCT[12-14,18]，包括160名受试对象。I^2 = 0，固定效应模型Meta分析结果显示两组差异无统计学意义[*MD*=−0.30，95%*CI*(−0.65，0.05)，*P* = 0.09]；治疗后12个月结果显示EMD使用可减少CAL，差异有统计学意义[*MD*=−0.38，95%*CI*(−0.71，−0.04)，*P* = 0.03]，见表2。

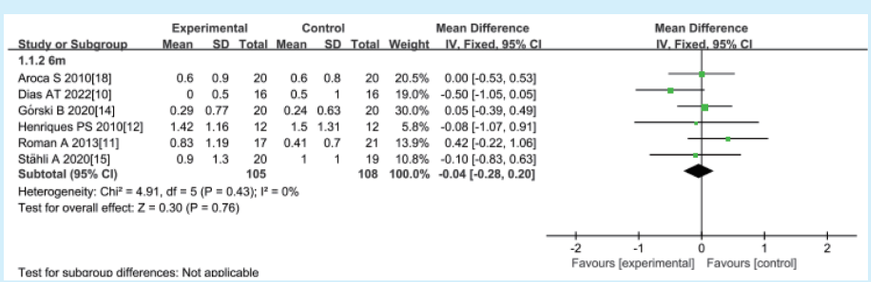

Figure 3　Meta-analysis of gingival recession height 6 months after enamel matrix derivative assisted treatment of gingival recession

图3　釉基质蛋白衍生物辅助治疗牙龈退缩后6个月牙龈退缩高度变化的Meta分析森林图

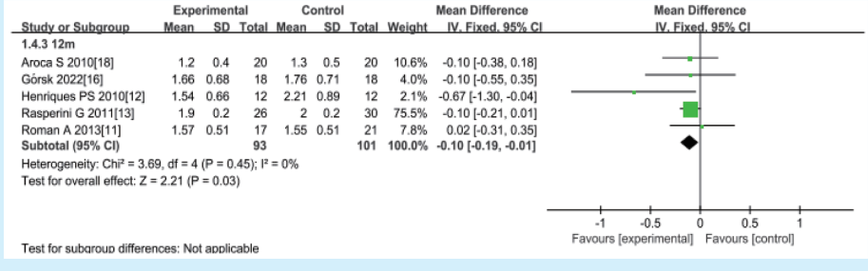

Figure 4　Meta-analysis of probing depth changes 12 months after enamel matrix derivative assisted treatment of gingival recession

图4　釉基质蛋白衍生物辅助治疗牙龈退缩后12个月探诊深度变化的Meta分析森林图

表2　釉基质蛋白衍生物辅助治疗牙龈退缩的Meta分析结果

Table 2　Meta analysis results of enamel matrix derivative assisted treatment of gingival recession

Outcome indicators	Number of included studies	Heterogeneity test results		Effect model	Meta analysis results	
		P	I^2		Effector(95%*CI*)	*P*
6-month GRH	6[11-12,14,15,18]	0.43	0	Fixed	−0.04(−0.28,0.20)	0.76
6-month GRW	3[10,14,18]	0.18	41	Fixed	−0.23(−0.85,0.40)	0.48
6-month KTW	6[10-12,14,15,18]	0.97	0	Fixed	−0.04(−0.34,0.27)	0.81
6-month PD	4[15-20,23]	0.91	0	Fixed	−0.08(−0.25,0.10)	0.39
6-month CAL	4[11,12,14,18]	0.41	0	Fixed	−0.30(−0.65,0.05)	0.09
12-month GRH	6[11-13,16-18]	0.10	46	Fixed	−0.14(−0.34,0.07)	0.19
12-month GRW	3[16-18]	0.88	0	Fixed	−0.02(−0.61,0.56)	0.94
12-month KTW	5[11-13,16,18]	0.008	71	Random	−0.01(−0.59,0.57)	0.97
12-month PD	5[11-13,16,18]	0.45	0	Fixed	−0.10(−0.19,−0.01)	0.03
12-month CAL	4[12,13,16,18]	0.29	21	Fixed	−0.38(−0.71,−0.04)	0.03

GRH: gingival recession height; GRW: gingival recession width; KTW: keratinized tissue width; PD: probing depth; CAL: clinical attachment loss

2.4　发表偏倚

针对治疗后6个月的GRH这一结局指标进行发表偏倚分析，Egger's检验结果显示不存在发表偏倚（P = 0.981）（图5）。

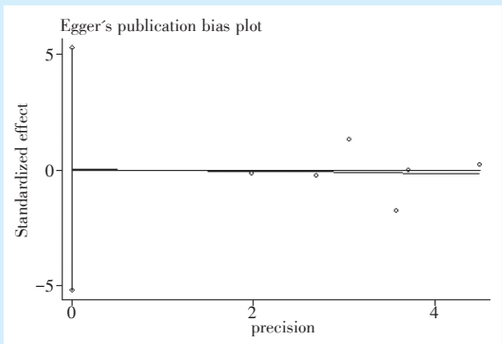

Figure 5　Egger's chart of probing depth at 6 months follow-up
图5　随访6个月时探诊深度的Egger's图

2.5　敏感性分析

通过逐一剔除纳入研究的方法进行敏感性分析，结果显示随访12个月PD及CAL这两个指标结局稳定性欠佳，其余指标分析结果均无方向性变化，稳定性较好。针对治疗后12个月的PD及CAL，当分别剔除Henriques等[12]和Rasperini等[13]这两个研究时结果转变为差异无统计学意义。

3　讨　论

EMD在国外已广泛用于牙周再生治疗，有研究显示EMD辅助治疗牙槽骨缺损可以取得比较良好的临床效果[19]。牙龈退缩作为口腔常见问题，临床曾采用游离龈移植术、侧向转位瓣等方法进行治疗，但目前CAF+CTG的方案仍然最具有可预测性，对Miller Ⅰ类及Ⅱ类的牙龈退缩可以达到完全的根面覆盖。近年隧道技术、改良隧道技术在牙周显微器械的加持下对于复杂且预测性低的MillerⅢ类及Ⅳ类牙龈退缩的治疗也可取得一定的疗效[20]。EMD以其生物学特性常辅助应用于牙龈退缩治疗，但针对治疗效果，仍存在一定争议。关于EMD辅助CTG治疗牙龈退缩的临床疗效，本研究结果显示仅在治疗后12个月的PD及CAL这两个结局指标上表现出一定益处，其余指标差异均无统计学意义。Dubey等[21]学者也认为EMD的使用对牙龈退缩位点根面覆盖率的提高没有明显作用，仅对PD及CAL有一定改善，与本研究结论一致。结缔组织瓣和根面的附着主要由冠方的长上皮附着和根方的新附着组成，根面覆盖的治疗对象一般仅存在牙龈退缩，并没有深牙周袋，但对于牙龈退缩较宽的区域EMD的使用可增加形成新附着的百分比，替代长结合上皮附着，提高附着质量，使疗效长期稳定。有学者在研究中发现EMD可以在根面覆盖术后6个月及12个月减少牙龈退缩量[22]，与本研究结果相悖。关于角化组织增加量，Meza Mauricio等[22]及Cheng等[23]均认为CTG联合CAF对KTW增加的贡献更大，而EMD的使用并不会带来更多益处，与本研究结论一致。但对于Miller Ⅲ类及Ⅳ类的牙龈退缩有学者却发现EMD的使用可以改善根面覆盖效果，有利于KTW的增加[24]。

本研究仍存在不足，包括：①纳入文献量少、研究对象的数量同样较少，针对盲法的使用、分配隐藏等偏倚部分文献没有详细描述，而且存在失访病例；②纳入研究的随访时间为6～12个月不等，缺少长期疗效证据；③在纳入研究的过程中部分试验采用的是改良隧道技术，部分是CAF技术，虽两种术式都需进行冠向复位，但技术不同可能会对结果带来一定干扰；④研究对象的牙龈退缩为Miller I～Ⅲ类不等，对于Miller Ⅲ类，由于邻面出现牙龈退缩，增加了根面覆盖的不确定性；⑤治疗后患者的依从性，口腔卫生措施是否到位没有严格的统一标准。

本研究结果显示，EMD辅助CTG治疗牙龈退缩相较于单纯CTG而言对于PD及CAL的改善具有一定益处，但对于减少牙龈退缩的量及增加角化龈宽度没有明显作用。

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参考文献

[1] Fan L,Wu D. Enamel matrix derivatives for periodontal regeneration: recent developments and future perspectives[J]. J Healthc Eng, 2022. doi: 10.1155/2022/8661690.

[2] Tavelli L, McGuire MK, Zucchelli G, et al. Biologics-based regenerative technologies for periodontal soft tissue engineering[J]. J Periodontol, 2020, 91(2): 147-154. doi: 10.1002/JPER.19-0352.

[3] Klewin-Steinböck S, Adamski Z, Wyganowska-Świątkowska M. Potential usefulness of enamel matrix derivative in skin and mucosal injury treatment[J]. Postepy Dermatol Alergol, 2021, 38(3): 351-358. doi: 10.5114/ada.2020.92318.

[4] Panahipour L, Sordi MB, Kargarpour Z, et al. TGF-β signalling mediates the anti-inflammatory activity of enamel matrix derivative *in vitro*[J]. Int J Mol Sci, 2022, 23(17): 9778. doi: 10.3390/

ijms23179778.

[5] Takeda K, Mizutani K, Matsuura T, et al. Antioxidant effect of enamel matrix derivative for early phase of periodontal tissue regeneration in diabetes[J]. J Periodontol, 2022, 93(8): 1206-1217. doi: 10.1002/JPER.21-0413.

[6] Liang Y, Luan X, Liu X. Recent advances in periodontal regeneration: a biomaterial perspective[J]. Bioact Mater, 2020, 5(2): 297-308. doi: 10.1016/j.bioactmat.2020.02.012.

[7] Imber JC, Kasaj A. Treatment of gingival recession: when and how?[J]. Int Dent J, 2021, 71(3): 178-187. doi: 10.1111/idj.12617.

[8] Bertl K, Spineli LM, Mohandis K, et al. Root coverage stability: a systematic overview of controlled clinical trials with at least 5 years of follow-up[J]. Clin Exp Dent Res, 2021, 7(5): 692-710. doi: 10.1002/cre2.395.

[9] Higgins JPT, Green S. Cochrane handbook for systematic reviews of interventions (version 5.1.0)[M/OL]. The Cochrane Collaboration, 2011.http://www.cochrane-handbook.org.

[10] Dias AT, de Menezes CC, Kahn S, et al. Gingival recession treatment with enamel matrix derivative associated with coronally advanced flap and subepithelial connective tissue graft: a split-mouth randomized controlled clinical trial with molecular evaluation[J]. Clin Oral Investig, 2022, 26(2): 1453-1463. doi: 10.1007/s00784-021-04119-9.

[11] Roman A, Soancă A, Kasaj A, et al. Subepithelial connective tissue graft with or without enamel matrix derivative for the treatment of Miller class Ⅰ and Ⅱ gingival recessions: a controlled randomized clinical trial[J]. J Periodontal Res, 2013, 48(5): 563-572. doi: 10.1111/jre.12039.

[12] Henriques PS, Pelegrine AA, Nogueira AA, et al. Application of subepithelial connective tissue graft with or without enamel matrix derivative for root coverage: a split-mouth randomized study[J]. J Oral Sci, 2010, 52(3): 463-471. doi: 10.2334/josnusd.52.463.

[13] Rasperini G, Roccuzzo M, Francetti L, et al. Subepithelial connective tissue graft for treatment of gingival recessions with and without enamel matrix derivative: a multicenter, randomized controlled clinical trial[J]. Int J Periodontics Restorative Dent, 2011, 31(2): 133-139.

[14] Górski B, Górska R, Wysokińska-Miszczuk J, et al. Tunnel technique with enamel matrix derivative in addition to subepithelial connective tissue graft compared with connective tissue graft alone for the treatment of multiple gingival recessions: a randomized clinical trial[J]. Clin Oral Investig, 2020, 24(12): 4475-4486. doi: 10.1007/s00784-020-03312-6.

[15] Stähli A, Imber JC, Raptis E, et al. Effect of enamel matrix derivative on wound healing following gingival recession coverage using the modified coronally advanced tunnel and subepithelial connective tissue graft: a randomised, controlled, clinical study[J]. Clin Oral Investig, 2020, 24(2): 1043-1051. doi: 10.1007/s00784-019-03008-6.

[16] Górski B, Górska R, Szerszeń M, et al. Modified coronally advanced tunnel technique with enamel matrix derivative in addition to subepithelial connective tissue graft compared with connective tissue graft alone for the treatment of multiple gingival recessions: prognostic parameters for clinical treatment outcomes[J]. Clin Oral Investig, 2022, 26(1): 673-688. doi: 10.1007/s00784-021-04045-w.

[17] Aydinyurt HS, Tekin Y, Ertugrul AS. The effect of enamel matrix derivatives on root coverage: a 12-month follow-up of a randomized clinical trial[J]. Braz Oral Res, 2019, 33: e006. doi: 10.1590/1807-3107bor-2019.vol33.0006.

[18] Aroca S, Keglevich T, Nikolidakis D, et al. Treatment of class Ⅲ multiple gingival recessions: a randomized-clinical trial[J]. J Clin Periodontol, 2010, 37(1): 88-97. doi: 10.1111/j.1600-051X.2009.01492.x.

[19] Iorio-Siciliano V, Blasi A, Nuzzolo P, et al. Treatment of periodontal intrabony defects using enamel matrix derivative: surgical reentry after an observation period of at least 5 years[J]. Int J Periodontics Restorative Dent, 2019, 39(4): 537-543. doi: 10.11607/prd.4148.

[20] Lahham C, Ta´a MA.Clinical comparison between different surgical techniques used to manage advanced gingival recession (Miller´s class Ⅲ & Ⅳ)[J]. Heliyon, 2022, 8(8): e10132. doi: 10.1016/j.heliyon.2022.e10132.

[21] Dubey P, Narasimhan M, Sehgal NK, et al. Connective tissue graft with or without enamel matrix derivative for treating gingival recession defects: a systematic review and meta-analysis[J]. J Evid Based Dent Pract, 2021, 21(4): 101635. doi: 10.1016/j.jebdp.2021.101635.

[22] Meza Mauricio J, Furquim CP, Bustillos-Torrez W, et al. Does enamel matrix derivative application provide additional clinical benefits in the treatment of maxillary Miller class Ⅰ and Ⅱ gingival recession? A systematic review and meta-analysis[J]. Clin Oral Investig, 2021, 25(4): 1613-1626. doi: 10.1007/s00784-021-03782-2.

[23] 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]. J Periodontal Res, 2015, 50(2): 220-230. doi: 10.1111/jre.12199.

[24] Mercado F, Hamlet S, Ivanovski S. Subepithelial connective tissue graft with or without enamel matrix derivative for the treatment of multiple Class Ⅲ-Ⅳ recessions in lower anterior teeth: a 3-year randomized clinical trial[J]. J Periodontol, 2020, 91(4): 473-483. doi: 10.1002/JPER.19-0058.

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