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Efficacy of enamel matrix derivatives (Emdogain®) in treatment of replanted teeth – a systematic review based on animal studies

REVIEW ARTICLE

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Abstract – The objective of the current systematic review was to evaluate the efficacy of enamel matrix derivative (EMD) (Emdogain®) on healing of replanted or autotransplanted permanent teeth. A review of the published literature [search term: (Emdogain OR enamel matrix derivative OR enamel matrix protein] AND [avulsion OR replantation OR autotransplantation)] was conducted by two independent investigators according to defined selection criteria. For data extraction of the identified animal studies, the following histomorphometric findings were considered: (i) healed PDL, (ii) surface resorption, (iii) inflammatory resorption and (iv) replacement resorption. The heterogenity of data collection and the small amount of identified publications did not allow for statistical analysis. Four controlled trials (CT) conducted in animals, but no randomized controlled trials (RCT) or clinical controlled trials (CCT) could be received from the systematic search. From the selected studies, two CT gave evidence of EMD treatment to be effective in inducing healing of replanted teeth, while one CT found no differences between EMD treated teeth and controls. Finally, one CT compared EMD and sodium fluoride application, but revealed no differences between the treatments. The data of controlled trials available are limited and conflicting. No firm conclusion regarding the efficacy of EMD application on healing of replanted or autotransplanted permanent teeth can be drawn because of lack of RCT and CCT.

Tooth avulsion is a complex injury affecting pulp, periodontal ligament (PDL), cementum layer and alveolar bone and is usually followed by pulpal and periodontal complications, which might compromise tooth survival. Complicating sequelae of pulp necrosis, damaged PDL and cementum layer may result in external inflammatory resorption or replacement resorption, which may ultimately result in tooth loss.

With regard to pulpal sequelae, a timely endodontic therapy is usually required to prevent or inhibit pulpal infection. Bacteria, bacterial by-products and tissue breakdown products from the root canal system could stimulate inflammatory resorption in the adjacent periodontal tissue in cases where trauma results in severe damage to the root surface leaving dentinal tubules exposed. Replacement resorption takes place when large areas of the PDL are damaged and the viability of PDL is lost finally resulting in replacement of the periodontal attachment by cells of the alveolar bone (1, 2). As the formation of new tissue on the affected root surfaces may be considered as competitive healing from the socket wall and the adjacent PDL, therapeutic approaches that would regulate and promote PDL cell proliferation and differentiation are considered to improve the healing process of avulsed teeth. As the development of resorption may be directly related to the vitality of the periodontal ligament, the length of extra-alveolar time, the type of storage (wet or dry), kind of storage media and the pre-treatment of teeth prior to replantation are of high relevance (3, 4).

Enamel matrix derivative (EMD) has attracted interest to improve periodontal healing of avulsed and replanted teeth, as it was reported to be effective in the treatment of periodontal intrabony effects (5, 6). Emdogain® (Biora, Malmö, Sweden; incorporated into Straumann Biologic Division since 2004) is a commercial EMD, which is extracted from developing embryonal enamel of porcine origin and contains several matrix proteins from the amelogenin family. Several studies have shown that EMD influences the migration, attachment, proliferative capacity and biosynthetic activity of periodontal ligament cells (7–10). Thus, it is also considered effective in improving the healing process of replanted teeth and recommended as therapeutic agent for the management of avulsed permanent teeth (11, 12), but consensus on published guidelines and treatment protocols is still lacking.

The primary objective of this review was to analyse the impact of EMD treatment compared to controls not receiving any treatment on healing of replanted or transplanted teeth. Secondly, the effect of EMD in comparison with other conditioning media, e.g. sodium fluoride should be investigated.

Methods

Research question

According to the paradigm of evidence-based dentistry, the research question of this study was defined accordingly to the PICO format (13, 14) as:

P (Patients/Population): Replanted or transplanted teeth in *humans or animals*

I (Intervention): Application of EMD

C (Comparison): Compared to teeth *not receiving any treatment* (C1) or treated with *other conditioning media* (C2)

O (Outcome): *healing patterns*

Search strategy

The search of literature was carried out in March 2007 using the electronic databases PubMed, Medline and EMBASE. In the first step, databases were searched for the terms (Emdogain OR enamel matrix derivative OR enamel matrix protein) AND (avulsion OR replantation OR autotransplantation). The literature search was closely related to the MOOSE Guidelines for meta-analyses and systematic reviews of observational studies (15).

In the second step, two investigators independently screened each English publication for eligibility by examining the title, abstract and keywords. References from the identified publications were manually searched to identify additional relevant articles.

Selection criteria

In the third step, two reviewers (A.W. and T.A.) applied the following inclusion criteria: randomized controlled trial (RCT), clinical controlled trial (CCT) or controlled trial conducted in animals (CT), where EMD application was compared with controls not receiving any type of treatment. For the second objective of the review, RCT, CCT and CT, in which EMD application was compared with other surface conditioning treatment, were selected. Clinical trials without an adequate control as well as reviews and case reports were excluded. Authors of the identified studies were contacted for clarification of missing information.

Data extraction

In the fourth step, the following histomorphometric findings were considered as outcome measures of CT: (i) healed PDL, (ii) surface resorption, (iii) inflammatory resorption and (iv) replacement resorption. Outcome measures for RCT and CCT were defined as follows: (i) tooth loss, (ii) radiological evidence for surface resorption, inflammatory resorption or replacement resorption and (iii) clinical evidence for ankylosis. However, the selection criteria revealed no RCT and CCT to be included in the forth step.

Data extraction was performed in duplicate by both examiners.

Data synthesis

The results presented in this study are in form of an organized, qualitative and systematic review of the evidence gathered on the efficacy of EMD compared to controls not receiving any kind of treatment in healing of replanted or autotransplanted teeth. Given the paucity of relevant studies addressing this question as well as the variability in research designs, meta-analysis including an overall statistical analysis of the evidence seemed not appropriate.

Results

Study identification

In the first and second step, 22 relevant publications could be identified. Only five publications met the inclusion criteria applied in the third step. Thereby, the selection criteria revealed no RCT and CCT and only five CT to be included (16–20). Seventeen publications were excluded for the following reasons (Table 1): Case report or review (21–29), CT not in English and information could not be obtained from the author (30) and inadequate or missing control (31–37). Sound, non-explanted teeth (31–33) as well as historical controls (36, 37) were considered inadequate. During the data extraction (fourth step), one study (20) was excluded because of missing statistical analysis.

As a result, four studies were available for final analysis. Three studies, in which EMD treatment was compared with controls not receiving any kind of relevant treatment, could be obtained (16–18). For better

Table 1. Procedure of the literature search and applied selection criteria for inclusion or exclusion of publications

First step	
Keyword search in the relevant data bases	24 publications
Next step	**24 publications**
Second step	
Identified publications	22 publications
Search in reference list of selected 22 publications	0 publication
Next step	**22 publications**
Third step	
Met inclusion criteria	5 publications
RCT	0 publication
CCT	0 publication
CT	5 publications
Met exclusion criteria	17 publications
Neither an RCT, CCT or CT	9 publications
Not English language	1 publication
Inadequate (historic) control	7 publications
Next step	**5 publications**
Fourth step	
Screening for outcome measures of the remaining trials	5 publications
Met exclusion criteria because of inadequate report of the results/no statistical analysis performed	1 publication
Final analysis	**4 publications**

CT, controlled trials; RCT, randomized controlled trials; CCT, clinical controlled trials. Data in bold indicate the studies that are appropriate for the next step.

Table 2. Main results of the histomorphometric parameters in studies comparing EMD vs no treatment

					Hitomorphometric outcome			
						Type of resorption (%)		
Study	No. teeth	Follow-up time	Extra-alveolar time and root surface treatment	No. teeth under analysis	Normal PDL (%)	Surface resorption	Inflammatory resorption	Replacement resorption
Iqbal et al. (10)	102	8–12 weeks	15, 30, 60 min dried, *Emdogain*	36	60.2 (5.2)	20.2 (2.6)	15.12 (5.8)	4.5 (3.1)
			15, 30, 60 min dried (*Control*)	36	43.4 (5.2)	15.8 (2.6)	26.0 (5.8)	14.9 (3.1)
Lam et al. (11)	n.a.	16 weeks	Immediately replanted	10	98.9 (2.3)	n.a.	0	1.1 (2.3)
			1 h dried	12	16.6 (19.6)	n.a.	12.3 (13.9)	71.2 (18.4)
			1 h dried, PDL removed	4	5.2 (7.3)	n.a.	1.6 (3.2)	93.2 (10.4)
			1 h dried, *Emdogain*	10	22.2 (22.8)	n.a.	5.4 (6.5)	72.4 (21.8)
			1 h dried, PDL removed, *Emdogain*	6	20.3 (15.2)	n.a.	5.1 (7.4)	74.6 (14.9)
			1 h dried, PDL removed, *EDTA*, *Emdogain*	7	19.2 (13.9)	n.a.	8.9 (9.0)	71.9 (15.2)
Molina et al. (12)	63	7–60 days	20 min saline	21 (after 7, 20 and 60 days each $n = 7$)	7 days: 93.3 20 days: 30.7 60 days: 19.4	7 days: 0.1 20 days: 61.1 60 days: 14.5		7 days: 0 20 days: 12.2 60 days: 0
			20 min saline, PDL removed	21 (after 7, 20 and 60 days each $n = 7$)	7 days: 31.4 20 days: 4.0 60 days: 14.5	7 days: 0.6 20 days: 44.0 60 days: 38.7		7 days: 0 20 days: 17.0 60 days: 6.3
			20 min saline, PDL removed, *Emdogain*	21 (after 7, 20 and 60 days each $n = 7$)	7 days: 18.9 20 days: 7.1 60 days: 7.8	7 days: 0 20 days: 59.5 60 days: 50.7		7 days: 0 20 days: 13.1 60 days: 4.9

PDL, periodontal ligament; n.a., not available.

illustration, a short description of these studies including the most relevant results is provided in Table 2. One study compared the effects of EMD application with sodium fluoride (19).

EMD vs no treatment

Two controlled trials found EMD treatment to be superior to controls without any kind of treatment. Iqbal et al. (16) assessed the effect of Emdogain in re-implanted teeth of nine beagle dogs. One-hundred and two teeth were extracted and air dried for 15, 30 or 60 min. The necrotic PDL was not removed, and the teeth were assigned to Emdogain coating or no treatment (homologous teeth). Histomorphometric analysis was performed in three groups: (i) teeth splinted for 1 week and animals sacrificed after 8 weeks, (ii) teeth splinted for 1 week and animals sacrificed after 12 weeks or (iii) teeth were not splinted and animals sacrificed after 12 weeks. Eighty teeth could be followed-up and statistical univariate analysis found a significant higher percentage of normal PDL in the Emdogain group (60.2 ± 5.25%) compared with the control (43.4 ± 5.2%). Also, the replacement resorption was significantly less in the Emdogain treated teeth (4.5 ± 3.1%) compared with the control (14.9 ± 3.1), while surface and inflammatory root resorption did not differ significantly. The multivariate analysis was carried out for EMD, follow-up and extraalveolar period and found significantly less replacement and inflammatory resorption for the EMD group. The incidence of root resorptions between splinted and non-splinted teeth was not significantly different.

In the study by Lam et al. (17), incisors and mandibular posterior teeth of seven monkeys were endodontically treated, extracted, dried for 1 h and replanted after receiving one of the following treatments: (i) none, (ii) PDL removal, (iii) Emdogain application, (iv) PDL removal and Emdogain application, (v) PDL removal and EDTA treatment before Emdogain application. Teeth that were immediately replanted and considered as negative control showed the best outcome. Roots that were replanted with remaining PDL after dried for 1 h exhibited significantly less replacement resorption compared with the other groups. However, treatment with EDTA and Emdogain (group 5) led to significantly less replacement resorption compared with teeth with PDL removed (group 2). Healing patterns after application of Emdogain only (group 4) were not superior to group 2.

In contrast, in the study of Molina et al. (18), healing of EMD treated incisors of wistar rats was not significantly different from the teeth, which did not receive any treatment (18). Each 21 incisors were extracted and kept in saline for 20 min. Thereafter, the teeth were endodontically treated and either replanted (group 1), replanted after PDL removal (group 2) or replanted after PDL removal and EDTA followed by Emdogain treatment (group 3). Histometric analysis was performed after 7, 20 and 60 days and found significantly better healing for group 1 compared with groups 2 and 3, which were not significantly different.

EMD vs sodium fluoride treatment

Only one study compared the effects of Emdogain and sodium fluoride on the healing process of replanted teeth

(19). Central incisors of 24 Wistar rats were extracted and kept dry for 6 h. Root surfaces were treated with sodium hypochlorite for 10 min and assigned to 2% acidulated-phosphate sodium fluoride or Emdogain treatment for 10 min. The teeth were filled with calcium hydroxide, replanted and outcome parameter evaluated after 10 and 60 days. Statistical analysis was applied to the 60 days' data, but found no differences in healing parameters (19).

Discussion

The objective of the current study was to analyse systematically whether the application of EMD facilitates healing of replanted or autotransplanted teeth. However, three quarter of the published literature had to be excluded from the current systematic review because of lack of original data or adequate controls. Consequently, the small number of included trials does not contribute towards making a final verdict on the impact of EMD on healing of replanted teeth, not least because no RCT or CCT could be identified and the included CT gave conflicting results. Moreover, the CTs that were included were too heterogeneous for inference of the data. The heterogeneity was caused by variation in the *in vivo* animal models, such as duration of extraoral storage, kind of replanted teeth, EDTA conditioning prior to EMD treatment or observation period. In this context, it should be mentioned that the use of a rat model (18, 19) may diminish the impact of these studies, as the continuous eruption pattern and apical development of rat teeth are different from that of human teeth (38).

However, regarding the included CT, the study of Iqbal et al. (16) is considered most powerful as it was performed in split-mouth design rather than in parallel group design. The significance of the rat model used in the studies by Molina et al. (18) and Poi et al. (19) may be limited.

It has been considered that the biological process induced by EMD is different from what can be expected by the root surface conditioning commonly applied before replantation namely, using storage media such as tetracycline, fluoride or citric acid. Tetracycline treatment was shown to increase the pulp revascularization, presumably because of a decrease in bacterial decontamination of the root surface during the extraalveolar period (39, 40). Fluoride is applied to decrease resorption and ankylosis, while acid pretreatment is suggested to demineralise the surface and expose the collagenous matrix to achieve new connective tissue (41, 42).

The standard treatment mainly intends to reduce the risk of root resorption and ankylosis of teeth with damaged periodontium (11, 12). The intention to use EMD is to promote regeneration and reestablishment of PDL cells on the damaged root surface. This might explain the favourable outcome of EMD treatment in the studies of Iqbal et al. (16) and Lam et al. (17) compared to the study of Molina et al. (18). In the first mentioned study, EMD was applied to damaged PDL cells (16, 17), while PDL cells were mechanically removed in the study of Molina et al. (18).

Favourable PDL healing is a critical factor for success of replanted or autotransplanted teeth, not least as PDL cells might induce bone production and the repair of the mechanically damaged root surface with new cementum. PDL cells of avulsed or autotransplanted teeth can be damaged not only mechanically during the injury or during extraction, but also bio-chemically because of various extra-oral conditions (e.g. storage media). From the present systematic review, no conclusion can be drawn regarding the evidence for EMD being effective in supporting healing of replanted teeth. The results point to the need for high-quality studies in further research. To improve the evidence, the study design ought to be RCCts with a sample size that is large enough to detect possible effects of EMD treatment. Further research should also consider the effect of different storage conditions and media on efficacy of EMD conditioning. Moreover, it is unclear whether replanted teeth treated with EMD may benefit from smear layer removal by EDTA root conditioning, which is a suggested step when using EMD for regeneration of periodontal tissue. However, clinical studies on the healing of intrabony defects treated with EMD failed to show a significant effect of EDTA conditioning prior to EMD application (43, 44).

Finally, mature or immature teeth might perform differently with regard to replantation after EMD conditioning.

The present systematic search revealed only one study which compared the effect of EMD with other surface media, more precisely to sodium fluoride conditioning. Acidulated fluoride solutions have been employed for root conditioning of replanted teeth as the application of fluoride might reduce root resorption through the formation of less soluble fluorapatite on the root surface (11, 41). Thus, the biological process induced by fluoride application is quite different from the purpose of EMD treatment, which is mainly to promote growth and differentiation of PDL cells. Taking into consideration the different objections of fluoride and EMD treatment, the identified study (19) revealed no difference between the healing patterns of roots treated with EMD or sodium fluoride. As only one single study dealt with this topic, further research is required to allow for a general statement.

In conclusion, the number of publications that met all inclusion criteria was found to be very limited and did not allow for drawing evidence for EMD being effective in supporting healing of replanted teeth.

References

1. Ne RF, Witherspoon DE, Gutmann JL. Tooth resorption. Quintessence Int 1999;30:9–25.
2. Andreasen JO. External root resorption: its implication in dental traumatology, paedodontics, periodontics, orthodontics and endodontics. Int Endod J 1985;18:109–18.
3. Krasner P, Rankow HJ. New philosophy for the treatment of avulsed teeth. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1995;79:616–23.
4. Andreasen JO, Andreasen FM, Skeie A, Hjørting-Hansen E, Schwartz O. Effect of treatment delay upon pulp and

periodontal healing of traumatic dental injuries. Dent Traumatol 2002;18:116–28.
5. Venezia E, Goldstein M, Boyan BD, Schwartz Z. The use of enamel matrix derivative in the treatment of periodontal defects: a literature review and meta-analysis. Crit Rev Oral Biol Med 2004;15:382–402.
6. Esposito M, Grusovin MG, Coulthard P, Worthington HV. Enamel matrix derivative (Emdogain®) for periodontal tissue regeneration in intrabony defects. Cochrane Database Syst Rev 2005;19:CD003875.
7. Rodrigues TL, Marchesan JT, Coletta RD, Novaes AB, Grisi MF, Souza SL et al. Effects of enamel matrix derivative and transforming growth factor-beta1 on human periodontal ligament fibroblasts. J Clin Periodontol 2007;34:514–22.
8. Zeldich E, Koren R, Nemocovsky C, Weinreb M. Enamel matrix derivative stimulates human gingival fibroblast proliferation via ERK. J Dent Res 2007;86:41–6.
9. Takayanagi K, Osawa G, Naakaya H, Cochran DL, Kamoi K, Oates TW. Effects of enamel matrix derivative on bone-related mRNA expression in human periodontal ligament cells in vitro. J Periodontol 2006;77:891–8.
10. Sculean A, Schwarz F, Becker J, Brecx M. The application of an enamel matrix derivative (Emdogain) in regenerative periodontal therapy: a review. Med Princ Pract 2007;16:167–80.
11. Flores MT, Andreasen JO, Bakland LK, Feiglin B, Gutmann JL, Oikarinen K et al. Guidelines for the evaluation and management of traumatic dental injuries. Dent Traumatol 2001;17:193–8.
12. Trope M. Clinical management of the avulsed tooth: present strategies and future directions. Dent Traumatol 2002;18:1–11.
13. Faggion CM, Tu YK. Evidence-based dentistry: a model for clinical practice. J Dent Educ 2007;71:825–31.
14. Huang X, Lin J, Demner-Fushman D. Evaluation of PICO as a Knowledge Representation for Clinical Questions. AMIA Annu Symp Proc 2006:359–63.
15. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. JAMA 2000;283: 2008–12.
16. Iqbal MK, Bamaas N. Effect of enamel matrix derivative (EMDOGAIN) upon periodontal healing after replantation of incisors in beagle dogs. Dent Traumatol 2001;17:36–45.
17. Lam K, Sae-Lim V. The effect of Emdogain gel on periodontal healing in replanted monkey's teeth. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2004;97:100–7.
18. Molina GO, Brentegani LG. Use of enamel matrix protein derivative before dental reimplantation: a histometric analysis. Implant Dent 2005;14:267–73.
19. Poi WR, Carvalho RM, Panzarini SR, Sonoda CK, Manfrin TM, Rodrigues T. Influence of enamel matrix derivative (Emdogain) and sodium fluoride on the healing process in delayed tooth replantation: histologic and histometric analysis in rats. Dent Traumatol 2007;23:35–41.
20. Araujo M, Havacibara R, Sonohara M, Cardaropoli G, Lindhe J. Effect of enamel matrix proteins (Emdogain) on healing after re-implantation of 'periodontally compromised' roots. An experimental study in dogs. J Clin Periodontol 2003;30:308–10.
21. Al-Hezaimi K, Naghsbandi J, Simon JH, Oglesby S, Rotstein I. Sucessful treatment of a radicular groove by intentional replantation and Emdogain therapy. Dent Traumatol 2004;20:226–8.
22. Barrett EJ, Kenny DJ. Optimization of post-replantation healing for avulsed permanent teeth in children. Ont Dent 1999;76:23–7.
23. Caglar E, Tanboga I, Susal S. Treatment of avulsed teeth with Emdogain - a case report. Dent Traumatol 2005;21:51–3.
24. Cohenca N, Karni S, Eidlitz D, Nuni E, Moshonow J. New treatment protocols for avulsed teeth. Refuat Hapeh Vehashinayim 2004;21:48–53.
25. Hamamoto Y, Takahashi K, Sakurai H, Akiba K, Izumi N, Kanoh H et al. The use of enamel matrix derivative (Emdogain) for improvement for probing attachment level of the autotransplanted teeth. Dent Traumatol 2005;21:336–40.
26. Levin I, Ashkenazi M, Schwartz-Arad D. Preservation of alveolar bone of un-restorable traumatized maxillary incisors for future. Refuat Hapeh Vehashinayim 2004;21:54–9.
27. Kenny DJ, Barrett EJ, Casas MJ. Avulsions and intrusions: the controversial displacement injuries. J Can Dent Assoc 2003;69:308–13.
28. Kenny DJ, Barrett EJ, Johnston DH, Sigal MJ, Tenenbaum HC. Clinical management of avulsed permanent incisors using Emdogain: initial report of an investigation. J Can Dent Assoc 2000;66:21.
29. Ninomiya M, Kamata N, Fujimoto R, Ishimoto T, Suryono KJ, Nagayama M et al. Application of enamel matrix derivative in autotransplantation of an impacted maxillary premolar – a case report. J Periodontol 2002;73:346–51.
30. Hoshino S. Application of enamel matrix derivative for tooth transplantation and replantation. Kokubyo Gakkai Zasshi 2000;17:133–45.
31. Filippi A, Pohl Y, von Arx T. Treatment of replacement resorption with Emdogain – preliminary results after 10 months. Dent Traumatol 2001;17:134–8.
32. Filippi A, Pohl Y, von Arx T. Treatment of replacement resorption by intentional replantation, resection of the ankylosed sites, and Emdogain – results of a 6-year survey. Dent Traumatol 2006;22:307–11.
33. Filippi A, Pohl Y, von Arx T. Treatment of replacement resorption with Emdogain – a prospective clinical study. Dent Traumatol 2002;18:138–43.
34. Schjott M, Andreasen JO. Emdogain does not prevent progressive root resorption after replantation of avulsed teeth: a clinical study. Dent Traumatol 2005;21:46–50.
35. Chappuis V, von Arx T. Replantation of 45 avulsed permanent teeth: an 1-year follow-up study. Dent Traumatol 2005;21:269–75.
36. Barrett EJ, Kenny DJ, Tenenbaum HC, Sigal MJ, Johnston DH. Replantation of permanent incisors in children using Emdogain. Dent Traumatol 2005;21:269–75.
37. Pohl Y, Filippi A, Kirschner H. Results after replantation of avulsed permanent teeth. II. Periodontal healing and the role of physiologic storage and antiresorptive therapy. Dent Traumatol 2005;21:93–101.
38. Bosshardt DD, Schroeder HE. Cementogenesis reviewed: a comparison between human premolars and rodent molars. Anat Rec 1996;245:267–92.
39. Cvek M, Cleaton-Jones P, Austin J, Kling M, Lownie J, Fatti P. Effect of topical application of doxycycline on pulp revascularization and periodontal healing in reimplanted monkey incisors. Endod Dent Traumatol 1990;6:170–6.
40. Yanpiset K, Trope M. Pulp revascularization of replanted immature dog teeth after different treatment methods. Endod Dent Traumatol 2000;16:211–7.
41. Selvig KA, Bjortvatn K, Claffey N. Effect of stannous fluoride and tetracycline on repair after delayed replantation of root-planed teeth in dogs. Acta Odontol Scand 1990;48: 107–12.
42. Albair WB, Cobb CH, Killoy WJ. Connective tissue attachement to periodontally diseased roots after citric acid demineralisation. J Periodontol 1982;53:515–26.
43. Sculean A, Berakdar M, Willershausen B, Arweiler NB, Becker J, Schwartz F. Effect of EDTA root conditioning on the healing of intrabony defects treated with an enamel matrix derivative. J Periodontol 2006;77:1167–72.
44. Parashis AO, Tsiklakis K, Tatakis DN. EDTA gel root conditioning: lack of effect on clinical and radiographic outcomes of intrabony defect treatment with enamel matrix derivative. J Periodontol 2006;77:103–110.