

SURGICAL REGENERATION OF INTRABONY DEFECTS WITH HYALURONIC ACID

ABSTRACT

The predictable regeneration of intrabony defects often represents a particular challenge for the dental practitioner. Today the combination of Enamel matrix derivative (EMD) with an appropriate flap design represents the gold standard. Meanwhile there is increasing evidence from preclinical and clinical studies, that hyaluronic acid (HA) features a wide range of positive biologic effects on periodontal wound healing and regeneration. Recently, both animal and clinical data have shown the positive effects of HA when used in conjunction with reconstructive periodontal surgery for the regenerative treatment of intrabony defects. The present article explains the surgical procedure for the regeneration of typical intrabony defects with HA based on two clinical cases.



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SCIENTIFIC BACKGROUND AND CASE REPORTS

Intrabony defects are defined as specific osseous defects with a base apical to the interdental alveolar crest and can be a result of persistent periodontitis.¹ In case they are untreated, there is an increased risk for disease progression and additional attachment loss.²

In case deep intrabony defects couldn't be stabilized by a cause-related periodontal therapy, surgical interventions, especially using barrier membranes or enamel matrix derivatives (EMD), represent the preferred treatment.^{3,4}

In addition, to optimize wound stability and reduce morbidity, the use of specific flap designs with maximum preservation of the interdental soft tissue or limiting flap elevation through a single flap approach (SFA), are highly recommended.^{4,5}

Hyaluronic acid is an anionic, non-sulfated glycosaminoglycan that is found in practically all tissues. Among others, HA plays an important role in wound healing as well as for soft and hard tissue repair.⁶⁻⁸ Hyaluronic acid is highly biocompatibility, promotes the proliferation and migration of periodontal and gingival fibroblasts, positively influences angiogenesis and stabilizes the blood coagulum.^{8,9} Due to these positive properties, hyaluronic acid is used successfully in periodontal soft tissue surgery. The results of a randomized clinical study which was performed in my group showed that the treatment of Miller class I recessions with a coronally advanced flap and the use of hyaluronic acid (hyaDENT BG, REGEDENT GmbH) resulted in a greater reduction of the recession depth and more frequent complete recession coverage than the use of the coronally advanced flap alone.¹⁰

Up to date, two systematic reviews (i.e. only one with a meta-analysis) have been published on the effects of HA when used in conjunction with surgical periodontal therapy. The results have shown that HA in conjunction with access flap may provide positive effects demonstrated by an additional reduction in probing depth (PD) and clinical attachment level (CAL) gain in intrabony defects compared with access flap alone.^{11,12}

Recently it could be shown that HA supports periodontal regeneration histologically as well. In an animal trial two-wall intrabony defects were surgically created in beagle dogs and treated with several regenerative protocols. The use of HA alone or combinations thereof resulted in statistically significantly higher formation of cementum with inserting collagen fibers compared to flap surgery (Open flap debridement OFD) alone.¹³

In a randomized controlled clinical trial we compared the clinical outcomes obtained in intrabony defects following regenerative periodontal surgery using the single flap approach (SFA) in conjunction with either HA or EMD.

At 24-months, both treatments resulted in statistically significant clinical improvements evidenced by PD-reduction and CAL-gain. For the CAL-gain there was no statistically significant difference between HA and EMD groups.¹⁴

The following two case reports describe the surgical procedure with HA for regenerative treatment of typical intrabony defects.

As known for EMD, HA can be applied either alone or in combination with a bone filler, depending on the respective defect size and configuration. Thus, Narrow defects (Fig. 1, 2) can be treated with HA only, whereas for wide extended bone defects (Fig. 7, 8) a mixture with a bone filler is recommended.

After local anaesthesia, surgical access is obtained by preserving the integrity of the interdental soft tissue. Briefly, the buccal gingival tissue is incised at least one tooth mesial and distal to the defect site to provide access for visualization and instrumentation of the defect. Vertical releasing incisions are placed mesial and/or distal to the treated defect, if they are considered necessary to improve visibility and/or to achieve a tension free flap closure.

After flap reflection, granulation tissue is removed from the defect. Scaling and root planing is performed with hand and ultrasonic instruments and the defect is rinsed with sterile saline solution. (Fig. 3, 9)

The application procedure of HA is clearly facilitated compared to EMD. Thus, HA can be applied directly into the defect without the need of root conditioning. Furthermore the surgical site doesn't need to be dried before application. In opposite to EMD which is washed out the defect by blood, HA binds to blood and thus helps to stabilize the defect space. (Fig. 4) In case a particulate bone filler is used, mixture with HA leads to a moldable paste ("sticky bone") that facilitates graft application and ensures better defect stabilization. (Fig. 10)

The periosteum at the base of the flap is gently dissected to allow tension release and the flap is positioned at the pre-surgical level or slightly coronal without any tension. Monofilament non-resorbable 6-0 nylon suturing material is used. Selection of the suturing technique is on the basis of the flap design.⁵ Extreme care is taken to obtain primary closure of the interdental soft tissues. Figures 11–13 show the excellent early wound healing potentially induced by HA at 24h (Fig.11) and 72h (Fig. 12, 13).

Patients usually are recalled weekly for the first 6 weeks to perform gentle supragingival professional tooth cleaning and reinforcement of oral hygiene. Afterwards, the patients are enrolled into monthly recall visits during the first 6 months, and every 3 months thereafter. At the follow-up visits,

professional oral hygiene/maintenance procedures and oral hygiene instructions reinforcement were performed. Probing and subgingival instrumentation is not performed \leq 12-month re-evaluation. Figures 5, 6 and 14, 15 show the long-term result with complete defect resolution and stable hard and soft tissue conditions.

CONCLUSION

Due to the broad range of effects accompanied by the facilitated application and the reduced material costs, especially compared to EMD, the application of HA in periodontology is indicated for a wide range of clinical situations. Within the limits of the present scientific data, it can be summarized that HA appears to represent a valuable alternative for regenerative treatment in intrabony periodontal defects as well.



Fig. 1:
Initial Situation: PPD of 8 mm



Fig. 2:
OPG shows narrow intraosseous defect



Fig. 3:
Situation after flap preparation and thorough degranulation of defect.



Fig. 4:
The defect was filled with crosslinked hyaluronic acid (hyaDENT BG)



Fig. 5:
Situation after 7 years shows significant reduction of probing depth to 2 mm



Fig. 6:
OPG after 7 years shows complete defect resolution and stable tissue level.



Fig. 7:
Initial Situation: PPD of 10mm



Fig. 8:
OPG shows wide extended intraosseous defect

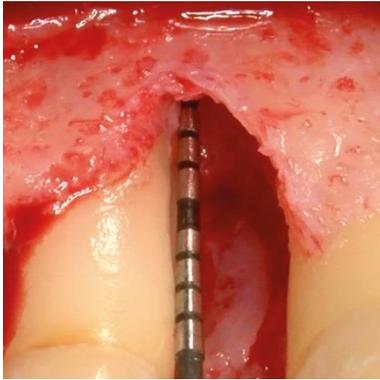


Fig. 9:
Situation after flap preparation and thorough degranulation of defect.



Fig. 10:
Defect filled with a mixture of crosslinked hyaluronic acid (hyaDENT BG) and a bone filler.



Fig. 11:
Excellent wound healing induced by HA at 24h



Fig. 12-13:
Situation 72h post-OP shows accelerated healing

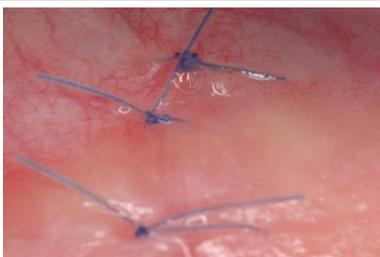


Fig. 13:
Situation 7 days post-OP shows accelerated healing



Fig 14:
Situation after 8 years shows significant reduction of probing depth to 2-3mm



Fig. 15:
OPG after 8 years shows complete defect fill and stable tissue level.

LITERATURE

1. Lang NP. Focus on intrabony defects – conservative therapy. *Periodontology* 2000. 2000; 22:51-58. doi: 10.1034/j.1600-0757.2000.2220105.x.
2. Papapanou PN, Wennstrom JL. The angular bony defect as indicator of further alveolar bone loss. *J Clin Periodontol.* 1991;18:317-322. doi: 10.1111/j.1600-051x.1991.tb00435.x.
3. Reynolds MS, Kao RT, Camargo PM, et al. Periodontal regeneration – intrabony defects: a consensus report from the AAP Regeneration Workshop. *J Periodontol.* 2015;86(2):105-107. doi: 10.1902/jop.2015.140378.
4. Nibali L, Koidou VP, Nieri M, Barbato L, Pagliaro U, Cairo F. Regenerative surgery versus access flap for the treatment of intrabony periodontal defects. A systematic review and meta-analysis. *J Clin Periodontol.* 2019;Dec 20. doi: 10.1111/jcpe.13237. [Epub ahead of print]
5. Trombelli L, Farina R, Franceschetti G, Calura G. Single-flap approach with buccal access in periodontal reconstructive procedures. *J Periodontol.* 2009;80(2):353-360. doi:10.1902/jop.2009.080420
6. Chen WY, Abatangelo G. Functions of hyaluronan in wound repair. *Wound Repair Regen.* 1999;7(2):79-89. doi: 10.1046/j.1524-475x.1999.00079.x.
7. Bertolami CN, Messadi DV. The role of proteoglycans in hard and soft tissue repair. *Crit Rev Oral Biol Med.* 1994;5(3-4):311-337. doi: 10.1177/10454411940050030601.
8. King SR, Hickerson WL, Proctor KG. Beneficial actions of exogenous hyaluronic acid on wound healing. *Surgery.* 1991;109(1):76-84.
9. Asparuhova MB, Kiryak D, Eliezer M, Mihov D, Sculean A. Activity of two hyaluronan preparations on primary human oral fibroblasts. *J Periodontol Res.* 2019;54(1):33-45. doi: 10.1111/jre.12602.
10. Piloni A, Schmidlin PR, Sahrman P, Sculean A, Rojas MA. Effectiveness of adjunctive hyaluronic acid application in coronally advanced flap in Miller class I single gingival recession sites: a randomized controlled clinical trial. *Clin Oral Investig.* 2019;23(3):1133-1141. doi: 10.1007/s00784-018-2537-4. Epub 2018 Jun 30. Erratum in: *Clin Oral Investig.* 2018;22(8):2961-2962. PMID: 29961138.

11. Bertl K, Bruckmann C, Isberg PE, Klinge B, Gotfredsen K, Stavropoulos A. Hyaluronan in non-surgical and surgical periodontal therapy: a systematic review. *J Clin Periodontol.* 2015;42(3):236-246. doi: 10.1111/jcpe.12371
12. Eliezer M, Imber JC, Sculean A, Pandis N, Teich S. Hyaluronic acid as adjunctive to non-surgical and surgical periodontal therapy: a systematic review and meta-analysis. *Clin Oral Investig.* 2019;23(9):3423-3435. doi: 10.1007/s00784-019-03012-w.
13. Shirakata Y, Nakamura T, Kawakami Y, Imafuji T, Shinohara Y, Noguchi K, Sculean A. Healing of Intrabony Defects Following Reconstructive Surgery with Hyaluronic Acid. IADR Meeting 2020, Final Presentation ID: 0225.
14. Pilloni A et al. 2021, manuscript in preparation.