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HISTOLOGICAL AND RADIOGRAPHIC EVALUATION OF THE USE OF HYALURONIC ACID AFTER IMPACTED MANDIBULAR THIRD MOLAR SURGERY

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ABSTRACT

This study was aimed to assess histological the radiographic outcomes of the use of hyaluronic acid HA after impacted mandibular third molar extractions. Twenty extractions of bilateral impacted mandibular third molars were performed in 10 patients (4 males, 6 females; 19 to 23 years old). After extraction of right and left mandibular third molars, the socket at one side received 1% HA gel soaked onto a pre-cut absorbable collagen sponge (test group) and the other was filled with blood clot (control group). Digital panoramic radiographs were obtained on (7 days and 4 months) postoperatively for bone density evaluation. Additionally, bone cores were harvested after 4 months from three patients and prepared for histologic evaluation.There were no statistically significant differences in bone density between the two groups at follow up periods. The biopsies harvested from the test and control sites exhibited various stages of bone maturation with mature osteocytes and formation without any inflammatory response or fibrous encapsulation. The application of 1% HA gel did not improve the histological and radiographic outcomes of osseous tissue after mandibular third molar extraction.

KEYWORDS: Bone healing, hyaluronic acid, impacted third molar extraction, mandibular third molar socket healing.

INTRODUCTION

Socket healing is a highly coordinated sequence of biochemical, physiologic, cellular, and molecular responses involving numerous cell types, growth factors, hormones, cytokines, and other proteins, which is directed toward restoring tissue integrity and functional capacity after injury.[1-3] After dental extraction, socket healing necessarily occurs by secondary intention; 4- 6 months are required for tissue to heal to a point where it is radiologically indistinguishable from surrounding bone.[4] Various methods have been suggested to enhance socket healing and to minimize the postoperative sequelae after third molar surgery.[5-8] Hyaluronic acid (HA) is a high molecular weight polysaccharide (glycosaminoglycan) and a major component of extracellular matrix almost in all living tissues.[9,10] It plays a critical part in the function of extracellular mineralized and non-mineralized matrices, including tissue hydrodynamics and cell migration, proliferation and differentiation.[11] Previous studies demonstrated the ability of exogenous hyaluronic acid in enhancing bone healing both experimentally[12-15] and clinically.[16-18] This study was aimed to assess histological the radiographic outcomes of the use of hyaluronic acid after impacted mandibular third molar extractions.

MATERIALS AND METHODS

Patient Selection

All patients were informed of the risks and benefits of the procedure after which they signed the consent form. The study protocol was approved by an ethical committee of Al-Andalus University for Medical Sciences. We selected 10 patients (4 males, 6 females) between the ages of 19 and 23 years, have American Society of Anesthesiologists physical status I, have bilateral mesioangular or horizontally impacted mandibular third molars, have the same difficulty level of bilateral third molars based on the Pederson classification (sum score of the spatial direction of tooth value, depth of impaction, and relation with the ramus on the panoramic radiograph)[19] and all were nonsmokers. The following patients were excluded from the study: those with signs of peri-coronitis and/or pain before surgery, those in whom the extraction of the retained third molar lasted for more than 30 min or the operation time differed by more than 5 min between the two sides, those who had undergone antibiotic or other medication therapies during the preceding 2 weeks, and those who had contraindications to the drugs or anaesthetics used in the surgical protocol. After extraction of right and left mandibular third molars, the socket at one side received 1% HA gel soaked onto a pre-cut absorbable collagen sponge (test group) and the other was filled with blood

clot (control group). The test and control sides were switched according to the order of patients. Each patient underwent two surgical operations, separated by 1 weeks.

Surgical procedure

Before surgery patients rinsed with 0.12% chlorhexidine for 2 minutes; they were not given pre-operative antimicrobica, or others drugs that might influence healing. All of the surgeries were performed by the same surgeon using a standard oral surgical procedure under local anaesthesia by nerve block of the inferior alveolar, lingual and buccal nerves, using 4% articaine containing 1:100,000 epinephrine (Medicaine, Septodont, France). The access was prepared with a mucoperiosteal envelope flap without releasing; bone removal and bone contouring were performed with a low-speed handpiece under sufficient sterile normal saline irrigation; sockets were irrigated with normal saline. After the tooth extraction the socket was thoroughly irrigated and freed from pathological tissue e.g. granulation tissue, follicular remnants and bony spicules. In the test group, the socket received 1% HA gel soaked onto a pre-cut absorbable collagen sponge Fig (1) and then the flap was sutured with 3-0 silk sutures. Post-operatively all patients were given antibiotics (amoxicillin and clavulanic acid 1000mg every 12 hours for 7 days), oral anti-inflammatory treatment (ibuprofen 1800 mg every day for 3 days) and 0.12% chlorhexidine gluconate rinses every 12 hours for 10 days. Oral hygiene was assessed and supportive periodontal therapy was provided for all patients at 2, 4, and 6 weeks after surgery. All patients were given instructions on the importance of maintenance of oral hygiene. Suture removal was done on the 7th post-operative day. All surgeries were performed by 1 surgeon, while a second surgeon performed the measurements without being aware of what therapeutic approach was used for the different sites of treatment.

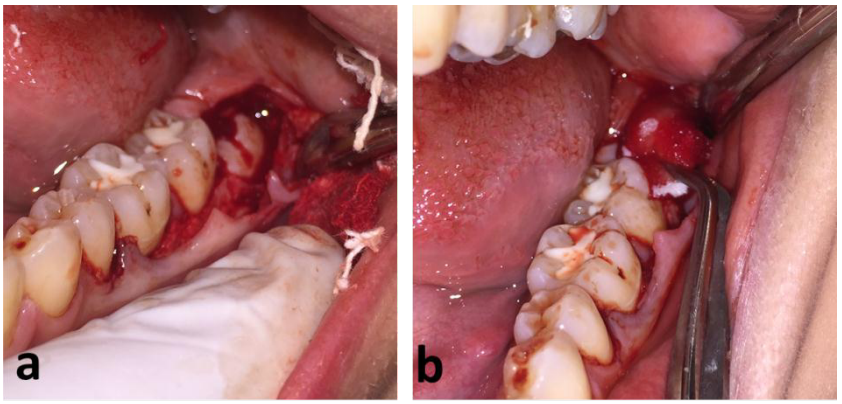

Figure 1: (a) exposure the impacted third molar , (b) application the HA with collagen sponge.

Radiographic analysis

Bone repair was assessed by digital panoramic X-rays immediately after extraction and 4 months postoperatively (Fig. 2). Radiographs were analyzed 3 times by the same examiner at different moments and the mean was calculated, using computerized image J program, which provides a reading of areas with a predefined size (in this case, the third molar extraction socket) for grayscale analysis, on a scale where absolute white has a value of 255 and black has a value of 0 (zero). Bone density was measured from "ROI" manager, "Measure" command was selected to give the mean gray value of the "ROI". The "ROI" was selected from the area corresponding to the extraction socket and was standardized for each patient. (Fig. 2)

Histological analysis

Bone cores of approximately 5 × 2mm were harvested from three patients with a trephine bur and prepared for histological evaluation. The specimens were fixed for 72 h in 10% formalin, after which they were decalcified and embedded in paraffin. Then, 5 mm plane sections were prepared and stained using hematoxylin–eosin.

RESULTS

The mean bone density was 131.30±4.14 in test group and it was 130.55±4.39 in control group immediately after extraction, after 4 month the mean bone density was 150.50±4.44 in test group and it was 151.85±4.60 in control group. There were no statistically significant difference in bone density between the two groups at follow up periods. (Table 1).

Table 1: Measurement of bone density (mean ± SD in mm).

Groups	first week	After 4 months
Control	130.55±4.39	151.85±4.60
Test	131.30±4.14	150.50±4.44
P values	0.582	0.354

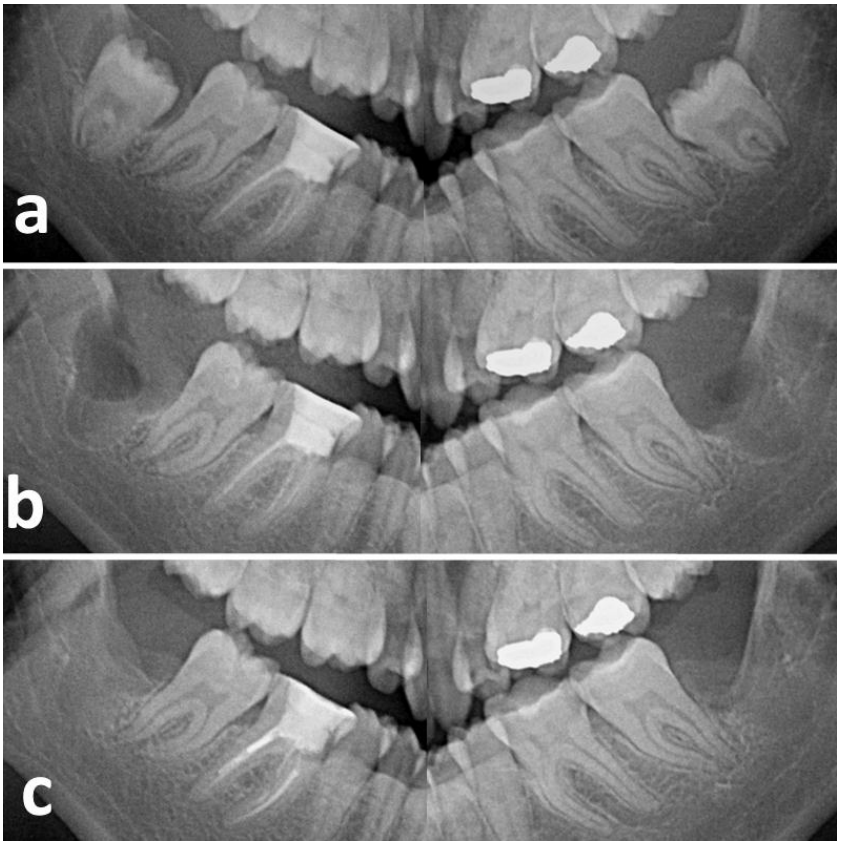

Figure 2: Panoramic radiograph of surgical site of patient with bilateral impacted mandibular third molars : (a) before extraction, (b) immediately after the extraction, (c) after 4 months.

Histological Evaluation

Histological analysis of specimens extracted from control and test sites exhibited various stages of bone maturation with mature osteocytes and formation without any inflammatory response or fibrous encapsulation. All sections showed osteoblasts adjacent to areas of woven bone, and mature bone surrounded by considerable bone marrow spaces. Fig (3)

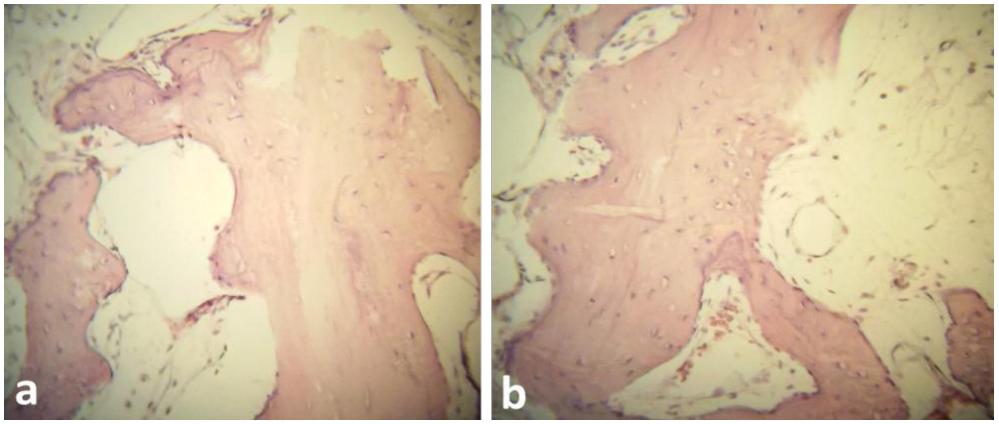

Figure 3: (a) Histologic analyses of 6months biopsy sample, a:test group, b:control group: (H&E staining, X 100).

DISCUSSION

This study was aimed to assess histological the radiographic outcomes of the use of hyaluronic acid after impacted mandibular third molar extractions. HA accelerated bone regeneration by means of chemotaxis, proliferation and successive differentiation of mesenchymal cells.[11] It significantly increased alkaline phosphatase and hence stimulate cell mineralization.[13] HA allowed the early deposition of osteoid tissue by providing a scaffold on which osteoprogenitor cell attached and so stimulated osteoblastic differentiation.[17] Aslan et al.[15] confirmed that HA needs an osteoconductive scaffold to be effective, as their findings showed that associating HA with bone grafts improved the rate of bone formation in each evaluation period. In the present study the Hyaluronic acid is loaded in

absorbable collagen sponge. Collagen sponges are well-characterized carrier systems that provide a sustained release of biomolecules with a putative role in bone regeneration.[21,22] It act as a carrier system, allowing the HA gel to remain in the wound for a longer period of time.[23] Radiographic evaluation of the extraction sockets in in the present study demonstrated that there were no statistically significant difference in bone density between the two groups at follow up periods. These results were confirmed by histological analysis of specimens extracted from control and test sites. All specimens exhibited the same histological features. In contrary to these results, Mendes et al.[24] revealed that HA could enhance healing in tooth sockets by promoting the expression of bone morphogenetic protein-2 and osteopontin. Kim et al.[25] demonstrated that the use of HA that can promote wound healing , it may be beneficial and indicated when treating infected sockets. Other clinical studies stated that combination of HA and autologus bone introduced good capabilities in accelerating bone formation when used in extractive socket and periodontal bony defect.[16-18] On the other, histomorphometric measurements in the study of Segari et al[26] revealed that, there was no influence of adding HA to CP as adjunctive to osseous tissue healing. The variations in the formulation, dose and configuration of used HA may could be the explanation of these contrary results , it was suggested that HA has a molecular weight-specific and dose-specific mode of action that may enhance the osteogenic and osteoinductive properties of bone graft materials.[12]

CONCLUSION

Within the limits of the present study, the use of hyaluronic acid after impacted mandibular third molar extractions does not improve the histological and radiographic outcomes of osseous tissue.

REFERENCES

1. Devlin H, Sloan P. (Early bone healing events in the human extraction socket). Int J Oral MaxillofacSurg, 2000; 31: 641.
2. Werner S, Grose R. (Regulation of wound healing by growth factors and cytokines). Physiol Rev, 2003; 1283:835.
3. Lieberman JR, Daluiski A, Einhorn TA. (The role of growth factors in the repair of bone). Biology and clinical applications. J Bone Joint Surg Am, 2002; 84: 1032.
4. Ellis III E, Hupp JR, Peterson LJ. Cirurgia oral e maxilofacialcontemporânea, 4th ed. São Paulo: Elsevier., 2005; pp. 59.
5. Artzi Z, Tal H, Dayan D. (Porous bovine bone mineral in healing of human extraction sockets. Part 1: Histomorphometric evaluations at 9 months). J Periodontol, 2000; 71: 1015.
6. Carmagnola D, Adriaens P, Berglundh T.(Healing of human extraction sockets filled with Bio-Oss) . Clin Oral Implants Res, 2003; 14: 137.
7. Filho RL, Silva OE, Camargo IB. (The influence of cryotherapy on reduction of swelling, pain and trismus after third molar extraction A preliminary study). J Am Dent Assoc, 2005; 136.
8. Rutkowski JL, Fennell JW, Kern JC. (Inhibition of alveolar osteitis in mandibular tooth extraction sites using platelet-rich plasma). J Oral Implantol, 2007; 13: 11.
9. Laurent TC, Fraser R. (Hyaluronan). Faseb J, 1992; 6: 2398-404.
10. Necas J, Bartosikova L, Brauner P, Kolar J. (Hyaluronic acid (hyaluronan): a review). Veterinarni Medicina, 2008; 53: 397-411.
11. Sasaki T, Watanabe C. (Stimulation of osteoinduction in bone wound healing by high-molecular hyaluronic acid) . Bone, 1995; 16: 9-15.
12. Solchaga LA, Dennis JE, Victor M, Goldberg VM, Caplan AI. (Hyaluronic acid-based polymers as cell carriers for tissueengineered repair of bone and cartilage). J Orthop Res, 1999; 3: 205-13.
13. Hunt DR, Jovanovic SA, Wikesjo UM, Wozney JM, Bernard GW. (Hyaluronan supports recombinant human bone morphgenetic protein-2 induced bone reconstruction of advanced alveolar ridge defects in dogs. A pilot study). J Periodontol, 2001; 72: 651-8.
14. Lisignoli G, Fini M, Giavaresi G, Aldini NN, Toneguzzi S, Facchini A. (Osteogenesis of large segmental radius defects enhanced by basic fibroblast growth factor activated bone marrow stromal cells grown on-woven hyaluronic acid-based polymer scaffold). Biomaterials, 2002; 23: 1043-51.
15. Aslan M, Simsek G, Day E. (The effect of hyaluronic acid supplemented bone graft in bon healing: experimental study in rabbits). J Biomater Appl, 2006; 20: 209-20.
16. Ballini A, Cantore S, Capodiferro S, Grassi F. (Esterified hyaluronic acid and autologous bone in the surgical correction of the infra-bone defects). Int J Med Sci, 2009; 6: 65-71.
17. Prato GP, Rotundo R, Magnani C, Soranzo C, Muzzi L, Cairo F. (An autologous cell hyaluronic acid graft technique for gingival augmentation: a case series). J Periodontol, 2003; 74: 262-7.
18. Baldini A, Zaffe D, Nicolin G. (Bone-defects healing by highmolecular hyaluronic acid: preliminary results). Annali di Stomatologia, 2010; I: 2-7.
19. Pedersen GW. Surgical removal of teeth. In: Pedersen GW (ed). Oral Surgery, Philadelphia, PA, WB Saunders., 1988; 63.
20. Jentsch H, Pomowski R, Kundt G, G€ocke R. (Treatment of gingivitis with hyaluronan) . J Clin Periodontol, 2003; 30: 159-64.
21. Friess W, Uludag H, Foskett S, Biron R, Sargeant C. (Characterization of absorbable collagen sponges as rhBMP-2 carriers). International Journal of Pharmaceutics, 1999; 187: 91–99.
22. Geiger M, Li RH, Friess W. (Collagen sponges for bone regeneration with rhBMP-2). Advanced Drug Delivery Reviews, 2003; 55: 1613–1629.

23. de Brito Bezerra B, Mendes Brazao MA, de Campos ML, Casati MZ, Sallum EA, Sallum AW. (Association of hyaluronic acid with a collagen scaffold may improve bone healing in critical-size bone defects). Clin Oral Implants Res, 2012; 23: 938-942.
24. Mendes RM, Silva GA, Lima MF. (Sodium hyaluronate accelerates the healing process in tooth sockets of rats). Arch Oral Biol, 2008; 53(11): 55-1162.
25. Kim JJ1, Song HY, Ben Amara H, Kyung-Rim K, Koo KT. (Hyaluronic Acid Improves Bone Formation in Extraction Sockets With Chronic Pathology: A Pilot Study in Dogs). J Periodontol, 2016; 87(7): 790-5.
26. Segari W, Radwan D, Abd El Hamid M.(The effect of adding hyaluronic acid to calcium phosphate on periapical tissue healing following periradicular surgery in dogs). Tanta Dental Journal, 2014; 11:122-129.