ASDJ
AINSHAMS DENTAL JOURNAL

Print ISSN 1110-7642
Online ISSN 2735-5039

AIN SHAMS DENTAL JOURNAL
Official Publication of Ain Shams Dental School
June 2021 • Vol. XXIV

Regeneration ability of immature teeth with necrotic pulp using hyaluronic acid a scaffold (clinical study)

Engy Ahmed Mohamed Mazen[1], Kareem Mostafa Al Batoty[2],Mohamed Mokhtar Nagy[3]

Abstract:

Aim: Is to assess Hyaluronic acid as scaffold for regenerative endodontic procedures (REPs).
Methodology: A sample of 30 patients have been chosen randomly from Endodontic department of faculty of Dentistry Ain shams University and divided randomly into 2 groups (15 patients in each one) (n=15). The 2groups were treated with classic protocol of ERT **(acc. To AAE considerations)** by blood clot formation (B.C), but the second one was received additional step which is injecting a scaffold using cross-linked injectable Hyaluronic acid gel as scaffold.
Results: The percentage of difference in tooth length, root thickness, apical diameter between the 2 groups were statistically analysed by calculating Mean and standard deviation. The significance level was set at P</= 0.05. Difference in percentage of root length change bett. 2groups P=0.963. Difference in percentage of root thickness change bett. 2groups P=0.035. Difference in percentage of apex diameter change bett .2groups P=0.035.
Conclusion: Cross linked Hyaluronic acid can be used as a scaffold in REPs.
Keywords Regenerative endodontics procedures, Scaffolds, Hyaluronic acid.

1 BDS, MSc Dept of Endodontics, Faculty of Dentistry, Ain Shams University
2 Prof. Dept of Endodontics, Faculty of Dentistry, Ain Shams University
3 Ass.Prof. Dept of Endodontics, Faculty of Dentistry, Ain shams University

Introduction:

The most dramatic event that may happen to a developing tooth is loss of ability of completing root development because of pulp necrosis due to caries or trauma. Treating immature non vital teeth is considered a challenge. Greatest challenge against survival of these teeth is the thin root with open apex. Open apex provides no stopping point at which endo-filling ends. Also, thin walls remain liable to perforation or fracture during mechanical preparation. Previously, these cases were treated with apexification where, calcium hydroxide is used to induce calcified barrier formation against which guttapercha can be condensed. Unfortunately, this treatment doesn't improve the root. Also, long-term use of calcium hydroxide has a negative weakening effect on the radicular dentin. The need for pulp regeneration appeared as a treatment option for such difficult cases to achieve complete root formation. Guided tissue and guided bone regeneration therapies have been established as viable treatment options with high success rates (1, 2). In the field of endodontics Regenerative endodontic procedures (REPs) represents tissue engineering aiming at achieving pulp regeneration in immature teeth that suffer from pulp necrosis and apical periodontitis (3). Tissue engineering is fundamentally based on the interaction among stem cells, three-dimensional scaffold materials, and biochemical molecules (4). Stem cells can differentiate into odontoblastic like cells, and fibroblast to produce functional dentin pulp complex like tissue, achieved by seeding the stem cells into a scaffold in presence of controlling factors. Scaffolds are 3D structures that mimic extracellular matrix, which plays basic role in cells adhesion and proliferation during tissue formation. Hyaluronic acid gel was tested in this study regarding ability to act as scaffold in REPs.

Methodology:

A sample of 30 patients have been chosen randomly and divided into 2 groups (15 patients in each one). The first group was treated with classic protocol of ERT **(acc. To AAE considerations)** by blood clot formation (B.C). The second one was treated by classic protocol along with cross-linked injectable Hyaluronic acid gel as scaffold. Hyaluronic acid was confirmed to be safe and doesn't induce inflammatory reactions by

reviewing the properties of the used product, also it was used in cosmetic dermatological fields without any documented inflammatory response to it. The 2 groups were treated on 2 visits. In the first visit the canals were cleaned by minimal mechanical prep. Then, disinfected with disinfection protocol including (20 ml/5 min. Naocl then 20ml saline), then canals were dried and Metapaste was injected inside the canal. In the second visit after 2weeks absence of any inflammatory signs and symptoms were confirmed then, canals were irrigated with EDTA 17% 20 ml/5 min. Followed by saline. Canals were dried and inducing bleeding periapically using pre bent hedstorm file 40# in the 2groups. In the second group there was one more step of injecting H.A inside the canals, after blood clot was formed inside each tooth MTA plug was put on the canal orifice and the teeth were restored finally with composite. The 2 groups were followed up every 3months for a year. The evaluation was based on clinical examination for any signs of failure as pain, fistula, abscess and radio graphically to exclude any apical lesions. Also, digital tracing the change in root length, thickness and apical closure using (J Graph).

Results:

The percentage of difference in tooth length, root thickness, apical diameter between the 2 groups were statistically analyzed by calculating Mean and standard deviation. The significance level was set at p </= 0.05.

Regarding the change in root length.

The change in group (II) (12.49±3.10) was higher than that of group (I) (12.33±8.19) yet the difference was not statistically significant (p=0.963). **Figure (1)**

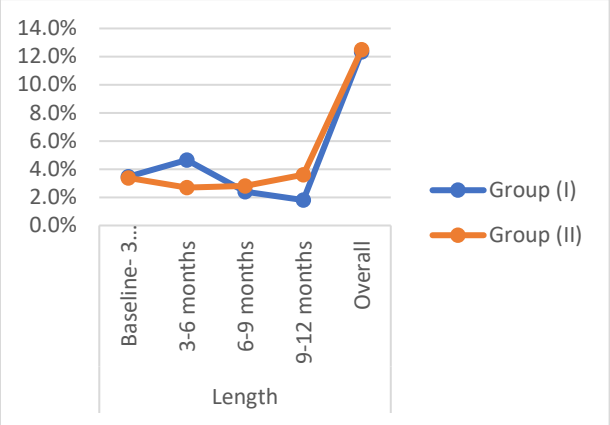


Figure (1) Line chart showing percentage difference change of root length

Regarding change in root thickness:
The change in group (II) (58.69±30.16) was significantly higher than that of group (I) (23.33±14.28) (p=0.035). **Figure (2)**

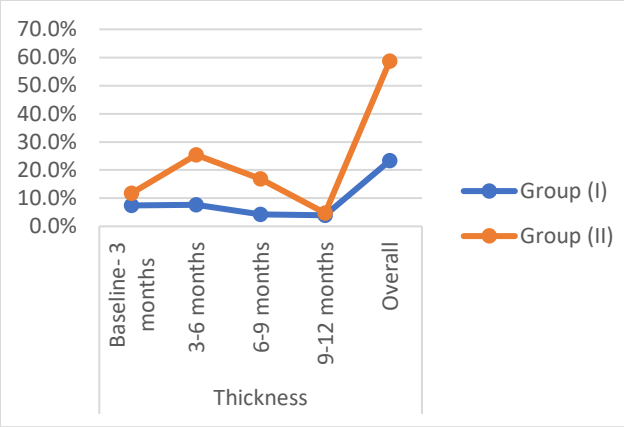


Figure (2) Line chart showing percentage difference change of root thickness

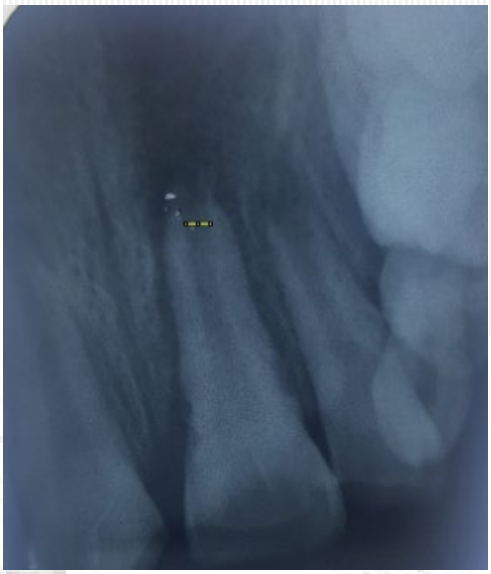


Figure (4) Baseline x ray

Regarding change in apical closure. The change in group (II) (58.69±30.16) was significantly higher than that of group (I) (23.33±14.28) (p=0.035). **Figure (3)**

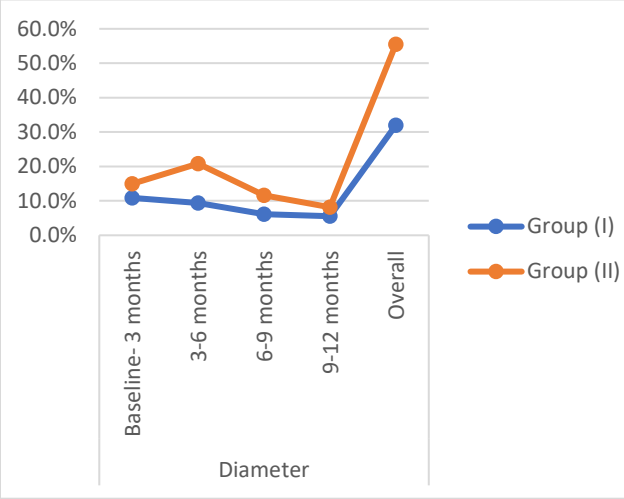
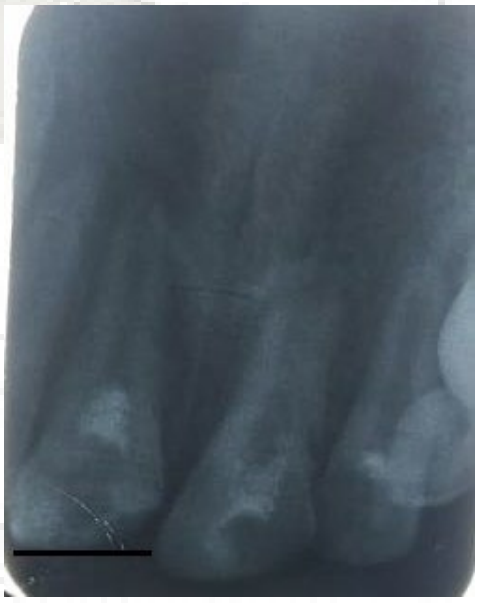


Figure (3): Line chart showing percentage difference change of apical diameter.



Discussion:

Scaffolds play an important role in ERPs. They're considered 3D structures that mimic extracellular matrix. They represent a structure base for cell adherence, proliferation and intercellular signals.

The choice of an appropriate scaffold is a crucial step for tissue engineering strategies such as endodontic regenerative approaches [5,6]. Several synthetic scaffolds have also been proposed for dental pulp engineering; the majority are polymers [7,8] and hydrogels [9,10] Inside the root canal system, an ideal scaffold should be able to attach to the dentinal walls, provide a sufficient structural support in the centre of the canal space [11]. The basic requirements for ideal scaffold are being source for growth factors, biocompatible and, has suitable degradation rate. Scaffolds can be classified according to biodegradability into biodegradable scaffolds, and biostable or permanent scaffolds [12], according to form into solid blocks, sheets, porous sponge, and injectable hydrogel [9] according to presence or absence of cells into cell free scaffolds, and scaffolds seeded with stem cells [13] and according to Origin into natural scaffolds, and synthetic scaffolds [14]

Hyaluronic acid is a natural biodegradable gel. Hyaluronic acid (HA) has been proposed as a promising scaffold in dental pulp regeneration because of its biocompatibility and biodegradation properties and most importantly because of its role in dental hard tissue formation [15,16]. However, the main disadvantage is rapid degradation and low mechanical properties which were overcome by crosslinking. Different types of scaffolds were suggested to be used in RET [7,17,9] but, not FDA approved.

Stylg (injectable H.A gel) is FDA approved as filler for skin injection was tested as scaffold in this study.

Results in this study demonstrated clear difference between group (I) treated with (BC) without scaffold and group (II) treated with (BC) along with scaffold. Difference in percentage of change in root thickness was significantly higher in group (II) than in group(I) especially at (3m- 6m) follow up (23.24+/-18.10) (6.99+/-4.57) respectively and at the final follow up (12m) (58.69+/-30.16) (23.33+/-14.28) respectively.

Also, percentage of change in difference in apical closure was significantly higher in group (II) than in group(I) at (3m-6m) follow up where, it was (22.78+/-9.67) (9.32+/-5.89) respectively and, at(12m) where the result was (54.4+/-6.01) (30.99+/-7.65) respectively. This promoting effect of H.A may be due to it is capable of stimulating (SCPA) mineralization and odontogenic

differentiation. Also, cross-linked H.A degradation rate which is about (6m) makes it provides structural base for the new formed tissue for reasonable time. These results are similar to other studies indicating the role of HA in dentine formation [16,18,19,20].

Finally, our conclusion is supported by another research investigated different brand of injectable hyaluronic acid gel in an in vitro study. This research stated that Restylane, an FDA-approved HA-based injectable gel, promoted cell viability, mineralization, and odontoblastic-like differentiation when cultured with SCAP (11). These results indicated for the first time that an FDA-approved product can be a promising scaffold for chairside REPs and that it may, along with other factors, lead to dental pulp regeneration [11] .

Conclusion:

Cross linked Hyaluronic acid can be used as a scaffold. It's to be considered a promising potential scaffold that needs more and more investigations to make use of its benefits at the best way.

References

1. **Costello BJ, Shah G, Kumta P, Sfeir CS.** Regenerative medicine for craniomaxillofacial surgery. Oral Maxillofac Surg Clin North Am 2010;22:33–42.
2. **Villar CC, Cochran DL.** Regeneration of periodontal tissues: guided tissue regeneration. Dent Clin North Am 2010;54:73–92.
3. **Murray PE, Garcia-Godoy F, Hargreaves KM**. Regenerative endodontics: a review of current status and a call for action. Journal of Endodontic2007;33:37790.
4. **Langer R, Vacanti JP**. Tissue engineering.Science1993May;14:260(5110):920 6.
5. **Hargreaves KM, Diogenes A, Teixeira FB.** Treatment options: biological basis of regenerative endodontic procedures. Journal of Endodontics 2013;39:S30–43.
6. **Nakashima M, Akamine A**. The application of tissue engineering to regeneration of pulp and dentin in endodontics. Journal of Endodontics 2005;31:711–8.
7. **Bohl KS, Shon J, Rutherford B, Mooney DJ.** Role of synthetic extracellular matrix in development of engineered dental pulp. J Biomater Sci Polym Ed 1998;9:749–64.
8. **Huang GT, Yamaza T, Shea LD, et al.** Stem/progenitor cell-mediated de novo regeneration of dental pulp with newly deposited continuous layer of dentin in an in vivo model. Tissue Eng Part A 2010;16:605–15.
9. **Cavalcanti BN, Zeitlin BD, Nor JE.** A hydrogel scaffold that maintains viability and supports differentiation of dental pulp stem cells. Dent Mater 2013;29:97102.
10. **Prescott RS, Alsanea R, Fayad MI, et al**. In vivo generation of dental pulp-like tissue by using dental pulp stem cells, a collagen scaffold, and dentin matrix protein 1 after subcutaneous transplantation in mice. J Endod 2008;34:421–6.
11. **Chrepa V, Austah O, Diogenes A**. Evaluation of a Commercially Available Hyaluronic Acid Hydrogel (Restylane) as Injectable Scaffold for Dental Pulp Regeneration: An In Vitro Evaluation. Journal of endodontics. 2017 feb.;43(2):257-262.

12. **Sureshchandra B, Roma M.** Regeneration of dental pulp: A myth or hype. Endodontology. 2013; 13: 139-54.

13. **Zhu W, Zhu X, Huang GJ, Cheung GS, Dissanayaka WL, Zhang C.** Regeneration of dental pulp tissue in immature teeth with apical periodontitis using platelet‐rich plasma and dental pulp cells. International endodontic journal. 2013 Oct 1; 46(10):962-70.

14. **Galler KM, D'Souza RN, Hartgerink JD, Schmalz G.** Scaffolds for dental pulp tissue engineering. Adv Dent Res 2011; 23:333–9.22.

15. **Inuyama Y, Kitamura C, Nishihara T, et al.** Effects of hyaluronic acid sponge as a scaffold on odontoblastic cell line and amputated dental pulp. J Biomed Mater Res B Appl Biomater 2010;92:120–8. 23.

16. **Chen KL, Yeh YY, Lung J, et al.** Mineralization effect of hyaluronan on dental pulp cells via CD44. J Endod 2016;42:711–6..

17. **Gronthos S, Mankani M, Brahim J, et al**. Postnatal human dental pulp stem cells (DPSCs) in vitro and in vivo. Proc Natl Acad Sci U S A 2000;97:13625–30.

18. **Felszeghy S, Meszar Z, Prehm P, Modis L.** The expression pattern of hyaluronan synthase during human tooth development. Arch Oral Biol 2005;50:175–9.

19. **Felszeghy S, Hyttinen M, Tammi R, et al.** Quantitative image analysis of hyaluronan expression in human tooth germs. Eur J Oral Sci 2000;108:320–6.

20. **Sasaki T, Kawamata-Kido H.** Providing an environment for reparative dentine induction in amputated rat molar pulp by high molecular-weight hyaluronic acid. Arch Oral Biol 1995;40:209–19.