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Assessment of outcome of regenerative endodontics for treatment of periapical lesions

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***Abstract*---**Background: Three key elements are essential for performing REPs: stem cells, scaffolds, and activators. The present study was conducted to assess outcome of regenerative endodontics for treatment of periapical lesions. Materials & Methods: 40 patients with mature incisors, canines, or mandibular premolars showing pulp necrosis and apical periodontitis were divided into group I (REP) and conventional root canal treatment (ENDO) group II. Calcium hydroxide medication was used,and the cavity was sealed. 3 weeks later, patients were treated following their assigned protocolof ENDO or REP. Clinical follow-up examinations were performed at 6 months and 12 months. Results: At 6 months, success was seen in 20 teeth in group I and 18 in group II and failure in2 in group II. At 12 months, success was seen

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in 20 in each group. The mean height (mm) at 6 months was 2.5 and 2.8 in group I and II, at 12 months was 1.6 and 1.9. Anterior-posterior dimension at 6 months was 2.6 and 2.7 and at 12 months was 1.8 and 2.2. Mesiodistal dimension at 6 months was 3.1 and 2.5 and at 12 months was 1.8 and 2.1 in group I and II respectively. The difference was non- significant (P>0.05). Conclusion: The use of allogenic umbilical cord mesenchymal stem cells encapsulated in a plasma-derived biomaterial is a promising alternative for the treatment of periapical pathology.

***Keywords*---**allogenic umbilical cord, stem cells, periapical pathology.

Introduction

Regenerative endodontic procedures have been defined as 'biologically based procedures that intend to physiologically replace damaged tooth structures, including dentine and root, as well as cells of the pulp–dentin complex'.[1] REPs were first exclusively developed for the treatment of immature teeth, with the purpose of achieving a complete root development, increasing the root length, thickening the root wall, and accomplishing apical closure.[2]

Three key elements are essential for performing REPs: stem cells, scaffolds, and activators. These techniques begin with the disinfection of the root canal system, followed by the induction of bleeding in the periapical region with the purpose of obtaining a blood clot.[3] This mass would behave as a natural scaffold for the migration of undifferentiated stem cells that come from outside the apex, mostly from the alveolar bone and periodontal ligament, while providing growth factors that stimulate cell differentiation and proliferation, inducing the formation of new tissue.[4] The benefit of regenerative endodontics over apexification is that with regenerative endodontics root lengthening and thickening is possible whereas with apexification it is not possible. Moreover, regenerative endodontics prevent reinfection by providing adequate coronal seal.[5] It utilizes scaffold which offers the framework for cell growth and differentiation at a local site. For the successful outcome of regenerative endodontics, a porous, biocompatible and correct shaped scaffold is of paramount importance.[6] The present study was conducted to assess outcome of regenerative endodontics for treatment of periapical lesions.

Materials & Methods

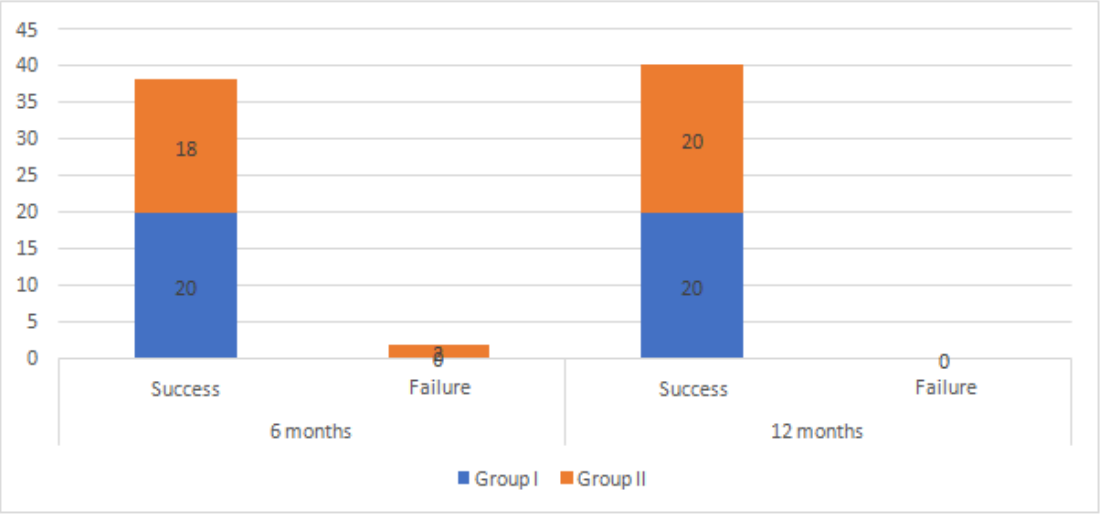
The present study comprised of 40 patients with mature incisors, canines, or mandibular premolars showing pulp necrosis and apical periodontitis. Patients were divided into group I (REP) and conventional root canal treatment (ENDO) group II. On the first visit, cavity access and mechanical preparation of the root canal were performed. Calcium hydroxide medication was used, and the cavity was sealed. 3 weeks later, patients were treated following their assigned protocol of ENDO or REP. Clinical follow-up examinations were performed at 6 months and 12 months. Data thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

Results

Table I Assessment of success and failure in both groups

Time period	Outcome	Group I	Group II	P value
6 months	Success	20	18	0.01
	Failure	0	2	
12 months	Success	20	20	0.05
	Failure	0	0	

Table I shows that at 6 months, success was seen in 20 teeth in group I and 18 in group II andfailure in 2 in group II. At 12 months, success was seen in 20 in each group. The difference was significant (P< 0.05).

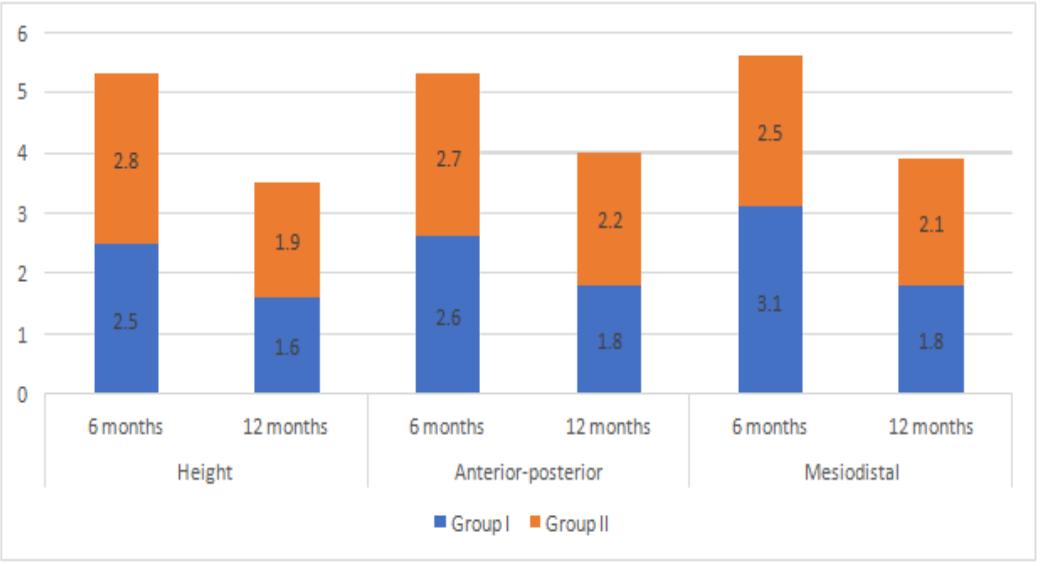


Graph I Assessment of success and failure in both groups

Table II Measurement of apical lesions

Dimension	Outcome	Group I	Group II	P value
Height	6 months	2.5	2.8	0.91
	12 months	1.6	1.9	
Anterior-posterior	6 months	2.6	2.7	0.82
	12 months	1.8	2.2	
Mesiodistal	6 months	3.1	2.5	0.57
	12 months	1.8	2.1	

Table II, graph II shows that mean height (mm) at 6 months was 2.5 and 2.8 in group I and II, at 12 months was 1.6 and 1.9. Anterior-posterior dimension at 6 months was 2.6 and 2.7 and at 12 months was 1.8 and 2.2. Mesiodistal dimension at 6 months was 3.1 and 2.5 and at 12 months was 1.8 and 2.1 in group I and II respectively. The difference was non- significant (P>0.05).



Graph II Measurement of apical lesions

Discussion

Optimized cell delivery systems are key for successful therapy. Cell encapsulation presents important benefits by circumventing current issues related to stem cell transplantation, such as low cell viability and poor retention in vivo.[7] In addition, scaffold containing growth factors can leverage the stem cell properties by providing tissue-like environments with specific cellular signals sustaining therapeutic cell stabilization for prolonged periods in the engraftment site.[8] Scaffolds promoting cell proliferation are classified as natural or synthetic. Some examples of natural scaffolds are blood clot and platelet-derived scaffolds.[9] Platelet-poor plasma (PPP) is the blood fraction with a reduced count of platelets. Finally, growth factors stimulate cellular proliferation and differentiation and are placed in the dentin matrix and scaffolds.[10] The present study was conducted to assess outcome of regenerative endodontics for treatment of periapical lesions.

We found that at 6 months, success was seen in 20 teeth in group I and 18 in group II and failure in 2 in group II. At 12 months, success was seen in 20 in each group. Brizuela et al[11] evaluated the safety and efficacy of encapsulated human umbilical cord mesenchymal stem cells in a plasma-derived biomaterial for regenerative endodontic procedures (REPs) in mature permanent teeth with apical lesions. The trial included 36 patients with mature incisors, canines, or mandibular premolars showing pulp necrosis and apical periodontitis. Patients were randomly and equally allocated between experimental (REP) or conventional root canal treatment (ENDO) groups. On the first visit, cavity access and mechanical preparation of the root canal were performed. Calcium hydroxide medication was used, and the cavity was sealed. Three weeks later, patients were treated following their assigned protocol of ENDO or REP. Clinical follow-up examinations were performed at 6 and 12 mo. The evolution over time of the percentage of perfusion units and the dimensions of lesion and cortical

compromise were explored. After the 12-mo follow-up, no adverse events were reported, and the patients showed 100% clinical efficacy in both groups. Interestingly, in the REP group, the perfusion unit percentage measured by laser Doppler flowmetry revealed an increase from 60.6% to 78.1% between baseline and 12-mo follow-up. Sensitivity tests revealed an increase of the positive pulp response in the REP group at 12-mo follow-up (from 6% to 56% on the cold test, from 0% to 28% on the hot test, and from 17% to 50% on the electrical test).

We found that mean height (mm) at 6 months was 2.5 and 2.8 in group I and II, at 12 months was 1.6 and 1.9. Anterior-posterior dimension at 6 months was 2.6 and 2.7 and at 12 months was 1.8 and 2.2. Mesiodistal dimension at 6 months was 3.1 and 2.5 and at 12 months was 1.8and 2.1 in group I and II respectively. Garrido-Parada et al[12] from the 539 studies identified through the initial search, 23 studies were qualified for the final analysis (3 randomized controlled trials and 20 case reports). The results in mature adult teeth indicate a success rate of 96.35 and 100% in bone healing through the randomized controlled trials and case reports, respectively; 100% in absence of clinical symptoms, and 58 and 62.5% in positive response tosensibility tests. The success rate in the case reports in teeth with open apex reported a 61.5% of root development, 100% of bone healing, 96.15% of absence of clinical symptoms, and 43.7% of positive response to sensibility tests. The current evidence is scarce but emerging, soREPs may be a promising alternative for treating adult necrotic teeth. The clinical protocol proposed is based on the evidence available and age considerations, and should be updated in the future.

Nangia et al[13] determined the overall clinical and/or radiographic success rate (O) of REP (I) in mature permanent teeth (P) and to compare it (C) with nonsurgical endodontic treatment (NSET). The overall success rate of REP was calculated using data from both randomized clinical trials and single-arm prospective studies. Sensitivity analysis and subgroup analysis were performed. Ten studies (n = 552) were included. R.D between REP and NSET was 0.032 (95% C.I: 0.023–0.087; P = 0.258). Overall success rate of REP was 96.0% (95% confidence interval: 94%–98%). No significant difference was found in sensitivity analysis (P = 0.551), orany of the subgroup analysis

Conclusion

Authors found that the use of allogenic umbilical cord mesenchymal stem cells encapsulated in a plasma-derived biomaterial is a promising alternative for the treatment of periapical pathology.

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