Clinical and Radiographic Assessment of the Efficacy of a Collagen Membrane in Regenerative Endodontics: A Randomized, Controlled Clinical Trial

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Abstract

Introduction: Recent reviews confirm a general lack of randomized, controlled clinical studies on the efficacy of regenerative endodontics in immature teeth affected by pulp and periapical diseases. Moreover, we have no evidence of the curative efficacy of collagen membranes used as scaffolds in regenerative endodontics. Here, we evaluated whether a Bio-Gide collagen membrane (Geistlich Pharma AG, Wolhusen, Switzerland) has efficacy in promoting dentin formation in regenerative endodontics. **Methods:** Forty-three patients yielding a total of 46 nonvital immature teeth were divided randomly into 2 groups. Subsequent to chemomechanical preparation, regenerative endodontics with (the experimental group) and without (the control group) Bio-Gide were performed. All cases were followed up clinically and radiographically every 3 months for at least 6 months. Quantitative analyses using an imaging program yielded percentage changes in root dimensions based on a comparison between preoperative and recall radiographs. **Results:** The results of 40 patients (43 teeth) were included in the final analyses. All patients from both groups showed clinical success with complete resolution of signs and symptoms. Radiographically, the thickness of the dentin wall at the middle third of the root was higher for the experimental group than the control group. However, other indicators were comparable between both groups. **Conclusions:** The use of the Bio-Gide collagen membrane promoted the development of the dentin wall in the middle third of the root in patients undergoing regenerative endodontic procedures. The convenience of operation and the assured positioning of the sealing material make the Bio-Gide collagen membrane especially suitable for handling wide root canals. *(J Endod 2017;■:1–7)*

Key Words

Dental pulp necrosis, immature teeth, radiography, regenerative endodontics, revascularization

Significance

This randomized, controlled clinical study evaluated the efficacy of a Bio-Gide collagen in promoting dentin formation in regenerative endodontics and provided evidence to support the use of collagen matrix in regenerative endodontics.

Pulp necrosis in an immature tooth with an open apex can lead to devastating consequences for the patient and represents a distinct challenge for the endodontist. Before 2004, clinicians relied on a "traditional" apexification procedure or the use of apical barriers (1, 2). However, neither procedure allows for thickening of the root wall or continued development of the root. In 2004, a novel treatment procedure for immature, nonvital teeth called "regenerative endodontics" (revascularization) was introduced by Banchs and Trope (3). In contrast to traditional apexification or the use of apical barriers, this procedure allowed for increasing both the length of the root and dentin wall thickness. Many case reports have since shown favorable outcomes after the eradication of bacteria from the root canal system, the formation of a scaffold in the canal space, and the creation of a bacteria-tight coronal seal (4–8). Although following a similar concept of regenerative endodontics, their treatment protocols vary in terms of the use of irrigants (8–10), intracanal disinfectant medications (3, 4, 6, 10), canal scaffolds (7, 11), and sealing materials (4, 9, 10, 12, 13). The search for an optimal revascularization protocol is ongoing.

In terms of the scaffold, most reported cases induce a blood clot from the apical foramen to allow the growth of a new tissue into the canal. However, in clinical practice, we cannot always induce sufficient blood to serve as a scaffold, which also increases the likelihood of sealing material collapse. In 2008, a resorbable collagen membrane was introduced to prevent the mineral trioxide aggregate (MTA) from collapsing and to serve as a scaffold to allow new tissue growth into the pulp space in cases with insufficient blood (5). However, to date, no randomized, controlled clinical study has provided persuasive evidence of the efficacy of collagen membranes in inducing root maturation.

The Bio-Gide (Geistlich Pharma AG, Wolhusen, Switzerland) (Fig. 1) is an absorbable, pure collagen membrane used widely as a scaffold material in periodontal tissue regeneration (14, 15). It consists of types I and III collagen extracted from quarantined pigs and refined to remove antigens; it has no antigen-sensitizing effects. Its degradation products include carbon dioxide and water, and the degradation period is in the range

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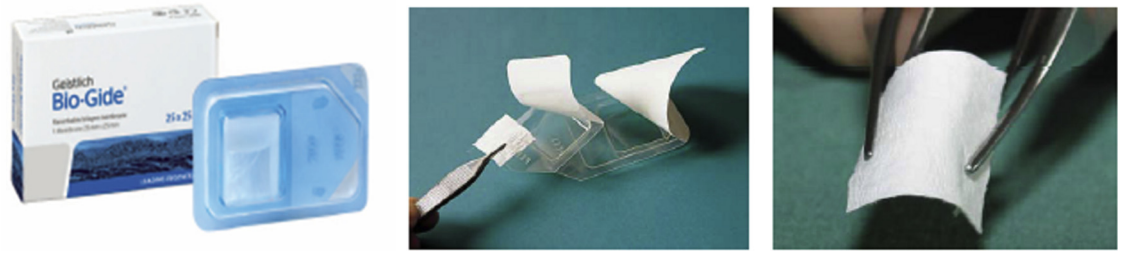

Figure 1. The Bio-Gide.

of 4 to 6 months to provide time for tissue reconstruction (16, 17). To date, no study of the curative efficacy of it used as a scaffold in regenerative endodontics has been reported. Experiments have shown that it can promote the adherence, migration, proliferation, and differentiation of ectomesenchymal cells (17, 18). It has many advantages, such as the ability to stabilize blood clots, maintain growth factor levels, and promote tissue regeneration (14–17). Therefore, its use in regenerative endodontics is desirable, especially in cases in which we cannot induce sufficient blood into the pulp space. We decided to use the Bio-Gide membrane as a scaffold material because it may promote the formation of the dentin in case we could not induce enough blood into the pulp space and may even help to promote the overall curative effect.

In this randomized, controlled clinical study, we investigated the efficacy of the Bio-Gide collagen membrane in promoting dentin formation in regenerative endodontics following the Consolidated Standards of Reporting Trials guidelines. The null hypothesis was that the use of the Bio-Gide collagen membrane would not promote dentin formation in regenerative endodontics.

Materials and Methods

Study Design and Sample Size

This 2-arm, parallel, randomized, controlled clinical study compared dentin formation in a regenerative endodontic procedure between an experimental group in which a Bio-Gide collagen membrane served as a scaffold and a control group without its use.

This study was performed in the Department of Pediatric Dentistry, Peking University School and Hospital of Stomatology, Beijing, China. The study protocol was approved by the Ethics Committee of Peking University School and Hospital of Stomatology (ref no. PKUSSIRB-201523072).

The present study was designed based on the work of Nagy et al (19) to have 80% power in detecting a difference between the 2 groups. The increases of root thickness in the 2 groups after 6 months were 5.8% ± 1.2% and 4.5% ± 1.6%, respectively. A sample size of 46 teeth to detect differences at the 5% level of significance using the *t* test for testing 2 independent means was calculated with an anticipated loss to follow-up of 10% included.

Children who underwent dental treatment at the Department of Pediatric Dentistry, Peking University Hospital of Stomatology, from January 2014 to February 2016 were recruited. In all cases, the following protocol was followed. It was explained to all patients and their caregivers that regenerative endodontic procedures were relatively new and that, to date, there were no guidelines for treatment protocols in the literature. A comprehensive discussion of the risks, complications, and alternative treatment options was undertaken, and parental consent was obtained. The informed consent form also explained that data from the procedure would be used for research purposes and that patient anonymity would be protected.

A simple random sampling method was used to recruit patients. Forty-six group information notes (23 for controls and 23 for the experimental group) were packed randomly into 46 opaque envelopes after generating a random sequence, and each envelope was numbered sequentially and handed over to each patient according to the time the participant joined the study. Inclusion criteria were an open apex >2 mm in diameter, absence of systemic or immune disease, and absence of known allergies to the medications used in the procedure. Exclusion criteria were a closed apex, apical cysts, and existing disease that needed long-term anti-inflammatory treatment.

Interventions

All of the regenerative endodontic procedures were performed by experienced faculty members of the department following similar protocols according to the clinical considerations for a regenerative procedure advised by the American Association of Endodontists. Clinical examinations, pulp sensitivity, and radiographic examinations were performed. A medical history, clinical symptoms, and preoperative examination of the tooth were collected before the operation.

During the first treatment visit, the access cavity was prepared under rubber dam isolation using 4% articaine with epinephrine 1:100,000. Copious, gentle irrigation was provided twice: first with 1.25% sodium hypochlorite (20 mL, 5 minutes) using an irrigating needle positioned ~1 mm from the root end to minimize cytotoxicity to stem cells in the apical tissues and then again with saline (20 mL/canal, 5 minutes). Canals were dried with paper points. Calcium hydroxide paste was delivered into the canal system using a syringe, and the canal was temporarily sealed using a 3–4 mm glass ionomer.

Teeth were reviewed 2 weeks later to assess the response to the initial treatment. If there was any sign or symptom of persistent infection, additional treatment was considered with intracanal medications.

For the second surgery, anesthesia was induced with 2% lidocaine without a vasoconstrictor. The tooth was isolated with a dental dam. Copious, gentle irrigation was provided with 20 mL 17% EDTA. The canal was dried with paper points. Bleeding in the canal system was infused by rotating a precurved K-file at 2 mm past the apical foramen. The Bio-Gide collagen membrane was placed at the middle third of the root, over the blood clot, and ProRoot MTA (Dentsply Tulsa Dental, Johnson City, TN) was used as a capping material. A layer of Filtek Z250 composite resin (3M ESPE, Irvine, CA; 3–4 mm) was placed over the capping material for the final restoration. For the control group, all steps were similar as for the experimental group, except that no Bio-Gide was used before adding the MTA.

All patients were evaluated at 3-month intervals for at least 6 months. Treatment outcomes were assessed clinically and radiographically at each follow-up visit.

Evaluation of Treatment Outcomes

Treatment outcomes were assessed in a blinded manner by 2 independent reviewers, both pediatric dentists. When an evaluation was not