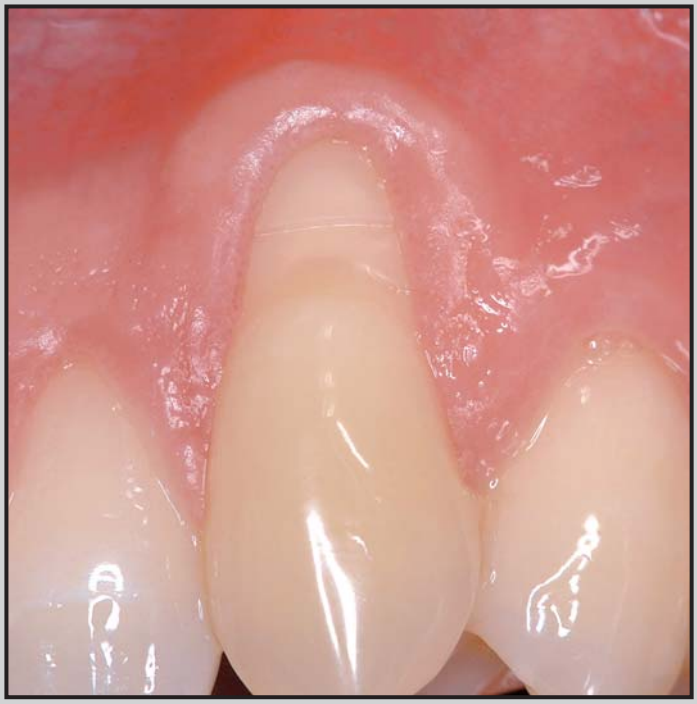

Comparison of Recombinant Human Platelet-Derived Growth Factor-BB Plus Beta Tricalcium Phosphate and a Collagen Membrane to Subepithelial Connective Tissue Grafting for the Treatment of Recession Defects: A Case Series

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When mixed with an osteoconductive scaffold, recombinant human platelet-derived growth factor (rhPDGF-BB), a potent wound-healing protein, has been shown to promote clinical attachment gain, radiographic bone fill, and regeneration of the periodontium. This human case series evaluated the clinical outcome of rhPDGF with beta tricalcium phosphate (β-TCP) and a collagen membrane in the treatment of recession-type defects. The control was the clinical gold standard for root coverage: the subepithelial connective tissue graft (CTG). Seven patients with recession defects ≥ 3 mm in contralateral quadrants of the maxilla, excluding molars, were treated in this series. Patients were followed postoperatively, and healing was evaluated at 8, 16, and 24 weeks, with recession depth as the primary outcome measure. This case series revealed a favorable tissue response to rhPDGF-BB + β-TCP and a collagen membrane and comparable clinical outcomes to CTG, warranting a controlled clinical trial of greater magnitude. (Int J Periodontics Restorative Dent 2006;26:127–133.)

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Recession defects around teeth are treated for a variety of reasons including, but not limited to, root sensitivity, increased potential for root caries, difficulty with plaque control, and esthetics. Although a variety of surgical techniques are available to the clinician to cover denuded root surfaces, many papers indicate that the subepithelial connective tissue graft (CTG) has not only the highest percentage of mean root coverage, but also the least variability.[1–3] Recently, a systematic review of the literature[4] that included a meta-analysis reinforced the experience of many clinicians by confirming that the CTG is the most predictable technique for root coverage in many situations. The analysis, however, did not find the CTG to be statistically significantly better than the coronally advanced flap in attaining complete root coverage. Furthermore, the CTG is limited both by the requirement of a remote surgical site needed to harvest the connective tissue and by the amount of donor tissue available for any given

surgical procedure. In addition, the donor site often has more morbidity than the recipient site.

As an alternative to connective tissue, collagen membranes have been used with reasonable success in root coverage grafts.[5–8] As an attractive guided tissue regeneration (GTR) membrane, collagen is not only an abundant, naturally occurring protein that is well-tolerated and bioabsorbable, but it also encourages migration of adjacent autogenous connective tissue and epithelial cells over its surfaces.[9] In addition, collagen's hemostatic properties promote initial clot formation and wound stability.[10] The use of a collagen membrane also precludes the need for a donor site and the associated problems.

The creation and maintenance of space between the root surface and the membrane is one of the basic principles of GTR techniques. Many clinicians believe this space facilitates the wound-healing process, leading toward regeneration.[11,12] Because the collagen membrane adapts intimately to the root surface, Kimble et al[13] evaluated the treatment of gingival recession using a collagen membrane with or without the use of demineralized freeze-dried bone allograft (DFDBA) for space maintenance. They concluded that root coverage using a collagen membrane with or without DFDBA yielded similar results.

Tissue engineering may allow the clinician to achieve improved outcomes with less invasive procedures. Platelet-derived growth factor (PDGF) is the most thoroughly studied growth factor in periodontics. Since the late 1980s, when it was first discovered that PDGF promoted regeneration of bone, cementum, and periodontal ligament (PDL),[14] nearly 100 studies have been published on its effects on PDL and alveolar bone cells and regeneration of the periodontium in both animals and humans. These studies have clearly demonstrated the mechanism of action of PDGF, showing the presence of cell-surface receptors for PDGF on PDL and alveolar bone cells and elucidating PDGF's stimulatory effect on the proliferation and chemotaxis of these cells.[15] Additionally, recombinant human PDGF-BB (rhPDGF-BB) has been shown to promote the regeneration of periodontal tissue, including bone, cementum, and PDL, in numerous animal studies[14,16–22] and in landmark human histologic reports.[23,24]

Beta tricalcium phosphate (β-TCP) is a purified, multicrystalline, porous form of calcium phosphate with a $Ca:PO_4$ ratio similar to that of natural bone mineral. When placed under a membrane, the β-TCP prevents membrane collapse against the root surface and provides a matrix or scaffolding for new bone formation.[25] It also facilitates the stabilization of the blood clot.[25] In a recent pivotal clinical trial involving 180 patients, the combination of β-TCP and rhPDGF-BB was shown to accelerate clinical attachment level gain and significantly increase linear bone growth and percent bone fill in severe intrabony defects when compared with β-TCP alone as well as with currently used grafting materials.[26]

It was the aim of this case series to compare rhPDGF-BB + β-TCP and a collagen membrane to the subepithelial CTG with a coronally advanced flap in patients with recession-type defects. Comparable results would therefore justify a controlled clinical trial.

Method and materials

Case population and evaluation

Seven patients with Miller Class II[27] buccal gingival recession of ≥ 3 mm and gingival width ≥ 3 mm on teeth in contralateral quadrants of the same jaw who met the inclusion/exclusion criteria were selected from patients seeking treatment in the authors' private practices. A signed institutional review board–approved consent form regarding the study was obtained from each patient. Of the seven patients, all were Caucasian nonsmokers. All teeth had ≤ 2.0 mm of keratinized tissue at baseline and a minimum of 3 mm of recession. Occlusal interferences were identified and eliminated through occlusal adjustment, and hard acrylic resin bite guards were constructed for those patients with parafunctional habits. Each patient served as his or her own control, so that extraneous factors such as oral hygiene and compliance were controlled within each subject.

Following screening examination, all subjects received instruction in proper oral hygiene measures. At the treatment sites, a brushing technique was prescribed that minimized apically directed forces to the soft tissue. Surgical treatment of the recession defects was not scheduled until the patient could demonstrate adequate supragingival plaque control.

For each subject, the first surgery was performed on the left side, with the second surgery performed immediately after the first. A randomization list determined whether the exposed and cleaned root surface was treated with either rhPDGF-BB + β-TCP and a collagen membrane or a subepithelial CTG. The randomization was revealed after the first surgical site was prepared.

Test materials

The test materials were composed of three components: rhPDGF-BB, β-TCP, and an approved collagen membrane. Together these materials promote wound healing by improving and promoting cellular ingrowth into the recession defect. In addition, they physically prevent the collapse of the soft tissues onto the root surface and facilitate stabilization of the blood clot by providing a biocompatible, osteoconductive scaffold for new tissue formation.

Surgical procedure

Treatment of test sites

The surgical technique used to achieve soft tissue coverage was a coronally advanced flap. Following administration of local anesthesia, the exposed portion of the root was prepared using, as needed, chisels, curettes, and finishing burs. Following root preparation, an intracrevicular incision was made with a scalpel at the affected tooth or teeth to mobilize a full-thickness mucosal flap. The incision was extended to involve the papilla region on each side of the tooth to be treated. Vertical releasing incisions, extending from the papilla out into the lining mucosa, were placed at each side of the tooth to facilitate the planned coronal repositioning of the flap tissue over the exposed root surface. The full-thickness flap was then elevated in an apical direction just beyond the mucogingival junction. The periosteum was then cut, and a blunt dissection into the vestibular lining mucosa was performed, eliminating muscle tension and facilitating coronal positioning of the mucosal flap at the level of the cementoenamel junction (CEJ).

The facial portions of the interdental papillae were de-epithelialized to create a connective tissue bed to which the coronally advanced flap could later be sutured. The pocket epithelium was also removed in the lateral portion of the defect. No further instrumentation of the root surface was performed.

The exposed root surface was conditioned with ethylenediaminetetraacetic acid (EDTA) (Prefgel, Straumann) for 2 minutes to remove the smear layer and thoroughly rinsed with sterile saline. Any remaining PDL tissue coronal to the alveolar bone was preserved. The rhPDGF-BB solution was then applied to the exposed root surface and to the coronal ligament fibers.

A small amount of β-TCP was saturated with the rhPDGF-BB solution and placed below the CEJ, over the denuded root surface and extending approximately 2 to 3 mm onto the adjacent bone. The collagen membrane was also saturated with the PDGF solution prior to membrane placement. Once saturated, the membrane was placed over the β-TCP according to standard GTR surgical procedure and sutured bilaterally to the de-epithelialized papilla region. Subsequently, the membrane was covered with the coronally advanced flap. The tissue flap was then secured at the level of the CEJ by suturing the flap to the de-epithelialized papilla regions with 5-0 gut sutures. The vertical incisions were closed with 6-0 gut sutures. Any remaining rhPDGF-BB solution was dispensed onto the coronally advanced flap. No pressure was applied after suturing.

Treatment of control sites

A procedure identical to that used at the test sites (with the exception that the mucosal flap was partial thickness, not full thickness), including root surface conditioning with EDTA, was performed at the control sites. However, instead of PDGF and β-TCP, the control sites received a subepithelial CTG placed over the denuded root surface. The donor area was the palate in the premolar region, with graft procurement following the procedure for CTG as outlined by Langer and Langer.[28] The graft was sutured to the papilla region and coronal to the mucogingival junction on either side of the denuded root. In addition, a suspensory suture was placed in the periosteum apical to the graft and positioned around the neck of the tooth in an effort to tightly adapt the graft to the root surface. The coro-

Fig 1a (left) *Preoperative view of control tooth.*

Fig 1b (right) *Intraoperative measurement of the alveolar crest to CEJ.*

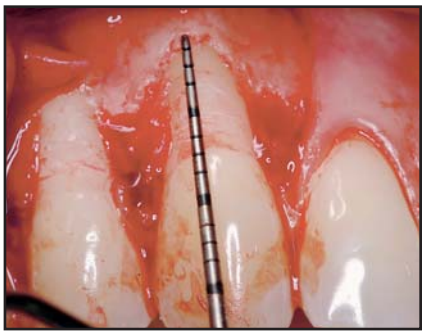

Fig 1c (left) *Clinical situation following suturing of connective tissue over the denuded roots.*

Fig 1d (right) *The mucogingival flap has been advanced and sutured over the CTG.*

nally advanced flap was then placed over the graft as previously described. Pressure was applied after suturing. A dressing (Coe-Pack, GC America) was placed in the area of the donor region.

Postoperative management

Antibiotics and analgesics were prescribed for the management of postoperative infection control and discomfort. All subjects received instruction in proper oral hygiene measures. Patients were instructed not to brush the teeth in the treated areas, but to use 0.12% chlorhexidine gluconate mouthwash for 1 minute twice daily for the first 3 weeks following surgery. Patients were also instructed to avoid excessive muscle tractioning or trauma to the treated areas for the first 3 weeks. Following this period, patients were instructed in a brushing technique that minimized apically directed trauma to the soft tissue of the treated teeth. Postoperative examinations were conducted at 1, 2, 4, 8, 12, 16, 18, and 24 weeks. At weeks 8, 16, and 24, clinical measurements were made and periodontal maintenance performed. Any adverse events, as well as adverse device effects, were recorded.

Case example

This patient, a 28-year-old systemically healthy man, presented with Miller Class II recession on both maxillary canines and the maxillary right first premolar. The control tooth was found to have 3 mm of recession, with a recession width of 5 mm (Fig 1a). CTGs were performed as previously described (Figs 1b to 1d). The test tooth presented with 5 mm of recession and a recession width of 5 mm (Fig 2a). The test surgery was performed as described and can be seen in Figs 2b to 2f. At 6 months there was no residual recession for either the control (Fig 3a) or test (Fig 3b) sites. The tissues at both sites appeared healthy, with no visible signs of inflammation.

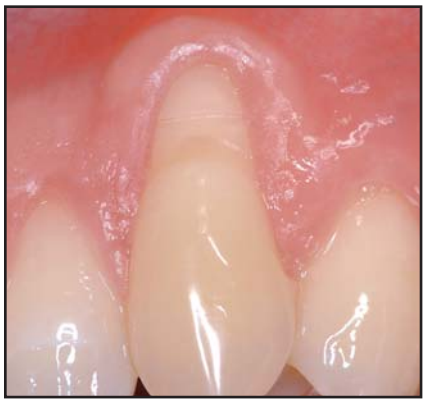

Fig 2a (left) *Baseline view of tooth randomized to receive the test treatment.*

Fig 2b (right) *The growth factor is applied to the root surface.*

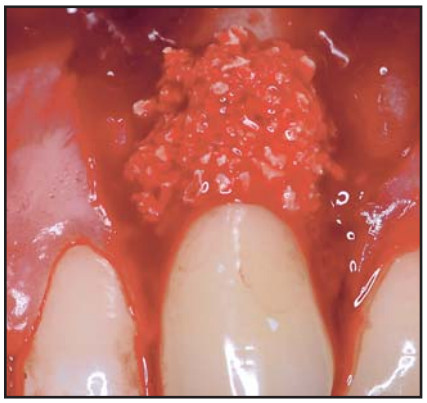

Fig 2c (left) *TCP is placed over the denuded root surface after it was saturated with the rhPDGF-BB.*

Fig 2d (right) *After it was soaked in the growth factor, the membrane is carefully trimmed and placed over the β-TCP.*

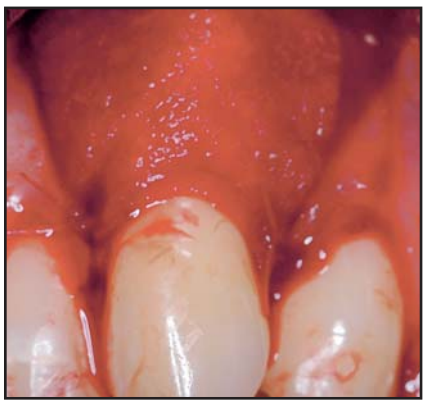

Fig 2e (left) *The membrane is placed with interrupted sutures in the papilla region.*

Fig 2f (right) *The mucogingival flap is coronally advanced and sutured over the membrane.*

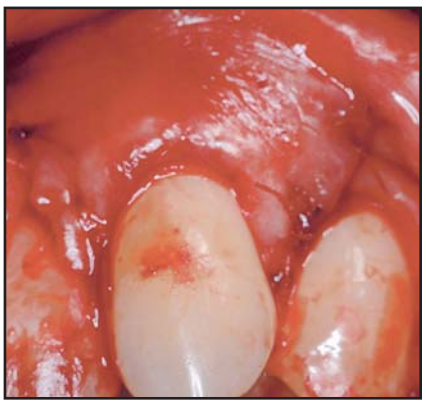

Fig 3a (left) *Control site (treated with CTG) at 6 months.*

Fig 3b (right) *Test site (treated with rhPDGF-BB + β-TCP and the collagen membrane) at 6 months.*

Discussion

The purpose of this case series was to compare two methods for treating recession-type defects: *(1)* rhPDGF-BB +β-TCP and a collagen membrane with a coronally advanced flap and *(2)* the subepithelial CTG with a coronally advanced flap. The summary of evidence indicates that both procedures are effective in covering recession defects within this case series. Since no serious adverse events were reported in any of the test or control cases, both treatment modalities can be considered safe and effective methods of treating recession-type defects.

The clinical handling characteristics of the rhPDGF-BB + β-TCP and collagen membrane compare favorably to those of the CTG. The β-TCP hydrates well in the rhPDGF-BB and is easily transported and placed over the denuded root surface. As the case series progressed, the surgeons learned that it was important to place the β-TCP at least 3 mm away from the CEJ with vertical releasing incisions. The collagen membrane was easily adapted over the β-TCP.

Because of the limited number of cases treated in this feasibility study and the minimal differences in clinical results, statistical comparison could not be made between the test and control groups as would be done in a larger, more adequately powered trial. Nevertheless, both procedures predictably achieved root coverage, and after 6 months of healing, all patients—both test and control—had no more than 1 mm of residual recession. All tissues appeared healthy and stable, and the test grafts appeared less bulky and more esthetic. This case series proves the principle that it is possible to treat periodontal recession-type defects with rhPDGF-BB + β-TCP and a collagen membrane with a coronally advanced flap.

The seven cases in the present case series provide adequate justification for further investigation in a larger study of the safety and efficacy of rhPDGF-BB + β-TCP and a collagen membrane with the coronally advanced flap as compared to CTG with the coronally advanced flap. Furthermore, we plan to evaluate the histologic outcome of these two treatment modalities on at least one patient to assess the type of attachment gained over the root surface. The positive results of this feasibility study support the need for a properly powered clinical study to determine the viability of this approach to treat root coverage.

Conclusion

Within the limits of this case series, the use of rhPDGF-BB + β-TCP and a collagen membrane may represent an acceptable alternative to the CTG for covering gingival recession defects. The use of this new procedure and material eliminates the need for the palatal donor site and thus represents a less invasive surgery for the patient as well as relieving the clinician from relying on a limited supply of donor tissue.

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