Platelet-Derived Growth Factor Stimulates Bone Fill and Rate of Attachment Level Gain: Results of a Large Multicenter Randomized Controlled Trial

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Background: Growth factors are generally accepted to be essential mediators of tissue repair via well-established mechanisms of action that include stimulatory effects on angiogenesis and cellular proliferation, ingrowth, differentiation, and matrix biosynthesis. The aim of this study was to evaluate in a large-scale, prospective, blinded, and randomized controlled clinical trial the safety and effectiveness of purified recombinant human platelet-derived growth factor (rhPDGF-BB) mixed with a synthetic beta-tricalcium phosphate (β-TCP) matrix for the treatment of advanced periodontal osseous defects at 6 months of healing.

Methods: Eleven clinical centers enrolled 180 subjects, each requiring surgical treatment of a 4 mm or greater intrabony periodontal defect and meeting all inclusion and exclusion criteria. Subjects were randomized into one of three treatment groups: 1) β-TCP + 0.3 mg/ml rhPDGF-BB in buffer; 2) β-TCP + 1.0 mg/ml rhPDGF-BB in buffer; and 3) β-TCP + buffer (active control). Safety data were assessed by the frequency and severity of adverse events. Effectiveness measurements included clinical attachment levels (CAL) and gingival recession (GR) measured clinically and linear bone growth (LBG) and percent bone fill (% BF) as assessed radiographically by an independent centralized radiology review center. The area under the curve (AUC), an assessment of the rate of healing, was also calculated for CAL measurements. The surgeons, clinical and radiographic evaluators, patients, and study sponsor were all masked with respect to treatment groups.

Results: CAL gain was significantly greater at 3 months for group 1 (rhPDGF 0.3 mg/ml) compared to group 3 (β-TCP + buffer) (3.8 versus 3.3 mm; $P = 0.032$), although by 6 months, this finding was not statistically significant ($P = 0.11$). This early acceleration of CAL gain led to group 1 exhibiting a significantly greater rate of CAL gain between baseline and 6 months than group 3 as assessed by the AUC (68.4- versus 60.1-mm weeks; $P = 0.033$). rhPDGF (0.3 mg/ml)-treated sites also had significantly greater linear bone gain (2.6 versus 0.9 mm, respectively; $P < 0.001$) and percent defect fill (57% versus 18%, respectively; $P < 0.001$) than the sites receiving the bone substitute with buffer at 6 months. There was less GR at 3 months in group 1 compared to group 3 ($P = 0.04$); at 6 months, GR for group 1 remained unchanged, whereas there was a slight gain in gingival height for group 3 resulting in comparable GR. There were no serious adverse events attributable to any of the treatments.

Conclusions: To our knowledge, this study is the largest prospective, randomized, triple-blinded, and controlled pivotal clinical trial reported to date assessing a putative periodontal regenerative and wound healing therapy. The study demonstrated that the use of rhPDGF-BB was safe and effective in the treatment of periodontal osseous defects. Treatment with rhPDGF-BB stimulated a significant increase in the rate of CAL gain, reduced gingival recession at 3 months post-surgery, and improved bone fill as compared to a β-TCP bone substitute at 6 months. *J Periodontol 2005;76:2205-2215.*

KEY WORDS

Bone regeneration; periodontics; platelet-derived growth factor; randomized clinical trial; tissue engineering.

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