Abstract: This case report describes the clinical efficacy of treatment with basic fibroblast growth factor (FGF-2) for periodontal regeneration. A patient with aggressive periodontitis participated in a clinical trial involving administration of 0.3% FGF-2 in comparison with a placebo control. To evaluate the efficacy of FGF-2, standardized radiographs were taken before surgery and at 12, 24, and 36 weeks after FGF-2 treatment. The rate of increase in alveolar bone height was 86.9% at 36 weeks. The 6-year post-operative radiograph showed significant development of alveolar bone in comparison with the first visit. FGF-2 treatment may be effective for periodontal regeneration in cases of aggressive periodontitis.

Keywords: FGF-2; periodontal regeneration; aggressive periodontitis; clinical trial.

Introduction

Periodontal regeneration is the main goal of periodontal therapy, and for this purpose guided tissue regeneration (GTR) (1) and application of enamel matrix derivative (2) are performed in clinical practice. Periodontal regenerative therapy uses mesenchymal stem cells that are present within the periodontal ligament. Improving the biological potential of mesenchymal stem cells may stimulate the regeneration of periodontal tissue (3). Recently, the use of cytokines has been considered physiologically effective for stimulating cells that can assist in periodontal regeneration. One of the cytokines used for this purpose is basic fibroblast growth factor (FGF-2).

Aggressive periodontitis is characterized by progressive destruction of periodontal tissue, and patients with this condition are considered to be at high risk of disease recurrence (4). This case report describes the clinical efficacy of 0.3% FGF-2 application for periodontal regeneration in a patient with generalized aggressive periodontitis.

Case Report

A 32-year-old Japanese man visited the Department of Periodontology at Nihon University School of Dentistry Dental Hospital, complaining of progressive and severe periodontitis. Otherwise, he was in good general health, his medical history was unremarkable, and family history was non-contributory. However, he smoked 10 or more cigarettes per day. He was diagnosed as having generalized aggressive periodontitis. After initial periodontal therapy and smoking cessation, he participated in a phase III clinical trial of 0.3% FGF-2 administration. This clinical trial was a multi-center, randomized, double-blind,
and placebo-controlled study involving 23 university dental hospitals in Japan, and conducted in accordance with Good Clinical Practice, having been approved by the institutional review boards of all the hospitals (approved by Nihon University School of Dentistry Dental Hospital on 8/26/08: Protocol number KC-B-1D-03). The clinical trial was designed by Kaken Pharmaceutical Co., Ltd. (Tokyo, Japan). Our patient was given adequate verbal and written information about the trial, and completed a signed informed consent form.

To evaluate the efficacy of FGF-2, standardized radiographs were taken before surgery and at 12, 24, and 36 weeks after administration of FGF-2. Five doctors specializing in dental radiography had been independently assigned to assess the rate of increase in alveolar bone height (RIBH). Clinical parameters (clinical attachment level [CAL], probing pocket depth [PPD], bleeding on probing [BOP], gingival index [GI], tooth mobility, width of keratinized gingiva, plaque index [PII]) were monitored for 36 weeks. Adverse events were assessed by laboratory tests.

Periodontal flap surgery was performed on tooth #35 (Fig. 1a), where CAL was 9 mm and PPD was 5 mm on the bucco-mesial side. Radiographic evaluation showed a vertical bony defect 6.02 mm in depth. After completion of the incision, the flap was raised, the tooth was meticulously scaled, and the root was planed. The intrabony defect component was 2 and 3 wall (Fig. 1b). After irrigation with saline, the agent in this trial was applied by means of a syringe to the exposed root surface. This case was allocated to 0.3% FGF-2 administration. At 36 weeks after periodontal flap surgery, CAL was 6 mm and PPD was 3 mm. Postoperative clinical evaluation revealed an attachment gain of 3 mm and pocket reduction of 2 mm. The alveolar bone height gradually increased during 36 weeks (Fig. 2 a-d), and RIBH was 86.9% (Table 1). Postoperative urinalysis demonstrated two events at 1 week: increases of β2 microglobulin and β-N-acetyl-D-glucosaminase. These laboratory data were improved during the next 2 weeks, and there were no other serious adverse events during the course of this clinical trial. After the 36-week observation period, the patient was recalled for supportive periodontal therapy (SPT) every 2 to 12 months for a period of 5 years. A postoperative radiograph at 6 years showed significant improvement of the alveolar bone defect in comparison with the first visit (Fig. 3a, b). At 6 years after periodontal surgery, the interproximal space was filled with a gingival
papilla (Fig. 1c); CAL was 4 mm and PPD was 2 mm. Postoperative clinical evaluation revealed an attachment gain of 5 mm and pocket reduction of 3 mm.

**Discussion**

Radiographic findings have suggested that FGF-2 induces new alveolar bone formation within 36 weeks. Administration of 0.3% FGF-2 has been shown to be efficacious for regenerating new bone in animal studies (5,6). Furthermore, FGF-2 treatment has been shown to be effective for human periodontal regeneration in a clinical trial (7). The mechanisms whereby FGF-2 facilitates periodontal regeneration are thought to include angiogenic activity and mitogenic effects on mesenchymal cells within the periodontal ligament (3). In the present case, a marked improvement of the bony defect was observed at 36 weeks after FGF-2 treatment (RIBH: 86.9%). GTR yields a RIBH of about 44% at 12 months (8), compared with a value of about 31% at 16 months with enamel matrix derivative (9) and about 51% at 36 weeks with FGF-2 (7). Thus FGF-2 treatment may have a higher capacity for new alveolar bone formation than other periodontal regenerative therapies.

Failure of compliance is associated with a higher rate of recurrence in patients with generalized aggressive periodontitis (4). The clinical parameters and radiographic findings in the present patient were stable at 6 years after FGF-2 treatment. This may have been related to compliance with SPT and smoking cessation (10).

Application of 0.3% FGF-2 may be effective for periodontal regeneration in patients with aggressive periodontitis.

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**References**


