Effect of concentrated growth factor combined with guided bone regeneration on cell proliferation and bone resorption in patients with severe periodontitis

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ABSTRACT

Objective: To study the effect of concentrated growth factor (CGF) combined with guided bone regeneration on cell proliferation and bone resorption in patients with severe periodontitis.

Methods: Patients with severe periodontitis who were treated in Stomatology Department of Shenmu Hospital between May 2014 and February 2017 were selected as the research subjects and randomly divided into two groups, surgery + CGF group received concentrated growth factor combined with guided bone regeneration, and pure surgery group received guided bone regeneration. The contents of inflammatory response, cell proliferation and bone resorption markers in gingival crevicular fluid were determined 1 week after treatment. Results: 1 week after treatment, HMGB1, ICAM1, E-selectin, Smac, FasL, Caspase-8, Caspase-9, Caspase-3, RANKL and NTX contents in gingival crevicular fluid of surgery + CGF group were significantly lower than those of pure surgery group while PD-L1, hBD-3, Wnt3a, BGP and OPG contents were significantly higher than those of pure surgery group. Conclusion: Concentrated growth factor combined with guided bone regeneration for severe periodontitis can inhibit inflammatory response, apoptosis and bone resorption, which is beneficial to the reconstruction of periodontal tissue.

1. Introduction

Periodontitis is a common stomatological disease, and the protracted periodontal tissue inflammation will increase the risk of tooth loss. Guided bone regeneration is a periodontitis therapy developed in recent years, which can promote the regeneration of periodontal tissue through graft materials and achieve the clinical healing of periodontal tissue[1]. However, for children with severe periodontitis, the guided bone regeneration alone can cause different levels of graft material absorption or rejection, which affects the healing of periodontal tissue[2]. Concentrated growth factor is the newly developed biological material, which can inhibit inflammation and promote osteoblastic differentiation and bone healing, has been used as the adjuvant therapy for the immediate implantation in inflammatory stage of patients with periodontitis and has achieved positive results. But there is still no report about the effects of concentrated growth factors combined with guided bone regeneration. The effect of concentrated growth factor combined with guided bone regeneration on cell proliferation and bone resorption in patients with severe periodontitis was analyzed in the following studies.

2. Case information and research methods

2.1 General information of patients with periodontitis

Patients with severe periodontitis who were treated in Stomatology Department of Shenmu Hospital between May 2014 and February 2017 were selected as the research subjects, all the patients were in line with the diagnosis for periodontitis, at least one site was with probing depth > 6 mm, tooth mobility was I-II degrees, and X-ray radiography showed alveolar resorption length was more than 1/2 of the root length. A total of 158 patients were enrolled and divided into two groups by random number table, each with 78 cases. Surgery + CGF group included 48 men and 30 women that were...
36-56 years old; pure surgery group included 51 men and 27 women that were 34-58 years old. There was no statistically significant difference in general information between the two groups (P>0.05).

2.2 Therapy

Both groups of patients received routine periodontal non-surgical treatment and started guided bone regeneration after 1 month, which was as follows: Widman flap surgery was used to expose the periodontal bone defect site, granulation was removed, the root surface was leveled, the alveolar bone was trimmed, then hydroxyapatite bioceramics was mixed with autologous plasma and water for injection and implanted in the alveolar bone defect site, pure surgery group received collagen membrane for covering, surgery + CGF group received CGF membrane for covering, and finally the gingival flap was fixed and sutured.

2.3 Gingival crevicular fluid index testing

1 week after treatment, the gingival crevicular fluid of corresponding parts was collected from the two groups of patients, and enzyme-linked immunosorbent assay kit was used to determine HMGB1, ICAM1, E-selectin, PD-L1, hBD-3, Smac, FasL, Caspase-8, Caspase-9, Caspase-3, Wnt3a, BGP, OPG, RANKL and NTX contents in gingival crevicular fluid samples.

2.4 Statistical methods

SPSS 18.0 software was used to input and analyze data, measurement data analysis between two groups was by t test and \( P < 0.05 \) indicated statistical significance in differences in test results.

3. Results

3.1 Inflammatory response marker contents

1 week after treatment, analysis of inflammatory response markers HMGB1 (pg/mL), ICAM1 (pg/mL), E-selectin (pg/mL), PD-L1 (ng/mL) and hBD-3 (ng/mL) contents in gingival crevicular fluid between the two groups of patients was as follows: HMGB1, ICAM1 and E-selectin contents in gingival crevicular fluid of surgery + CGF group were significantly lower than those of pure surgery group while PD-L1 and hBD-3 contents were significantly higher than those of pure surgery group. Differences in HMGB1, ICAM1, E-selectin, PD-L1 and hBD-3 contents in gingival crevicular fluid were statistically significant between the two groups of patients 1 week after treatment (\( P<0.05 \)).

3.2 Cell proliferation marker contents

1 week after treatment, analysis of cell proliferation markers Smac, FasL, Caspase-8, Caspase-9 and Caspase-3 contents in gingival crevicular fluid between the two groups of patients was as follows: Smac, FasL, Caspase-8, Caspase-9 and Caspase-3 contents in gingival crevicular fluid of surgery + CGF group were significantly lower than those of pure surgery group. Differences in Smac, FasL, Caspase-8, Caspase-9 and Caspase-3 contents in gingival crevicular fluid were statistically significant between the two groups of patients 1 week after treatment (\( P<0.05 \)).

3.3 Bone resorption marker contents

1 week after treatment, analysis of bone resorption markers Wnt3a, BGP, OPG, RANKL and NTX contents in gingival crevicular fluid between the two groups of patients was as follows: Wnt3a, BGP and OPG contents in gingival crevicular fluid of surgery + CGF group were significantly higher than those of pure surgery group while RANKL and NTX contents were significantly lower than those of pure surgery group. Differences in Wnt3a, BGP, OPG, RANKL and NTX contents in gingival crevicular fluid were statistically significant between the two groups of patients 1 week after treatment (\( P<0.05 \)).

4. Discussion

The clinical treatment of severe periodontitis is much more difficult, it is mostly accompanied by different extent of periodontal tissue destruction and alveolar bone loss, and severe cases can cause tooth loss. Guided bone regeneration is a periodontal regeneration therapy.
developed in recent years, which can promote the proliferation of periodontal cells and the regeneration of periodontal bone through the implantation of nano-hydroxyapatite. Although the efficacy of guided bone regeneration technique for periodontitis has received more and more recognition, the efficacy of guided bone regeneration for patients with severe periodontitis is not ideal, and affected by the graft material resorption or rejection, the periodontal bone regeneration process can be affected[3,4]. CGF is a biological material rich in transforming growth factor β, vascular endothelial growth factor, insulin-like growth factor and other growth factors, which can not only adjust the activation of mononuclear macrophages and lymphocytes and affect the activation of inflammatory response, but can also promote the osteoblast differentiation and proliferation and promote bone regeneration through multiple signaling pathways downstream[5]. The value of CGF for the treatment of periodontitis has been reported, but the effect of CGF combined with guide bone regeneration is not clear.

The continuous activation of inflammatory response is the pathological feature of local tissues in patients with severe periodontitis, and various inflammatory regulators express abnormally in the inflammatory response activation process. PD-L1 and hBD-3 are the molecules that have a negative regulatory effect on inflammation, the former can mediate the apoptosis of lymphocytes and mononuclear macrophages and reduce the secretion of pro-inflammatory mediators, and the latter is a kind of low-molecular-weight peptide that is negatively charged and can inhibit the inflammatory response induced by LPS[6,7]. HMGB1, ICAM1 and E-selectin are the pro-inflammatory cytokines, HMGB1 has direct inflammatory damage effect and can cause periodontal tissue damage and alveolar bone resorption[8], ICAM1 and E-selectin are the cytokines that promote inflammatory cell adhesion and promote inflammatory factor infiltration, and they can mediate the cascade amplification of inflammatory response[9,10]. In the study, analysis of the differences in inflammation markers in gingival crevicular fluid showed that Wnt3a, BGP and OPG in gingival crevicular fluid of surgery + CGF group were significantly lower than those of pure surgery group.

The persistent inflammatory response in periodontal tissue can lead to periodontal tissue damage and alveolar bone resorption by affecting cell proliferation and apoptosis. Mitochondrial pathway apoptosis and death receptor pathway apoptosis are two different mechanisms that regulate apoptosis. Smac is the regulatory molecule of mitochondrial pathway apoptosis, which can be combined with various anti-apoptosis molecules in the mitochondrial pathway and weaken the anti-apoptotic capacity of the cells to promote the activation of downstream Caspase-9[11,12]; Fas/FasL are the regulatory molecules of death receptor pathway apoptosis, and the two can be combined with each other to facilitate the activation of downstream Caspase-8 by FADD pathway[13,14]. Activated Caspase-9 and Caspase-8 in cells can make Caspase-3 activate and mediate apoptosis through a series of cascade activation reactions. In the study, analysis of the differences in apoptosis markers in gingival crevicular fluid showed that Smac, FasL, Caspase-8, Caspase-9 and Caspase-3 contents in gingival crevicular fluid of surgery + CGF group were significantly lower than those of pure surgery group. This indicates that the CGF combined with guided bone regeneration can reduce the expression of pro-apoptosis molecules to further reduce the injury degree of periodontal tissue in patients with severe periodontitis.

The excessive inflammatory response and apoptosis in local tissue of periodontitis can lead to continuous resorption of bone tissue in the alveolar bone, which can lead to the tooth mobility and increase the risk of tooth loss[15]. Wnt3a is an important signal molecule regulating bone metabolism, and it can adjust the expression of alkaline phosphatase, osteocalcin, osteopontin, etc during the process of osteogenesis differentiation so as to accelerate osteogenesis differentiation, inhibit osteoclast differentiation and help bone formation; BGP is a hormone peptide secreted by osteoblasts, and its synthesis and secretion can reflect the activity of osteoblasts[16]; OPG is a secreted protein that participates in the regulation of osteoclast activity, it is secreted by osteoblasts and it can compete with RANKL to be combined with the RANK on osteoclast surface and inhibits the differentiation and maturation of osteoclasts[17,18]; NTX is a product of type I collagen fiber degradation in periodontal bone tissue, which is closely related to the bone resorption process and can produce direct damaging effect on periodontal tissue[19,20]. In the study, analysis of the differences in bone resorption markers in gingival crevicular fluid showed that Wnt3a, BGP and OPG
contents in gingival crevicular fluid of surgery + CGF group were significantly higher than those of pure surgery group while RANKL and NTX contents were significantly lower than those of pure surgery group. This means that the CGF combined with guided bone regeneration can enhance osteoblast activity and inhibit osteoclast activity to more effectively reduce the bone resorption of periodontal tissue in patients with severe periodontitis.

To sum up, it can be concluded that concentrated growth factor combined with guided bone regeneration is more valuable than guided bone regeneration alone for the treatment of severe periodontitis, and joint treatment can effectively inhibit the inflammatory response, apoptosis and bone resorption.

References


