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Effect of SDF-1 Expression in the Healing of Tooth Extraction Wounds in Diabetic Patients

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Abstract

At present, with the citizens' daily diet is more refined, people's jaw shows a trend of degeneration, so the incidence of impacted teeth is gradually increasing in the citizens. In addition, according to the data provided by the International Diabetes Federation, about 115 million adults in China are diabetic, and diabetes has a serious negative impact on tissue healing and defect repair. Especially for diabetic patients, the healing time after impacted tooth extraction is long and the effect is not ideal, which has a great impact on the recovery and postoperative quality of life of diabetic patients. The process of tissue repair and reconstruction after tooth extraction in patients with diabetes is complicated, and many factors are involved in the regulation of the healing process. According to current research, diabetes is called quench in Traditional Chinese medicine and is mostly caused by hot and dry Yin deficiency. Quench thirst caused by qi deficiency, qi deficiency, Yin loss and Yang caused by Yin and Yang two deficiency and yun accumulation into poison, change by poison evil and born, so bad healing after tooth extraction due to poison evil. In addition, there is evidence in cell biology that stromal cell-derived factor 1 (SDF-1) can mediate stem cell tissue repair after injury through the SDF-1/CXCR4 signaling pathway. So as to complete the chemotaxis of bone marrow stem cells, and then directional aggregation in the defect and injury tissue, and the formation of capillaries to complete tissue repair. However, up to now, there are few studies and reports on stromal cell derived factor 1 in the research of tooth extraction wound repair in diabetic patients. Therefore, it is necessary to review the effect of stromal cell derived factor SDF-1 expression in tooth extraction wound tissue healing in diabetic patients.

Keywords

Diabetic Patients; Tooth Extraction and; Tissue Healing; Stromal Cell Derived Factor 1; SDF-1 /CXCR4 Signaling Pathway; Defect.

1. Introduction

In the tissue healing process of diabetic tooth extraction patients, the biological repair process is relatively complex, which mainly includes inflammatory reaction, granulation tissue formation and tissue reconstruction. This process is reflected in histopathology for the expression of cell growth factor and repair of cell protein structure, so as to complete the repair of tissue injury caused by tooth extraction.

According to Jackson Edwin K et al., bone marrow mesenchymal stem cells (BMSCS) can release nutritional factors and migrate to the defect area to complete the repair of the defect tissue, and stromal cell derived factor 1 (SDF-1) is involved[1]. Stromal cell derived factor 1 is the expression of C-X-C motif chemokine receptor 4 (CXCR4), a G-protein-coupled receptor with seven transmembrane domains as SDF-1 receptor. In addition, studies have shown that SDF-1 can achieve the effect of stem cell recruitment in injured tissue areas.

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2. Cells Involved in the Repair of Injured Tissue

2.1 Fibroblast

In the process of tissue defect repair, fibroblast is one of the important functional cells, which can provide highly heterogenous mesenchymal cells needed by loose connective tissue repair after tissue defect, and provide a variety of growth factors to promote tissue repair, so as to maintain the dynamic balance between tissue repair and protease synthesis. In addition, some scholars have pointed out that fibroblasts can complete their biological behaviors such as activation and migration through the expression of SDF-1 and secrete extracellular matrix, so fibroblasts are called engineers of tissue defect repair.

2.2 Mesenchymal Stem Cells

When the body tissue is damaged, mesenchymal stem cells can be the first to differentiate into osteoblasts and chondrocytes. Due to their potential to differentiate into multicellular cells, mesenchymal stem cells have been proven to play a key role in tissue repair and functional recovery. Ryo Takahashi et al. showed that mesenchymal stem cells can be widely distributed in multiple parts of the body after differentiation into other stromal stem cells and can be regulated and affected by various growth factors[2]. A variety of growth factors can be used as signal transduction to promote the directional aggregation of pluripotent stem cells to the defect area, and then to repair the tissue defect.

2.3 Endothelial Progenitor Cell

Endothelial progenitor cells (EPC) can mainly be found in bone marrow stem cells, and a small amount of EPC can also be observed in peripheral blood. This cell is mainly active in the process of tissue defects and repair, and is active in wound healing and vascular diseases, and has the role of new capillaries. Studies have shown that endothelial progenitor cells can mobilize and recruit some cytokines, such as vascular endothelial growth factor, angiopoietin 1 and cell-derived factors [3]. When SDF-1/CXCR4 was expressed, the level of SDF-1 protein around the injured tissue increased rapidly, and chemotactic endothelial progenitor cells (ECPS) gathered at the injured site to achieve tissue repair after injury.

2.4 Macrophages

When the normal tissue of the body is damaged, a series of inflammatory reactions occur around the damaged tissue, at which time macrophages begin to play immune functions in the body. Macrophages achieve body immunity by phagocytosis of bacteria and viruses in tissues and presenting and processing antigens. Studies have found that activation and performance of macrophages are different under different injury microenvironments, and activated macrophages have bidirectional function. Therefore, macrophages were divided into classically activated macrophages (M1 type) and vicarially activated macrophages (M2 type) according to the inflammatory state and activation performance. Under the condition of high inflammation, M1-type macrophages can effectively remove necrotic tissue and pathogens, and realize the body's resistance to inflammation. M2 type shows anti-inflammatory response in a low inflammatory state. Macrophages can secrete TNF-α, IL-6 and other inflammatory responses during the anti-inflammatory process in vivo, which antagonizes the expression of SDF-1 and exerts a certain influence on tissue repair after injury[4].

3. Study on Correlation between Diabetes Mellitus and Tissue Defect Repair

3.1 Mechanism of Poor Prognosis in Diabetic Patients with Injury

After tissue injury, diabetic patients will have different degrees of infection and deeper tissue destruction, and the increase of blood glucose concentration and the mediations of various inflammatory factors will cause perivascular lesions to different degrees. The body of diabetic patients is in the disorder of endocrine metabolism for a long time, which directly leads to the

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accumulation of glycosylated end products in the body after injury and affects wound healing. In addition, the disturbance of blood glucose and lipid metabolism leads to vascular neuropathy, which in turn affects the production of a variety of cytokines, making the healing process more difficult and the inflammatory response more serious.

In addition, Rihua Zhang et al. pointed out that the expression of SDF-1 mrna in trauma tissues of diabetic patients was limited and even abnormal, resulting in localized inflammatory responses in deep target cells[5]. The highly inflammatory target cells limit the function of fibroblasts and vascular endothelial cells, resulting in impaired angiogenesis and thereby limiting the process of tissue healing in diabetic patients.

3.2 Expression of SDF-1 in Diabetic Patients

SDF-1 has the effect of promoting angiogenesis on wound surface in the body, and interferes with wound healing by affecting fibroblasts, mesenchymal stem cells, endothelial progenitor cells and macrophages. SDF-1 recruits fibroblasts and mesenchymal stem cells for proliferation and fresh granulation tissue formation in damaged areas. The accumulation of endothelial progenitor cells is highly correlated with the destruction of peripheral blood vessels and regeneration of capillaries, thus achieving adequate blood circulation and nutrient supply in the healing process of wound tissues. In diabetic patients, local oxygen tension is relatively scarce, and the tissue nutrient exchange and gas exchange are limited in the healing process, and the activities of various related factors promoting healing are inhibited[6]. The accumulation of endothelial progenitor cells in the peripheral blood of the trauma area can realize the establishment of vascular network and alleviate the problems of local oxygen deficiency and nutrient exchange disorder.

3.3 SDF-1relieves Tissue Hypoxia in Diabetic Patients

Local hypoxia is one of the important factors affecting the repair of tissue defects in diabetic patients due to the deficiency of local oxygen tension. Some scholars reviewed previous studies and pointed out that local tissue hypoxia can be induced by hypoxia-inducible factor-1 (HIF-1).HIF-1 can also be expressed in normal tissues, but the expressed protein is rapidly hydrolyzed by proteases in vivo. When the expression ofHIF-1 proteolytic enzyme is blocked after tissue injury,HIF-1 protein is highly expressed in the tissue, which activates the encoding of various inflammatory factor genes, thus resulting in high local inflammatory response and low oxygen tension. After SDF-1 is activated in hypoxic tissue, it promotes the recruitment of vascular endothelial growth factor (VEGF) by endothelial progenitor cells, accelerates the expression of nitric oxide synthase (NOS-2) and heme oxygenase (Hmox1), and effectively alleviates local basal oxygen tension错误!未找到引用源。. In addition, SDF-1-induced macrophage aggregation can effectively complete phagocytosis of inflammatory tissue and antigen presentation in the defect tissue. It has been suggested thatHIF-1 released in local hypoxia environment has a certain correlation with the promotion of SDF-1 protein expression level mediated by SDF-1/CXCR4 channel in injured tissues.HIF-1 can induce SDF-1 to complete homing of endothelial progenitor cells in injured tissues, so as to establish local microcirculation and improve oxygen tension[7]. Therefore, SDF-1 is the key to repair tissue defects in the hypoxic environment after local tissue damage in diabetic patients.

4. SDF-1and Angiogenesis after Local Injury

4.1 Synergistic Effect of SDF-1 and Vascular Endothelial Growth Factor

Vascular endothelial growth factor (VEGF) is the primary influencing factor of angiogenesis after local tissue injury. VEGF promotes the regeneration of vascular endothelial cells, thus completing the increase of blood vessel permeability in the body. Some scholars have pointed out in their studies on diabetic patients that the increase of VEGF concentration is positively correlated with the formation of tissue new capillaries and granulation tissue in new tissues. SDF-1 and VEGF are both key to angiogenesis, and they are co-expressed after injury. Studies have shown that the increase of VEGF concentration increases the concentration of CXCR4 in injured tissues and enhances the

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expression level of SDF-1 protein[9]. At the same time, the high expression of SDF-1 protein promotes the increased expression of VEGF in the PI3K/Akt/eNOS pathway, realizing the synergism of SDF-1 and VEGF to complete the granulation formation and local capillary angiogenesis of injured tissues错误!未找到引用源。.

4.2 Effects of DPP-4 Inhibitors on Angiogenesis in Diabetic Patients

Dipeptide base peptidase 4 inhibitors (DPP - 4) is a kind of specific cell surface of protease, have the function of the islet beta cells release insulin, at the same time can be achieved for inhibition of glucagon sample - 1, will be inactivated and insulin secretion of polypeptides so as to make the endogenous and GIP GIP - 1 the expression level of ascension to realize the control of blood sugar levels. Tony G.Walsh and other foreign scholars have shown that DPP-4 inhibitors can mediate high expression of SDF-1 protein, up-regulate SDF-1 activity and promote tissue healing [9].

In the context of low local oxygen tension, injured local tissues can be synergistic with SDF-1 expression by increasing the expression level of compensatory DPP-4 inhibitors. The increased expression level of compensatory DPP-4 inhibitor promotes the secretion of GLP-1 by islet α cells to achieve the regulation of immune response, and thus to complete the regulation of the overall healing process [10]. Valenzuela-fernaendez Agustin et al pointed out that DPP-4 inhibitors can directly induce the transformation of epithelial mesenchymal cells on the surface of trauma, and achieve the aggregation of fibroblasts through the synergic action of SDF-1 to promote wound healing[12].

5. Expectation

After the injury of diabetic patients, due to the influence of insufficient oxygen tension and nutrient circulation of local tissues, the regeneration ability of local tissues is deficient, and the expression of a variety of growth factors is obstructed, which seriously affects the wound healing of diabetic patients. SDF-1 can realize the recruitment of various growth factors involved in new tissue in the local trauma of patients and promote the healing of injured tissue, becoming a new direction in the treatment of local tissue injury in patients with diabetes. At present, TCM intervention methods such as Yiqi, detoxification and collaterals prescription have become one of the new methods to repair damaged tissue in patients with diabetes. Therefore, it is worthy of further discussion and research to explore effective drug treatment to enhance the expression of local SDF-1 in injured tissues of diabetic patients, and to analyze the safety and effectiveness of drugs, thus providing new ideas for the treatment of local injury healing in diabetic patients.

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