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ANALYSIS OF ROLE OF LEPTIN IN ORAL WOUND HEALING IN DIABETIC PATIENTS

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Abstract:
Introduction: *Leptin, a 16-kDa non-glycosylated polypeptide anti-obesity hormone consisting of 146 amino acids, is a product of the obese gene. Although leptin is mainly produced by white adipose tissue, recent studies have demonstrated that leptin is also produced by placenta, stomach, skeletal muscles, brain and pituitary gland.* ***Objectives of the study:*** *The basic aim of this study is to analyze the role of leptin hormone in oral wound healing of diabetic patients.* ***Methodology of the study:*** *This study was done at Bakhtawar Amin Medical & Dental College, Multan during Jan 2018 to March 2018. The diabetic patient of both genders were considered for this study. Those patients who was suffering from any kind of oral wound was selected for this study. For this purpose we collect the data to analyze the role of leptin hormone in wound healing process.* ***Results:*** *The differences between the control and diabetic groups at the three measuring time periods were extremely highly significant (P = 0.000). Totally, the means of expression after 21 days were noticed by higher values than that after 14 days in both control and diabetic groups, while the means of expression after 7 days were the lowest one.* ***Conclusion:*** *It is concluded that leptin plays an important role in oral wound healing in normal patients as compared to diabetic patients. But it is not clear that why leptin is not helpful in diabetic patients.*

Key words: *Leptin, Hormone, Diabetes, Level*

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INTRODUCTION:

Leptin, a 16-kDa non-glycosylated polypeptide anti-obesity hormone consisting of 146 amino acids, is a product of the obese gene [1]. Although leptin is mainly produced by white adipose tissue, recent studies have demonstrated that leptin is also produced by placenta, stomach, skeletal muscles, brain and pituitary gland. Leptin is known to exhibit a variety of physiological actions on body weight homeostasis, lipid metabolism, hematopoiesis, thermogenesis, ovarian function, bone formation, angiogenesis and wound healing [2]. The leptin receptor (Ob-R) is expressed in various tissues including the hypothalamus, adipose tissue, skeletal muscle and hepatocytes. The multifunctionality of leptin and the wide distribution of its receptor suggest that leptin plays a variety of physiological roles not only as a systemic hormone but also as a local growth factor[3].

Diabetes is a major cause of mortality globally, and it has been estimated that 400 million people worldwide will suffer from it by 2030. Despite the fact that hereditary qualities seems to assume an essential part in the advancement of diabetes, examine recommends that dietary decisions driven by natural and financial components are of critical significance. Amazing eating regimens assume an essential part in diabetes avoidance [4]. Suitable dietary adherence can enhance insulin affectability and glycemic control, and consequently add to way of life change and general personal satisfaction. Nonetheless, past research recommends that dietary adherence is seemingly among the most troublesome foundations of diabetes administration [5]. Higher HEI scores demonstrate nearer adherence to current dietary rules for singular food and supplement gatherings. For the sufficiency segments, for example, vegetables and natural product, a higher score demonstrates higher utilization. Dietary proposals depend on the useful effects of devouring products of the soil and expressly stress their constructive outcomes of decreasing corpulence and certain sorts of growths [6]. The last three segments of the HEI incorporate refined grains, sodium, and discharge (calories from strong fats, liquor, and included sugars) and a higher score demonstrates bring down utilization.

Wound healing requires a well-orchestrated integration of complex biological and molecular events of cell migration, cell proliferation, and extracellular matrix deposition. Over 100 known physiologic factors contribute to wound healing deficiencies in individuals with diabetes. These include decreased or impaired growth factor production, angiogenic response, macrophage function, collagen accumulation, epidermal barrier function, quantity of granulation tissue, keratinocyte and fibroblast migration, and proliferation and also the number of epidermal nerves. Injury induces tissue hypoxia leading to up regulation of growth factor, extracellular matrix degradation, and subsequently, activation of angiogenesis. This formation of new blood vessels is required to sustain the newly formed granulation tissue [7].

Objectives of the study

The basic aim of this study is to analyze the role of leptin hormone in oral wound healing of diabetic patients.

METHODOLOGY OF THE STUDY:

This study was done at **Bakhtawar Amin Medical & Dental College, Multan** during Jan 2018 to March 2018. The diabetic patients of both genders were considered for this study. That patient who was suffering from any kind of oral wound was selected for this study. For this purpose we collect the data to analyze the role of leptin hormone in wound healing process. The data were analyzed by using immunochemical assay. For the process of immunohistochemical staining, 5 µ sections were prepared from each paraffin block and were deparaffinized in xylene solution and then dehydrated in graded alcohol series. To block the internal peroxidase activity, hydrogen peroxide (3%) in phosphate buffer solution was used. Then, antigen retrieval was done in a microwave oven (Panasonic 1380W) for 10 min, under the pressure of almost 2 atmospheres in 120°C. Further incubations using pre-diluted ready to use primary mouse polyclonal antibodies against leptin (lab vision corporation, Fremont, USA) (dilution 1:10) were used as the primary antibody for 30 min and were incubated in a moist chamber in room temperature for 1 day, followed by the application of secondary antibody (for 15 min), diaminobenzidine (producing brown staining), and Meyer's hematoxylin (for background staining). The samples were placed in phosphate buffer saline (PBS) immediately after each mentioned step. The positive control was used according to the manufacturer's instructions. The negative control was prepared by the replacement of primary antibody with PBS.

STATISTICAL ANALYSIS

Unconditional logistic regression was used to find out the odds ratios (ORs) and 95% confidence intervals for relations between blood transfusion, and risk of leukemia. Other variables, for example smoking, alcohol consumption, time of blood transfusion and

family history, did not result in material changes in the observed associations. All *P* values presented in the results are two-sided, and all analyses were performed by using SAS software.

RESULTS:

The differences between the control and diabetic groups at the three measuring time periods were extremely highly significant ($P = 0.000$). Totally, the means of expression after 21 days were noticed by higher values than that after 14 days in both control and diabetic groups, while the means of expression after 7 days were the lowest one (Figure 01).

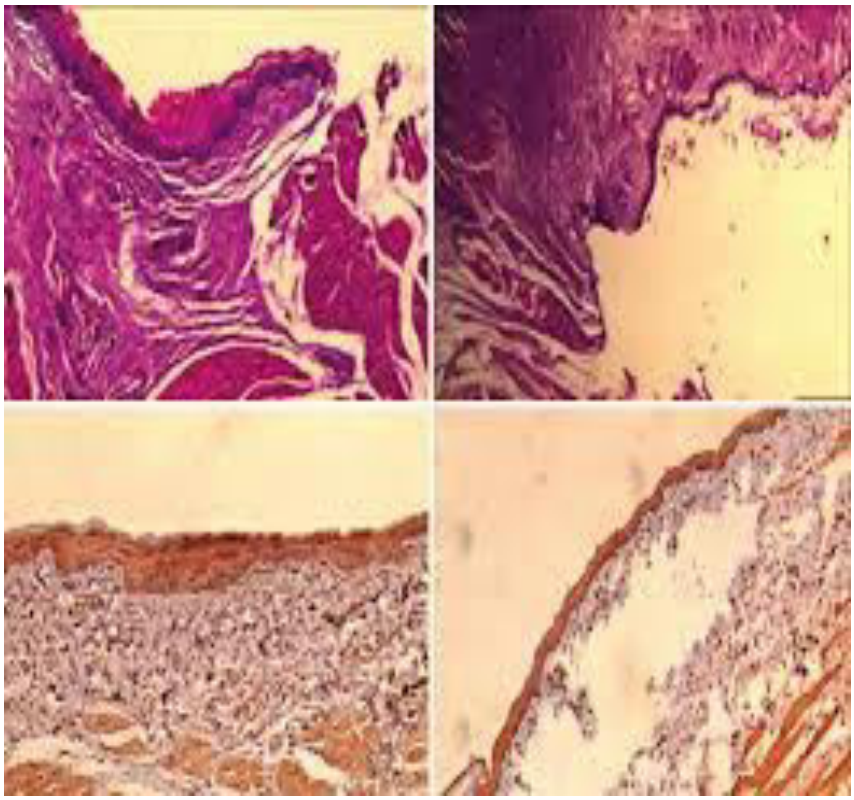

Figure 01: Expression of leptin in oral wound healing

The mean values of leptin expression in oral mucosa among control and diabetic rats at the three measuring points of time were demonstrated (Table 01). Control group showed higher means of expression of leptin after 7, 14, and 21 days than the diabetic group

Groups	After 7 days	After 14 days	After 21 days	*F* (*P* value)
Control				
Range	2.5–6	12–14.5	20–25	550.463 (0.000)***
Mean±SD	5.24±0.56[#]	13.01±0.85	22.78±1.78	
Diabetic				
Range	2–3.1	4–6	6–9	122.249 (0.000)***
Mean±SD	2.48±0.46	5.07±0.73	7.46±0.88	
t (*P* value)	13.192 (0.000)***	24.540 (0.000)***	26.726 (0.000)***	

Table 01: Analysis of expression of level of leptin in oral wound healing

DISCUSSION:

Despite the evidence shown by recent studies that local or systematic administration of cells and/or proangiogenic molecules could significantly improve angiogenesis and wound closure, diabetic wounds remain a significant clinical problem. However, it has been suggested that both systemic and topical leptin accelerate wound repair in diabetic mice, possibly through the direct interaction of leptin with its receptors in wounded skin, but do not appear to significantly stimulate wound angiogenesis [6-8]. In the present study, we evaluated the expression of leptin during healing of the incisional oral mucosal wound in both normal and diabetic rats to elucidate the role of leptin in promoting wound healing. The results of this study revealed that leptin was expressed in the epithelium and vascular endothelial cells and some stromal cells in subepithelial connective tissue. This expression is more intense in the control group than the diabetic group. These findings suggest several possibilities regarding the mechanisms by which leptin promotes wound healing. One possibility is that leptin promotes wound healing by enhancing the epithelial cell proliferation and maturation. Another possibility is that leptin stimulates angiogenesis in the connective tissue beneath the wound and promotes wound healing in the oral mucosa by accelerating the supply of nutrients, oxygen, and even some bioactive substances [9].

The oral mucosa serves many functions. The major one is the protection of the deeper tissues of the oral cavity; others include acting as a sensory organ and serving as the site of the glandular activity and secretion. Interruption in the continuity of this lining tissue compromises these functions. The oral mucosa is easily affected by many systemic factors including diabetes. Oral wounds in diabetes often fail to heal adequately, resulting in chronic ulcer formation followed by serious systemic infections [10]. This in accordance with the results of the present study in which H and E staining revealed that the healing of the surface epithelium in the control group was more than that in the diabetic group which was noticed by the thickness of the surface epithelium [11].

CONCLUSION:

It is concluded that leptin plays an important role in oral wound healing in normal patients as compared to diabetic patients. But it is not clear that why leptin is not helpful in diabetic patients.

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