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Research Article

Morphological Changes of Gingiva in Streptozotocin Diabetic Rats

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Abstract

Gingivitis and periodontitis are chronic bacterial diseases of the oral cavity. Diabetes mellitus is responsible for tooth deprivation both by decay and by periodontitis. Diabetes results in a diabetic status in experimental animals similar to that in humans. The aim of the study was to investigate the relationship between the gingival changes in streptozotocin-induced diabetes mellitus. Forty male Wistar rats (200 g, 4 weeks old, experimental). Diabetes mellitus was induced by 45 mg/kg IV streptozotocin. The results showed that the marginal gingival and the relevant gingival papilla showed inflammation and thickening of the epithelium as well as marked thickness of the arteriole in the diabetic group. The results suggested a probable application of a routine assay for the control of the disease in patients in order to control the progress of disease complications. This investigation can be used as a routine assay for the control of the disease.

1. Introduction

Gingivitis and periodontitis are chronic bacterial diseases of the oral cavity. One of the main factors in the development of the periodontal disease is the host response to bacterial stimuli. Systemic factors modify all forms of gingivitis and periodontitis through their effects on the immune and inflammatory defense. It has been reported [1] that the severity of periodontitis is related to the inflammation induced by mechanical or chemical irritations in the gingiva. It is also suggested that in diabetes mellitus the unmyelinated small diameter nerve fibers are affected, leading to peripheral neuropathy. Furthermore, many studies have been focused in the pathogenesis of periodontitis in diabetes mellitus. Microangiopathy at the bone tissue was suggested as a factor that can have an impact on the bone through multiple pathways, such as changes in insulin levels, higher concentrations of advanced glycation end products associated with glycosuria, reduced renal function, lower insulin levels, and increased inflammation [3].

Furthermore, diabetes mellitus is responsible for tooth deprivation. Periodontal diseases are associated with a higher experience of caries, a higher prevalence of gingival and periodontal problems. Patients with high blood pressure have poorer gingival or periodontal conditions, fewer teeth, and higher levels of periodontal inflammation. It was found that a larger number of oral *streptococci* adhered to the tooth surface in diabetic mice that spontaneously develop insulin-dependent diabetes mellitus.

The aim of the study was to investigate the relationship between the presence of microangiopathy in streptozotocin-induced diabetes mellitus and the severity of periodontitis.

2. Material and Methods

Forty male Wistar rats of average body weight of 200 g were divided into two groups: control (control, $n = 10$). They were housed five per cage at a constant temperature of 22°C and a light/dark cycle (light period 08.00-20.00 hours). Food and water were provided ad libitum and cared for accordance with the principles of the "Guide for the Care and Use of Mammals in Biomedical Research" (National Institutes of Health, Bethesda, MD). The animals of group A were injected once IV with streptozotocin 45 mg/kg body weight. The duration of the experiment was 90 days. The blood glucose levels were estimated by the glucose oxidase method (Glucose Division, Miles Laboratories, Rexdale, Ontario, Canada) in blood samples. Urine glucose was also qualitatively assayed in urine with urineteststrips (Glukotest, Glukotest, Glukotest). Food intake as well as their food intake was determined. The animals were sacrificed by perfusion of the heart with saline. The incisors obtained from the incisor area of the mandible were washed with distilled water and fixed for further histological examination with the light microscope. The sections were stained with haematoxylin-eosin by light microscope. The values are expressed as mean \pm SD. The statistical analysis was performed by Student's *t*-test. A $P < 0.05$ was considered an acceptable level of significance.

3. Results

The induction of diabetes mellitus was assessed the day after streptozotocin injection by signs such as frequent urination, increased appetite, and weight loss. In the streptozotocin animals exerted a hyperphagia accompanied with an increase in body weight. The streptozotocin animals had increased serum glucose and increased body weight. The severity of diabetes was indicated by the statistically significantly increased serum glucose levels in comparison to controls ($P < 0.001$, Table 1). The quantity of diabetes was compared to controls. Blood glucose levels were significantly increased in the streptozotocin group compared to the control group. The levels of Hb A1c were lower in the control group compared to the streptozotocin group. The frequency of diabetes was frequent and the shavings of the cages needed to be changed were increased.

Control animals	Streptozotocin diabetic animals
Body weight (g)	240 ± 10
Body weight change (%)	100 ± 5
Survival (%)	90 ± 5
Survival at 100 days (%)	80 ± 5

Table 1: Clinical indices and laboratory finding

The experimental animals had a mortality of 10% during the experiment. The remaining animals remained alive until the end of the experimental procedure.

The histological findings of the experimental group were as follows: hyperplasia of the marginal gingivae and the gingival papillae from the incisal area, formation of new vessels with various wall thicknesses, and hyperplasia of the gingiva, which was in contact with the tooth surface.

The gingival specimens obtained from the molar area of the mandible showed hyperkeratinization to high hyperkeratinization and mild inflammation. All the experimental findings were not observed in the control animals (see Table 2, Figure 2).

Parameter	Control animals	Streptozotocin diabetic animals
Hyperkeratinization	0	1
Inflammation	0	1
Hyperplasia	0	1
Angiogenesis	0	1

Table 2: Histological findings.**Figure 1:** (□) Focal perivascular and diffuse angiogenesis, and (*) hyperplasia of the squamous epithelium.**Figure 2:** (*) Hyperplasia of the squamous epithelium, inflammation of the lamina propria, and (†) thickening of the gingiva.**Figure 3:** (*) Normal gingival mucosa, normal vasculature, and absence of inflammation.

4. Discussion

Recent drastic increase in diabetic population poses serious problems for health services. The recent drastic increase in the diabetic population poses serious problems for socioeconomic services. The most important issue in the clinical practice is the complications that contribute to a high morbidity and mortality [7, 8].

Hyperglycaemia, as a common feature of diabetes mellitus, is a cause of endothelial dysfunction.

Diabetes mellitus results in the development of large and medium-sized arteries independently of the presence of atherosclerosis. The abnormalities

laminin, fibronectin, type IV collagen, and connective tissue with calcium. It is of particular interest that accumulation of PAS-positive materials are recognized as the histological markers of diabetic microangiopathy.

In this study, the administration of streptozotocin in rats induced changes similar to that observed in diabetic patients, as shown by the manifestations reported in the literature [2, 13, 14].

The changes observed in periodontal vasculature concerned macro- and microvasculature. It is known to impair the function of various organs and systems and includes nephropathy, and neuropathy [15]. Periodontal disease is considered a complication that has long been observed that diabetic patients have greater tooth loss than non-diabetic patients of comparable age [16]. The severity of the periodontal disease is about the same as in non-diabetic patients [17]. The phenomenon may be due to the high tissue glucose concentrations and the products of the impaired glucose metabolism and it is recognized as a narrowing of vessel lumen diameter. This process induces disabilities of vessel wall such as narrowed vessels and an abnormal vasculature [12, 18]. Our results are in agreement with those reported in the literature that vessel lumen diameter in diabetic subjects as observed by the incidence of periodontal disease [9].

These changes can be aggravated through inflammatory cell infiltration and treatment in the gingivomucosal tissue as reported by Fehér et al. [19]. The pathophysiology of diabetic microangiopathy and its pathogenesis is related to hyperglycemia, early stimuli elicit adaptive reactions of tissues such as changes of microangiopathy. The impaired glucose metabolism with a narrowing of vessel lumen diameter. This situation in dental extraction sockets, periradical lesions, and periodontal disease [4, 19].

In addition, it has been suggested that the unmyelinated small-diameter nerve fibers in diabetes mellitus, which indicates that in the streptozotocin-induced diabetes mellitus, a prerequisite for neurogenic inflammation induced by mechanical changes is the increased permeability. Furthermore, diabetic changes may be accompanied by changes in the connective tissue [21].

This process induces disabilities of vessel wall such as narrowed vessels and an abnormal vasculature [12, 19]. Since the ability of the diabetic subjects to maintain a good oral hygiene is especially during increased blood flow causing severe disturbances in oral health, poor nourishment, which, in relation to the high blood glucose levels, leads to a change in the microflora in the oral cavity [22]. The presence of PAS material deposits in the periodontium is an index of severe diabetic damage [9]. Therefore, slow flow of blood and the destruction process of the periodontium [23].

An important injury that leads to severe handicap in diabetic patients is the loss of vision, which leads to blindness [24]. Most recently, it has been proven that the loss of vision is related to the presence of the periodontal disease [25]. In addition, the loss of vision in diabetes is related to tooth loss and temporomandibular joint dysfunction.

Therefore, the investigation of the surrounding oral cavity tissue changes and the signs that may alert the physician to control or prevent the disease. The histological gingival analysis may be routinely utilized for the control of the disease, which is considered as a diagnostic method of the severity of the disease.

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