Effect of Streptozotocin Induced Diabetes on the Lingual Papillae of Albino Rat

Thesis
Submitted For Partial Fulfillment of the Requirements
of Master Degree in Oral Biology

By
Dina Mohamed Abdel-Khalek
B.D.S -2002
Demonstrator, Oral Biology
Faculty of Dentistry - Ain Shams University

Under Supervision of

Prof. Dr.
Suzy M. Farid Shinaishin
Professor and Head of Oral Biology Department
Faculty of Dentistry, Ain Shams University

Co-supervisor
Associate Prof.Dr.
Ahmed Mahmoud Halawa
Associate professor of Oral Biology
Faculty of Dentistry, Ain Shams University

Faculty of Dentistry
Ain Shams University
2009

دراسة تأثير داء السكرى المستحث بواسطة الستربتوزوتوسين علي الحليمات اللسانية للفأر الأبيض

رسالة مقدمة من الطبيبة

دينا محمد عبد الخالق

بكالوريوس طب و جراحة الفم و الأسنان

كلية طب الأسنان - جامعة عين شمس

2002

المعيدة بقسم بيولوجيا الفم

كلية طب الأسنان - جامعة عين شمس

كجزء من مقومات الحصول على درجة الماجستير

فرع بيولوجيا الفم

تحت إشراف

أ.د/ سوزى محمد فريد شنيشن

أستاذ ورئيس قسم بيولوجيا الفم

كلية طب الأسنان - جامعة عين شمس

المشرف المساعد

أ.م.د/أحمد محمود حلاوة

أستاذ مساعد بيولوجيا الفم

كلية طب الأسنان - جامعة عين شمس

كلية طب الأسنان - جامعة عين شمس

2009

Acknowledgement

Endless grateful thanks to ALLAH for helping me to finish this work.

First of all, I'd like to express my deep gratitude and appreciation to ***Prof. Dr. Souzi Farid Shinashin***, head of Oral Biology Department, Faculty of Dentistry, Ain Shams University for her extremely precious help, continuous support and valuable guidance throughout this work.

I am also equally thankful to ***Ass. Prof. Dr. Ahmed Mahmoud Halawa,*** Ass. Prof. of Oral Biology, Faculty of Dentistry, Ain Shams University for his effort, time and indeed valuable notices during all the different stages of this work.

And never forget my endless thankfulness to ***Prof. Dr. Medhat Ahmed El-Zeiny***, Prof. of Oral Biology and former vice dean, Faculty of Dentistry, Ain Shams University, for his immeasurable backing & encouragement since I was a first year student and until today.

Sincere thanks are also extended to all my senior staff and colleagues in the Oral Biology Department for their valuable remarks and faithful cooperation.

A final note of thanks goes to my family, my sweet Ali, for helping and encouraging me to finish this study.

Introduction

Diabetes mellitus (DM) is one of the most prevalent chronic diseases affecting mankind. It is defined as a multistage, complex, chronic metabolic disorder characterized by dysregulation of carbohydrate, protein and lipid metabolism **(Artino et al., 1998).**

The two main types of diabetes that correspond to these two mechanisms and are called insulin dependent (type I) and non-insulin dependent (type II) diabetes. In type I diabetes insulin is deficient or totally absent, while in type II diabetes, there is generally enough insulin but the cells upon it should act are not normally sensitive to its action **(American Diabetes Association, 2006)**.

Diabetes has different pathological effects on the body tissues and organs; it is associated with an increased risk for a number of serious, sometimes life-threatening complications as heart disease, stroke, high blood pressure, blindness, kidney disease and amputations **(Rother, 2007)**.

Affection of the oral mucous membrane, tongue and lingual papillae are more common in people with diabetes. Persons with poorly controlled diabetes are nearly three times more likely to

develop severe periodontitis than those without diabetes **(Gregg et al., 2007)**.

Few researches have been concerned with the effect of diabetes on different types of lingual papillae namely filliform, fungiform circumvallate and foliate.

Therefore, the diabetes induced effects on lingual papillae and taste buds are the scope of this study.

Review of Literature

Diabetes mellitus:

Diabetes affects every cell in the body and the biochemical processes of carbohydrate, lipid and protein metabolism is disrupted. The term diabetes came from Greek words meaning "siphon" or "run through". In medicine, it signifies the excretion of an excessive urine volume. Diabetes is characterized by the polytriad: polyuria (excessive urination), polydypsia (excessive thirst), and polyphagia (excessive hunger) **(Ophardt, 2003).**

The primary feature of this disorder is elevation in blood glucose levels (hyperglycemia), resulting from either a defect in insulin secretion from the pancreas, a change in insulin action, or both. Sustained hyperglycemia has been shown to affect almost all tissues in the body and is associated with significant complications of multiple organ systems, including the eyes, nerves, kidneys and blood vessels **(Mealey, 2006)**.

Diabetes Pathophysiology:

An understanding of the pathophysiology of diabetes rests upon knowledge of the basics of carbohydrate metabolism and

insulin action. Following the consumption of food, carbohydrates are broken down into glucose molecules in the gut. Glucose is absorbed into the blood stream elevating blood glucose levels. This rise in glycemia stimulates the secretion of insulin from the beta cells of the pancreas. Insulin is needed by most cells to allow glucose entry. Insulin binds to specific cellular receptors and facilitates entry of glucose into the cell, which uses the glucose for energy. The increased insulin secretion from the pancreas and the subsequent cellular utilization of glucose results in lowered blood glucose levels. Then the reduced blood glucose levels in turn results in decreased insulin secretion **(Mealey, 2006)**.

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In diseases that alter insulin production and secretion, glucose dynamics will subsequently be altered. The same effect will be seen if insulin is secreted from the pancreas but is not properly utilized by target cells. On the other hand, increased insulin secretion results in very low blood glucose levels (hypoglycemia) because large amounts of glucose enter tissue cells and little remain in the bloodstream **(Mealey, 2006)**.

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Insulin is the only hormone that lowers blood glucose levels. The counter-regulatory hormones such as glucagon,

catecholamines, growth hormone, thyroid hormone, and glucocorticoids all act to increase blood glucose levels **(Mealey, 2006)**.

Types of DM:

There are two main types of diabetes are called insulin dependent (type I) and non-insulin dependent (type II) diabetes **(Masharani, 2006).**

Type I DM:

This type is a catabolic disorder in which circulating insulin is virtually absent and plasma glucagon is elevated. It is usually associated with ketosis in its untreated state and occurs at any age but most commonly arises in children and young adults with a peak incidence before school age and around puberty. This form of diabetes is immune-mediated & the pancreatic B cells fail to respond to all insulinogenic stimuli and is characterized by ketonemia, ketonuria, or both. Also autoantibodies against Islet cells are frequently present **(Masharani, 2006)**.

Subtypes of type I DM:

1. Immune-mediated type 1 DM: it is believed to result from an infectious or toxic insult to persons whose immune system is

genetically predisposed to develop a vigorous autoimmune response .

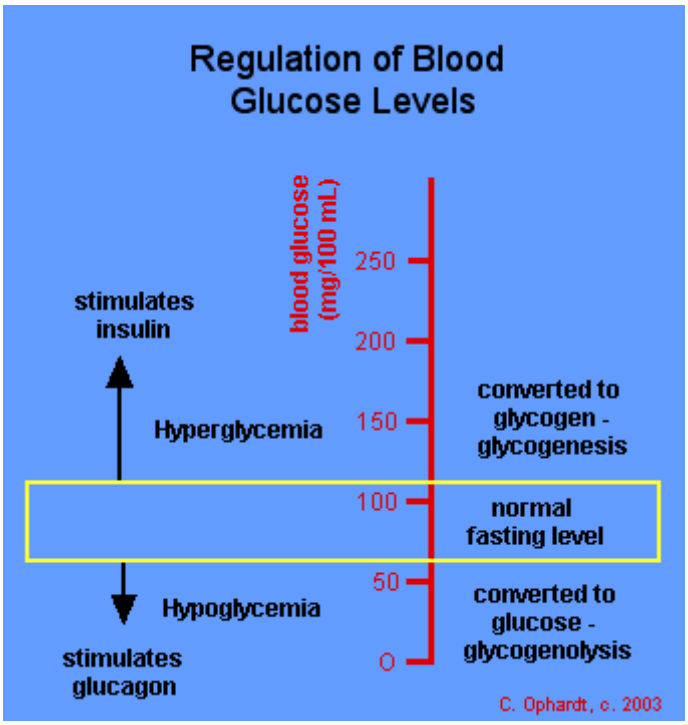
2. Idiopathic type 1 diabetes mellitus - Fewer than 10% of subjects have no evidence of pancreatic B cell autoimmunity to explain their insulinopenia and ketoacidosis. This subgroup has been classified as "idiopathic type 1 diabetes" and designated as "type 1B." **(Masharani, 2006)**.

Type II DM:

In this type, there is generally enough insulin but the cells upon it should act are not normally sensitive to its action. Most affected patients are over 40 years of age and are obese. Type II DM is characterized by polyuria and polydipsia. Ketonuria and weight loss generally are uncommon at time of diagnosis. Candidal vaginitis in women may be an initial manifestation. Many patients have few or no symptoms.

Plasma glucose of 126 mg/dL or higher after an overnight fast on more than one occasion. After 75 g oral glucose, diagnostic values are 200 mg/dL or more 2 hours after the oral glucose. Hypertension, dyslipidemia, and atherosclerosis are often associated **(Masharani, 2006)**.

Errors of metabolism associated with DM are shown in the following figures.



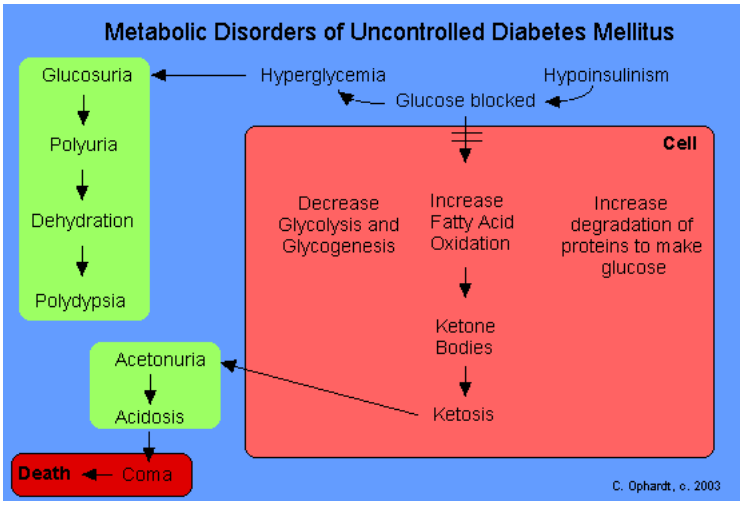


Fig. (1): Errors of metabolism in DM. **(Ophardt, 2003).**

GENERAL COMPLICATIONS OF DIABETES:

Diabetes has different pathological effects on the body tissues and organs. It causes serious, sometimes life-threatening complications as heart disease, myocardial infarction, stroke, high blood pressure, ocular complications as diabetic cataracts, retinopathies and blindness. Diabetic nephropathy, peripheral & autonomic diabetic neuropathy, amputations, complications of pregnancy and sexual dysfunctions are also frequent. **(American Diabetes Association, 2006)**.

The major cause of the high morbidity and mortality rate associated with diabetes is a group of microvascular and macrovascular complications affecting multiple organ systems **(Mealey, 2006).**

Vascular complications result from atherosclerosis and microangiopathy. Increased lipid deposition and atheroma formation is seen in the larger blood vessels, along with increased thickness of arterial walls. Proliferation of endothelial cells, alterations in endothelial basement membranes and changes in the function of endothelial cells induce microvascular damage. Since the function of cell membranes is determined largely by their

phospholipid bilayers; thus, changes in lipid metabolism can have major effects on cells **(Mealey,2006).**

Autonomic neuropathy affecting the gastrointestinal system is a major presentation of diabetic neuropathy. Increased number of substance P-containing nerve fibers in diabetes mellitus might be the reason for painful neuropathy and might amplify the inflammatory reaction in nerve axons **(Masharani, 2006).**

The oxidation of circulating low-density lipoprotein (LDL) in hyperglycemic individuals increases oxidant stress within the vasculature, which in turn induces chemotaxis of monocytes and macrophages into the vessel walls, where oxidized LDL causes changes in cellular adhesion and increased production of cytokines and growth factors resulting in stimulation of smooth-muscle cell proliferation and increase in vessel wall thickness that significantly alter wound healing. Other changes include increased atheroma formation and development of microthrombi in large blood vessels and alterations in vascular permeability and endothelial cell function in the microvasculature **(Rother, 2007)**.

Proper diabetes control can help reduce risk of complications. However, many people are not even aware that they have diabetes until they develop one of its complications. The onset and

progression of these complications is strongly linked to the presence of sustained hyperglycemia **(Mealey, 2006).**

Skin and Mucous membrane complications of DM:

Chronic pyogenic infections of the skin may occur, especially in poorly controlled diabetic patients. Eruptive xanthomas can result from hypertriglyceridemia associated with poor glycemic control, This inflammatory reaction results in the release of histamine, leukotrienes, cytokines, and chemokines which might cause inflammations and lesions of the mucosa **(Masharani, 2006)**.

Maruo et al., (2001) detected accelerated DNA fragmentation of the epithelial and connective tissue cells with induced diabetes.

Oral complications of diabetes:

Gregg et al., (2007) stated that affection of the oral mucous membrane, tongue and lingual papillae are more common in people with diabetes. Persons with poorly controlled diabetes are nearly three times more likely to develop severe periodontitis than those without diabetes.

Oral conditions that are seen in individuals with diabetes may include burning mouth, altered wound healing, increased incidence of infection, enlargement of the parotid glands , xerostomia and the prevalence of hyposalivation. These conditions elucidate the possible interrelationships between salivary dysfunction & diabetic complications **(Moore et al., 2001).**

Strong evidence suggests that, diabetes is a risk factor for the prevalence and severity of gingivitis and periodontitis. Diabetes is associated with increased gingival inflammation in response to bacterial plaque, it has been shown to significantly increase the risk of attachment loss and alveolar bone loss approximately threefold when compared to non-diabetic control subjects.

Recent epidemiological studies have incriminated diabetes mellitus as a risk factor for the development of oral squamous cell carcinomas, as well as oral premalignant lesions because it seems to promote signal transduction pathway leading to increased cellular proliferation. **(Vairaktaris et al., 2007)**.

It has also been found that patients with diabetes had significantly higher prelevance of fissured tongues, irritation fibromas, traumatic ulcers & delayed wound healing