ESTIMATION OF ACTH IN SALIVARY SECREATION OF DIABETICS

THESIS

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By

SALAH AHMED IBRAHIM MOHAMED
M.B.Ch.B.

Supervised By

Prof. Dr. MOGHAZI ALI MAHGOUB
Professor of Medicine
Faculty of Medicine
Ain Shams University

Dr. MOHAMED ALAA EL DINE HAMED
Assistant Professor of Medicine
Faculty of Medicine
Ain Shams University

Dr. FADILA GADALAH
Lecturer of Medicine
Faculty of Medicine
Ain Shams University

Faculty of Medicine
Ain Shams University

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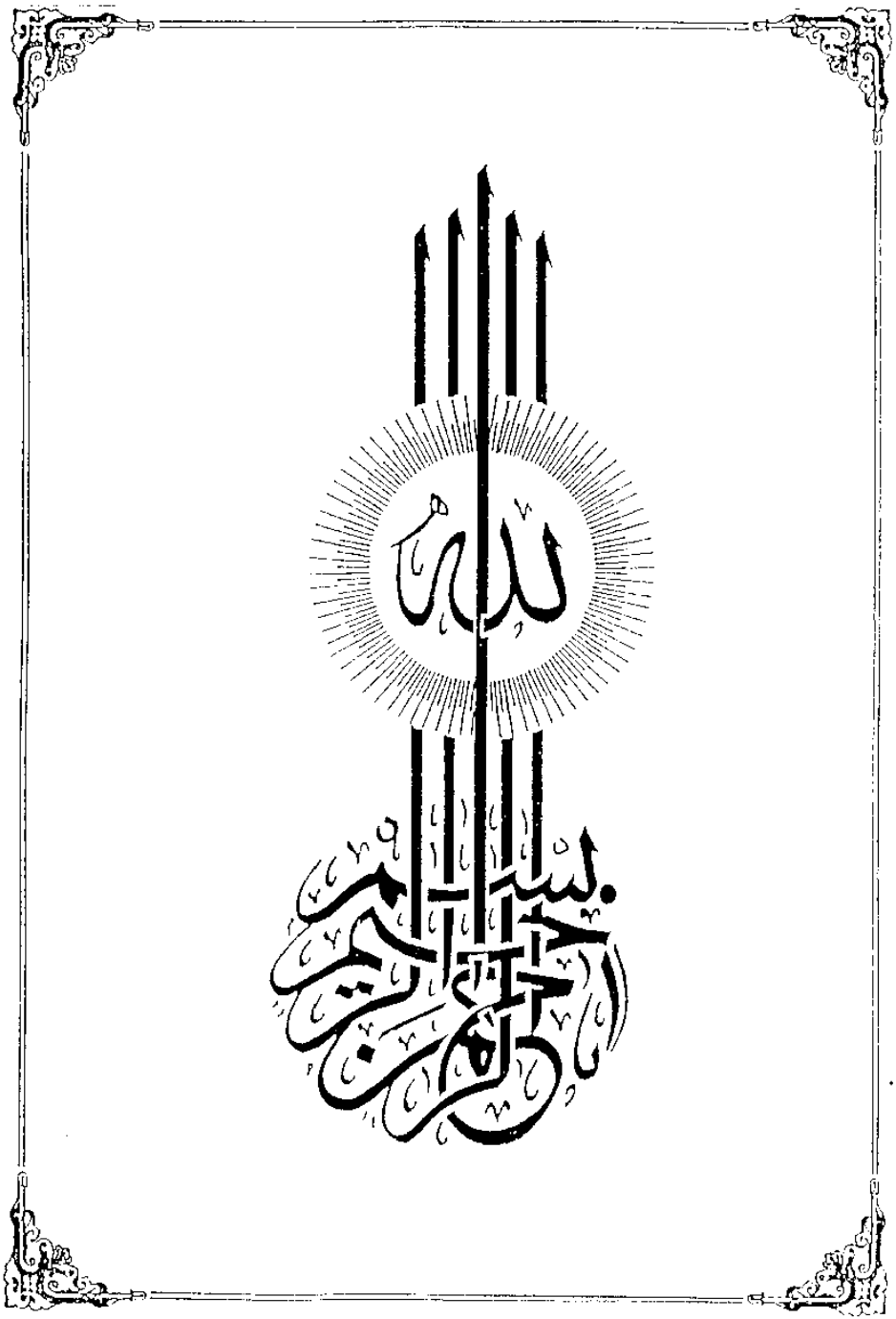

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INTRODUCTION AND AIM OF WORK

Introduction:

Assessment of hormones in saliva may be advantageous in researches, since saliva samples are easily obtainable and do not demand stressful venipuncture (Dirk et al., 1985).

The sampling and storage of saliva can be done by the patient, or experimental subject himself, thus not requiring the presence of laboratory equipment and personnel.

This gives a good prospect for research of endocrine response patterns during real life situations and field experiments.

Recent progress in radioimmunoassay (RIA) technique has made possible a sufficiently sensitive direct assay of salivary adrenocorticotrophic hormone (ACTH).

It is well known that saliva is composed mainly of water, salts and mucopolysaccharides (Davenport, H.W. et al., 1977).

Recently, it is observed that certain hormones can be found in salivary secretion (Avigdor Sharon et al., 1985).

Aim of Work:

The aim of this work is to demonstrate the level of salivary ACTH compared to plasma ACTH and in order to raise its usefulness as a non-invasive technique to follow up diabetic patients.

REVIEW OF LITERATURE

Diabetes Mellitus

History: (Kloppel, 1984):

The term "diabetes" [=running through a siphon] is based on the ancient idea that in this disease every fluid consumed runs immediately through the body, thus leading to polyuria. The first detailed description of the clinical syndrome of diabetes was given by Aretaios of Cappadocia [Ca.81-138 A.D.]. Who took up the apparently already known term "diabetes", which was probably coined by Demetrius of Apamaia about 200 years earlier. Aretaios believed that the cause of diabetes lies in the stomach, Galen implicated the Kidneys and Claude Bernard, in the middle of the 19th century, favoured the liver. It was not until 1889, that Mering and Minkowsky's experiments established the relation of the pancreas to diabetes, and this eventually led to the discovery of insulin by **Banting and Best in 1922.**

Definition of Diabetes Mellitus:

In 1980, The WHO expert committee on diabetes mellitus defined this disease as "a state of chronic hyperglycaemia (i.e. the state of having an excessive concentration of glucose in the blood), which may result from many environmental and genetic factors,

often acting jointly". The causes of hyperglycaemia are either an absolute or a relative insulin deficiency, which leads to a wide spectrum of defective carbohydrate metabolism.

Classification of Diabetes Mellitus

The classification of diabetes mellitus and associated states proposed by National Diabetes Data Group in 1979 and provisionally endorsed by WHO "1980" is still the latest accepted classification (Keen and Tang Fui, 1982, Genuth, 1982).

Classification of D.M. and other Categories of Glucose intolerance:

1- **Diabetes Mellitus:**

a- Insulin dependent "IDDM" or Type I.

b- Non-insulin dependent "NIDDM" or Type II:

- Non obese NIDDM.
- Obese NIDDM.

c- Other Types:

- Pancreatic disease.
- Hormonal.
- Drug or chemical induced.
- Insulin receptor abnormality.
- Certain Genetic Syndromes.
- Other Types.

2- **Impaired Glucose Tolerance "IGT":**

a- Non obese IGT.

b- Obese IGT.

c- Impaired Glucose Tolerance associated with certain conditions and syndromes; e.g.:

- Pancreatic disease.
- Hormonal.
- Drug or chemical induced.
- Insulin receptor abnormalities.
- Certain genetic syndromes.

3- Gestational diabetes.

4- Statistical risk groups:

a- Previous abnormality of glucose tolerance prev. AGT.

b- Potential abnormality of glucose tolerance pot. AGT.

- Insulin Dependent Diabetes Mellitus "IDDM" or Type 1:

With few exceptions diabetes mellitus in children is of the insulin dependent variety-previously called juvenile onset diabetes mellitus "JOD".

"IDDM", however, is not restricted to onset in the childhood, but it may occur at any age. Patient with IDDM usually present with an accelerating history of glucosuric symptoms for less than 3 months and only rarely discovered accidentally when they are asymptomatic (Fajan et al., 1978). This explains their state of absolute insulin dependance (Genuth, 1982). IDDM is characterized by insulinopenia (Genuth, 1973, 1982). Fasting plasma insulin levels are low, and there is little or no response to challenge with glucose, tolbutamide, aminoacids, glucagon or, other Beta cell stimulants.

Anatomically the islets are small with decreased number of beta cells, though hyperplasia of other islet cells that produce glucagon, somatostatin and pancreatic polypeptide is often seen (Gepts et al., 1977).

The decreased number of beta cells in the islets results in disappearance of the beta cell function

as shown by low plasma levels of the connecting peptide "C peptide" which is normally co-secreted with insulin (Malmquist et al., 1982, Werther et al., 1982).

Though patients with non insulin dependent diabetes of youth, which can be diagnosed very early in life, are usually treated with insulin, they are able to survive without it (Fajans et al., 1978).

Type I "IDDM" has been long associated with autoimmune diseases, such as Hashimoto's Thyroiditis or, Addison's disease. It is also known to be associated with an increased incidence of histocompatibility antigens, in particular, HLA-B_8-HLA-BW_{15}, DW_3, DW_4 (Irvine et al., 1977; Rotter and Rimoin, 1978).

- Subclassification of Type I Diabetes Mellitus, "IDDM":

Recent genetic studies, serum antibody measurements and tissue typing have provided strong evidence that type I diabetes is not individually homogeneous (Irvine et al., 1977; Fajans et al., 1978; Cudworth and Wolf, 1982).

It was subdivided by the WHO Expert Committee in 1980 into two groups: Type Ia, and Type Ib this subdivision may aid in better prognostic information and more assured genetic counselling (Genuth, 1982).

Type Ia:

This subtype occurs in young age with male prepoderance. It has a genetic vulnerability to an environmental agent, thus identical twins may not be concordant for the disease. It has a primary association with HLA-DR_3 and HLA-DR_4 (Cudworth and Wolf, 1982). The serum antibodies in this type are short term. They produce high titers of antibody to the exogenous insulin that is administered therapeutically (Genuth, 1982). It is not usually associated with other autoimmune disturbance.

Type Ib:

It occurs at middle age with a striking female preponderance (Cudworth and Wolf, 1982). In this group identical twins has a high degree of concordance for diabetes suggesting a genetically conferred inevitability of the disease. It has a strong association with HLA-DR_3. Islet cell antibodies tend to persist in the serum of the patients. These patients and their families have frequently other autoimmune disorders, such as Hashimoto's disease.

- Non-Insulin Dependent Diabetes Mellitus "NIDDM" or Type II:

This type of diabetes usually occurs after the age of 30 years. The prevalence is actually undetected