GASTRIC EMPTYING AS A DETERMINANT OF THE ORAL GLUCOSE TOLERANCE TEST

THESIS

Submitted for the Partial Fulfillment of the Master Degree in GENERAL MEDICINE

BY

SAAFAN MOUSTAFA ABDEL KHALEK SAAFAN

M.B.B.CH.

Supervisors

Prof. Dr. SAYED M. RAAFAT
Prof. of Inter. Medicine

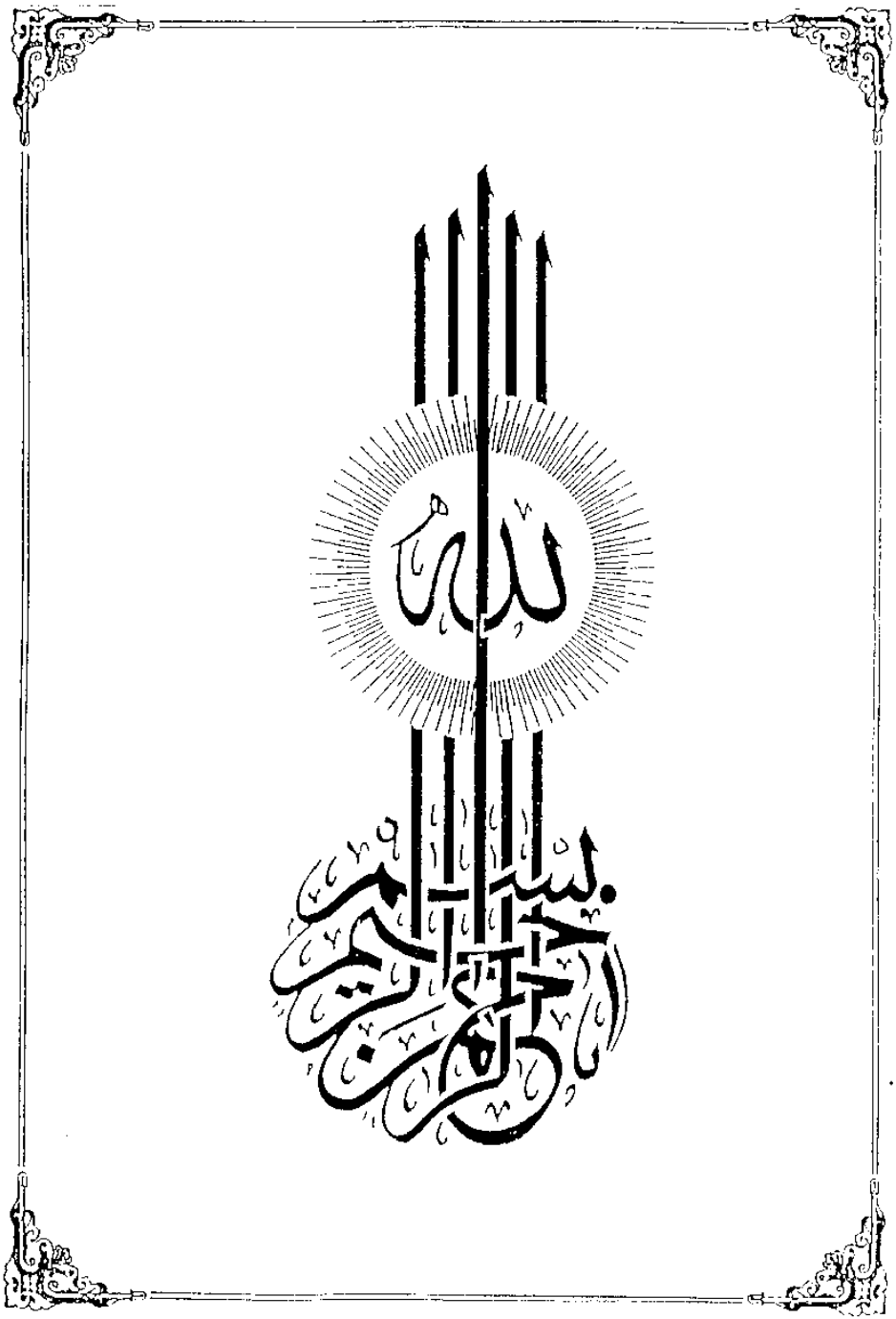
Prof. Dr. HUSSEIN EL-DAMASY
Prof. of Inter. Medicine

Dr. FADILA GAD ALLAH
Lec. of Int.Medicine

Faculty of Medicine
Ain Shams University
Cairo-Egypt

(1987)

بسم الله الرحمن الرحيم



TO MY SON :

TAMER

ACKNOWLEDGEMENT

I would like to express my deepest gratitude and most sincere thanks to prof. Dr. Sayed Saafat who gave me the broad outline of such subject, for close supervision and great co-operation . His constant advice and constructive criticism are beyond acknowlecgement.

I wish to express my deepest appreciation and thanks to Prof. Dr. Hussein El-Damassy whose encouragement, care, and support helped me a lot to complete this work.

I wish to express my thanks to Dr. Fadila Gad Allah who supervised this work in the very fine details , helping me collecting , interpreting, and arranging the data of the work.

I would like to thank all the biochemists of the endocrine lab.

Last but not least , I am grateful to all patients who have shared in this study by their own blood. To whom I am greatly indebted.

ABBRIVIATIONS

* dl : decilitre
* GHb : Glycosylated hemoglobin.
* GIP : Gastric inhbitory polypeptide.
* GLI : Glucagon like immunoreactivity.
* gm/m^2 : gram per meter square.
* GTT : Glucose tolerance test.
* IDD : Insulin dependent diabetes.
* IGT : Impaired glucose tolerance.
* mg% : milligram per cent.
* NDDG: National DataDiabetes Data Group.
* NIDD: Non insulin dependent diabetes.
* OGTT: Oral glucose tolerance test.
* Pot.AGT: Potential abnormality of glucose tolerance.
* PP : Pancreatic polypeptide.
* Pre-ABT: Previous abnormality of glucose tolerance.
* PYY : Peptide YY.
* SP : Substance-p.
* SS : Somatostatin.
* VIP : Vasoactive intestinal peptide.

Contents

INTRODUCTION

INTRODUCTION AND THE AIM OF THE WORK

Diabetes mellitus is the most common metabolic disease of humans (Foster, 1985). Some of the patients do not present with impressive symptoms and signs that provide the physician with a clue to the diagnosis . Thus the laboratory procedures for the diagnosis are of great value .

The oral glucose tolerance test is the most practical test for the routine use and is the most frequently performed (Dela Huergu, 1971) . On the other hand , this test has several disadvantages, the most important being its poor reproducibility (McDonald et al., 1965).

Recent interest in gastrointestinal factors that influence the post-prandial rise in the peripheral blood glucose has emphasized the importance of the rate of gastric emptying (Jenkines et al., 1982).

The aim of the present work is to study the effect of altering the rate of gastric emptying , induced by drugs, on the blood glucose levels during the oral glucose tolerance test.

REVIEW OF LITERATURE

I. DIABETES MELLITUS

definition, classification and diagnosis

Definition:-

Diabetes mellitus is a clinical syndrome characterised by chronic hyperglycemia and glucosuria (Toft et al.1981).It is not a single disease entity but it includes a variety of metabolic disorders which lead frequently to grave consequence (Marson and Boucher, 1978). The diminished effectiveness of insulin ultimately leads to hyperglycemia with the eminent danger of ketoacidosis.

Classification:-

Diabetes was classified according to patient's age at the onset of symptoms into juvenile onset and adult onset.In 1979 the national diabetes data group (NDDG)has classified diabetes as follow:

Class	Former terminology
1. Diabetes mellitus	
a.insulin dependent diabetes mellitus type I(IDDM)	juvenile onset type diabetes (i)Ketosis-prone diabetes (ii)juvenile onset diabetes (iii)severe diabetes (iv)brittle diabetes
b.non-insulin dependent diabetes mellitus type II (NIDDM):-	maturity onset type diabetes (i)adult onset diaetes (ii)ketosis-resistant diabetes
(i)non-obese NIDDM	(iii)mild diabetes

Class	Former terminolgy
(ii)obese NIDDM	(iv)obesity hyperglycemia (v)maturity onset diabetes (vi)stable diabetes
C-other types including diabetes mellitus associated with certain conditions and syndromes:- (i)pancreatic diseases (ii)hormonal (iii)drug or chemical induced (iv)insulin receptor abnormality (v)certain genetic syndromes	secondary diabetes
2.Impaired glucose tolerance (IGT) (i)non obese (ii)obese (iii)IGT associated with certain condition and syndromes as .pancreatic diseases .hormonal .drug or chemical induced .insulin receptor abnormality .genetic syndromes	asymptomatic diabetes , chemical diabetes, subclinical diabetes, border line diabetes.
3.Gestational diabetes(GD)	Gestational diabetes

4. Previous abnormality of glucose tolerance (Pre AGT)	Latent diabetes, prediabetes
5. Potential abnormality of glucose tolerance.	Prediabetes, potential diabetes.

TYPE I: INSULIN DEPENDENT DIABETES MELLITUS (IDDM):

This the the first subclass of diabetes. IDDM describes the clinical form of the diabetes syndrome, florid with symptoms,rapidly progressive in course and lethal in the absence of insulin treatment. In the majority of cases, onset is in the youth (NDDG,1979). It is characterized by insulinopenia (Genuth, 1973). Islet cell antibodies are present in 80 to 90 per cent of all patients with IDDM at the time of diagnosis.

According to the genetic studies, type I could be classified into Ia and Ib , the subgroup Ia,their HLA haplotype contains B8 and DW 3 , autoantibodies tend to persist in the serum of these patients. Associated autoimmmne disorders as grave's disease, Hashimoto's thyroiditis , Addison's disease are frequently encountered in these patients. Enviromental factors (viral, chemical) appear to be mainly responsible for B-cell dysfunction in these patients.

The subgroup Ib , their HLA haplotype contains BW15 and CW3 and B7. Other autoimmune disorders are not seen frequently in these patients. serum autoantibodies tend to disappear after the first year of disease. also the pattern of microvascular complications does not stand out, while in subgroup Ia retinopathy and renal microangiopathy are more common and more severe.

TYPE II : NON INSLULIN DEPENDENT DIABETES MELLITUS (NIDDM)

Persons in this subclass, frequently present with minimal or no symptoms referable to the metabolic aberrations of diabetes. Patients with NIDDM are not insulin dependent and are not prone to ketosis, however they may require insulin for correction of symptomatic or persistant hyperglycemia, if this can not be achieved with the use of diet or oral agents. Such patients may develop ketosis under special circumstances such as severe stress precipitated by infections or trauma. Serum insulin level may be normal, elevated or depressed (Genuth,1973).

Patients with NIDDM may be asymptomatic for years or decades and show only slow progression of the disease. However, the typical chronic associations and complications of diabetes, namely, macroangiopathy, microangiopathy, neuropathy and cataract may be seen in this type (Vracho, et al. ,1970).In the majority of cases the onset is after the age of 40 but NIDDM is known to occur at all ages, consequently age of onset is not recommended as a criterion by which to classify an individual. About 60-90% of NIDDM subjects are obese (Genuth, 1982), in these patients glucose tolerance is often improved by weight loss (Genuth, 1982). Hyperinsulinemia and insulin resistance characterise patients in this subclass (NDDG,1979).

In contrast to type I diabetes, NIDDM is characterised by absence of inflammatory cells in the islets, no circulating islet cell antibodies, no particular HLA association and no suggestion of association with viral illness (ALBIN and RIFKIN, 1982).
The insulin level may be increased, normal or depressed, these variable patterns of insulin secretion strongly suggest heterogenous causes, the site of abnormality may be either the Bcell, secretory

secretory response to glucose or target tissue response to insulin or both (Beaty et al. 1982).

The most impressive evidence for a genetic compnent in the pathogenesis of type II diabetes is the observation of the high concordance rate of NIDDM in monozygotic twins even when they are geographically separated, the rate was 93% when the index twin developed diabetes after the age of forty (Tattersal and pyke,1972). These findings suggest that enviromental modification may not modify the incidence of NIDDM but may affect the course and onset of disease (Albin and Rifkin, 1982).

Secondary diabetes

This class includes persons who have disorders characterised by the association of diabetes with another condition. Only a few of many types of secondary diabetes (according to NDDG, 1979) will be mentioned here:-

1) Pancreatic disorders:

Surgical removal of the pancreas, pancreatic disease due to chronic alcoholism and other forms of pancreatitis are associated with many of the clinical characteristics of IDDM. There is however a great tendency to develop insulin induced hypoglycemia because of concomitant lack of the counter regulatory hormone glucagon, at least 2/3 of the pancreas must be destroyed to develop the clinical syndrome.It is usually associated with exocrine pancreatic insufficiency as well.