Study of Proper Timing of Some Sulfonylureas in Relation to Meals

Thesis Submitted for Partial Fulfilment of Master Degree of Internal Medicine

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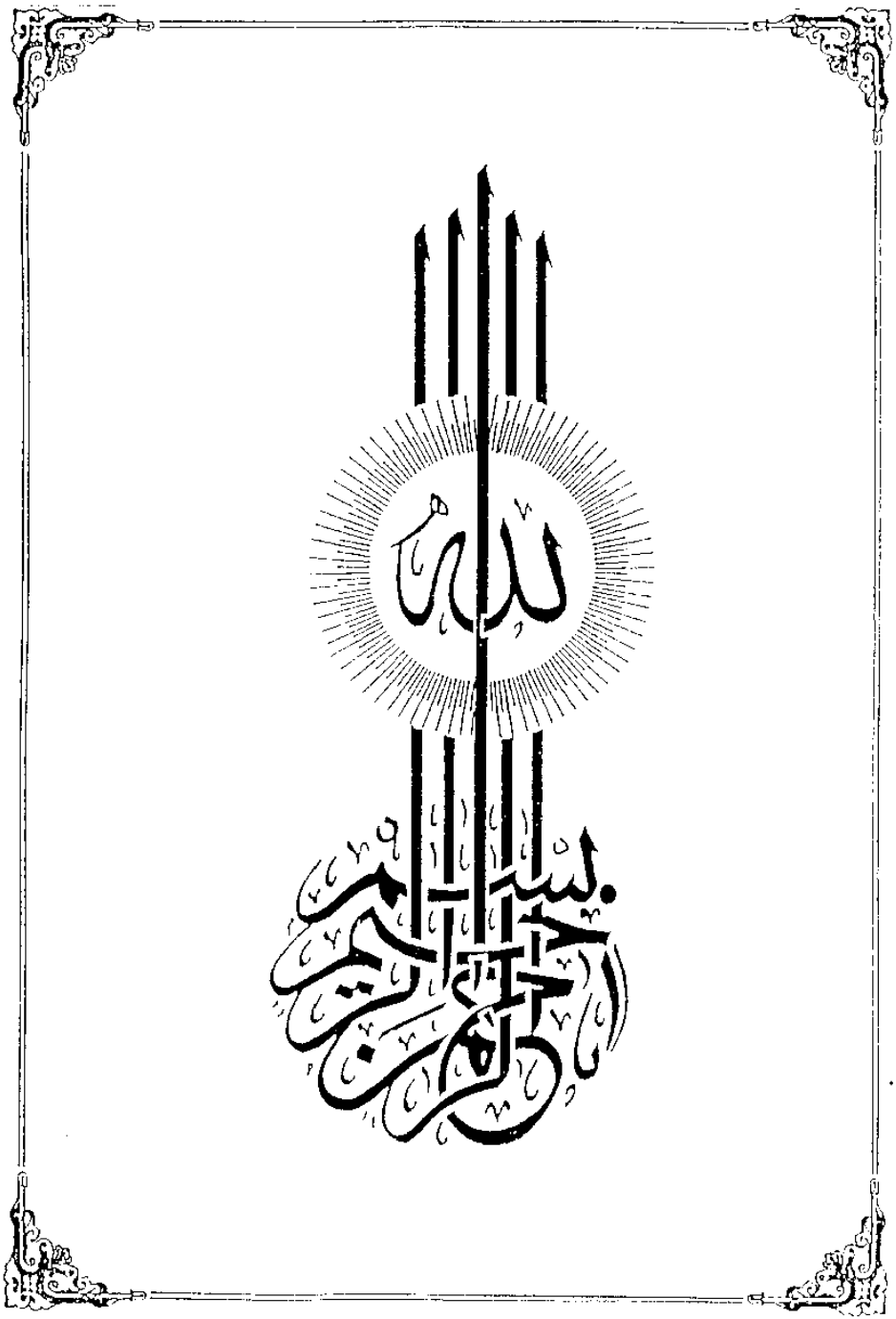

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NIDDM type can be controlled by diet regimen with or without oral hypolycaemic drugs especially sulfonylureas.

After sulfonylurea administration, primary maximum insulin secretion is expected during absorption of the drug. Since glucose and sulfonylurea synergestically affect insulin secretion, in order to insure maximum insulin secretion and to optimize the therapeutic responce, the drug should be absorbed during postprandial hyperglycaemia.

Due to synergy between sulfonylurea and glucose secondry insulin secretion stimulated by food ingestion can be also obtained during elimination phase, but these intensity will be unpredictably low depending on time elapsed since administration. This behaviour is what permit the single daily dose treatment. (Tamassia, 1977).

Our aim is to clarify the proper timing of some sulfonylureas administration in relation to meals on blood sugar.

Review

Review

Diabetes Mellitus

Definition

In 1980, The W.H.O Expert Committee on Diabetes Mellitus defined this disease as "a metabolic disorder of chronic hyperglycaemia, with or without glycosuria, which may result from many environmental and genetic factors, often acting jointly".

Incidence

The prevalence of diabetes mellitus varies from 2-5% in developing countries to 5-10% in developed countries. (American Diabetes Association, 1984).

The world wide incidence of diabetes has been rising yearly, more than 5.5 million Americans are diagnosed as having diabetes, it is estimated that there are another 5.5 million persons in the U.S who have the disease but who as yet remained undiagnosed. (Einhorn, 1992).

Arab et al., 1987, carried out a study of diabetes mellitus in different geographical sectors of Egypt, the total prevalence of diabetes was 4.18%. The essential feature revealed by comparison of different geographical areas was the higher prevalence of diabetes at the urban communities (Alexandria 5% and Damanhour 9.2%) compared to rural agricultural and desert communities (Ezbet Touch 2.6% and the Western Desert 0.8% respectively).

Diagnosis

The diabetic state may vary in its expression from being totally asymptomatic to being rapidly lethal, and this range is largely related to the degree of defect in insulin production and for insulin action. (Keen 1989).

Much is made of defining exact glycaemic diagnostic criteria for diabetes, even though this is seldom a real problem in clinical practice. When thirst, polyuria with glycosuria and weight loss are present, the blood glucose is usually so high that a single measurement of blood glucose is all that is required to establish the diagnosis of diabetes and more sensitive tests are unnecessary. (Keen-1989).

The diagnosis can be made when the patient plasma glucose level is higher than 200 mg/dl in the setting of classic symptoms and signs. (Einhorn 1992).

Other acceptable diagnostic criteria are a fasting plasma glucose concentration greater than 140 mg/dl on at least two separate occasions, or a single fasting plasma glucose of 140 mg/dl along with a glucose level above 200 mg/dl during at least two oral glucose tolerance tests (Olefsky 1992).

Impaired glucose tolerance exist if the fasting plasma glucose level is less than 140 mg/dl and if 30-, 60-, 90-, minutes plasma glucose concentrations exceed 200 mg/dl along with a 2-hours plasma glucose level between 140 and 200 mg/dl. Oral glucose tolerance test performed by ingestion of 75 gm glucose, 1-0.75 gm/kg of body weight in children, 100 gm for pregnant women. (Watkin et al 1990). Table 1.

Oral glucose Tolerance Test: W.H.O diagnostic criteria 1985

Glucose Concentration mmol/L - mg/dl						
	Venons whole blood		Capillary whole blood		Venous plasma	
	mmol/L	mg/dl	mmol/L	mg/dl	mmol/L	mg/dl
- Diabetes Mellitus						
. Fasting	≥6.7	≥120	≥6.7	≥120	≥7.8	≥142
. 2 hour after glucose load.	≥10.0	≥182	≥11.1	≥202	≥11.1	≥202
- Impaired glucose tolerance						
. Fasting	>6.7	>120	<6.7	>120	<7.7	<140
. 2 hour after glucose load.	6.7-9.9	120-180	7.8-11	142-200	7.8-11	142-200

Table 1 (Watkin et al., 1990)

Diabetes Mellitus

Classification

Aetiology

Pathogenesis

Classification of Diabetes Mellitus according to W.H.O Classification 1985

[A] Clinical Classes

1- Insulin dependant diabetes mellitus (IDD), Type I.

2- Non-insulin dependant diabetes mellitus (NIDD), Type II.

Non-obese.

Obese.

3- Malnutrition-related diabetes mellitus (MRDM) or tropical diabetes mellitus.

4- Other types of diabetes mellitus associated with certain conditions and syndromes:-

a. Pancreatic diseases.

b. Diseases of hormonal aetiology.

c. Drug induced or chemically induced conditions.

d. Abnormalities of insulin or its receptors.

e. Certain genetic syndromes.

f. Miscellaneous.

5- Impaired Glucose Tolerance (IGT)

Non-obese

Obese

Associated with certain conditions and syndromes.

6- Gestational diabetes mellitus.

[B] At-Risk Status

1- Previous abnormality of glucose tolerance.

2- Potential abnormality of glucose tolerance (Olfesky... 1992, Watkins ... 1990).

[1] Insulin Dependant Diabetes Mellitus

It is present in patients with little or no endogenous insulin secretory capacity. These patients develop extreme hyperglycaemia, ketosis, and the associated symptomatolgy unless treated with insulin, and they are therefore entirely dependant on exogenous insulin therapy for immediate survival. This form of the disease usually but not always, develops prior to early adulthood. (Olfesky 1992).

[2] Non-INsulin Dependant Diabetes Mellitus

Occurs in patients who retain significant endogenous insulin secretory capacity, although treatment with insulin may be necessary for control of hyperglycaemia, these patients don't develop ketosis in the abscence of insulin therapy and are not dependant on exogenous insulin for immediate survival. A person with diabetes mellitus may require insulin to treat symptomatic hyperglycemia, but if insulin is withheld, they do not generally develop ketoacidosis, such patients even if treated with insulin, have non-insulin dependant diabetes mellitus. (Horwitz 1984).

[3] Malnutrition-Related Diabetes Mellitus (MRDM) or Tropical Diabetes Mellitus

It is now included as a separate category, with its two types, fibrocalculous pancreatic diabetes (FCPD) and protein deficient pancreatic diabetes (PDPD). (Watkins et al 1990). Its supposally high prevelance in certain countries, in particular tropical

developing countries (e.g. India, Indonesia and Africa), its special clinical features are severe symptoms in young people below age of 30, with a history of severe malnutrition, without development of ketosis and there is insulin dependance, sometimes with servere but fluctuating insulin resistance.

Fibrocalculons Pancreatic Diabetes (FCPD)

This is associated with exocrine pancreatic defeciency, pancreatic fibrosis (often leading to calcification) and the presence of stones in pancreatic duct. Most population in which this condition arises are subject to malnutrition and have a diet based on Cassava. Cyanates are present in the Cassava root and may be a factor in the pancreatic damage.

Protein-Deficient Pancreatic Diabetes (PDPD)

This form appears to be a direct consequence of malnutrition. The main differences from the fibrocalculous variant are that exocrine pancreatic function is unimpaired and there is no evidence of pancreatic fibrosis or calcification. In both forms of tropical diabetes, insulin secretion is preserved, although impaired, this is the likely explanation for the observed resistance to ketosis. (Kumar and Clarck 1990).

[4] Other types of diabetes mellitus associated with certain conditions and syndromes.

(A) Pancreatic diseases

Diabetes may result from surgical removal or destructive disease of the pancreas. Severe IDD always occurs immediately following total pancreatectomy, acute pancreatitis can cause diabetes but frequently does not do so, patient with chronic pancreatitis and cystic fibrosis may develop diabetes. There is an association between carcinoma of pancreas and diabetes.

Two third of patients with haemochromatosis usually develop diabetes. (Dymock et al., 1972).

(B) Diseases of hormonal aetiology

Corticosteroids and ACTH, growth hormone, glucagon and catecholamines all induce insulin resistance. Patients with tumours producing such hormones often have diabetes.

Caushing's syndrome of either pituitary, adrenal or ectopic origin is commonly associated with mild diabetes, it tends to be more common and severe in patients with ectopic ACTH syndrome.

* In acromegaly, diabetes is common and almost occurs in one-third of patients. Pheochromocytoma produces simillar effects via the catecholamines excess.

* Though primary aldosteronism might be expected to produce glucose intolerance because of hypokalemia as potassium is essential for glucose uptake by cells under the influence of insulin.

. Addison's disease, coeliac disease and Addisonian Pernicious anaemia may occur in association with diabetes mellitus, as a part of autoimmune diasthesis.