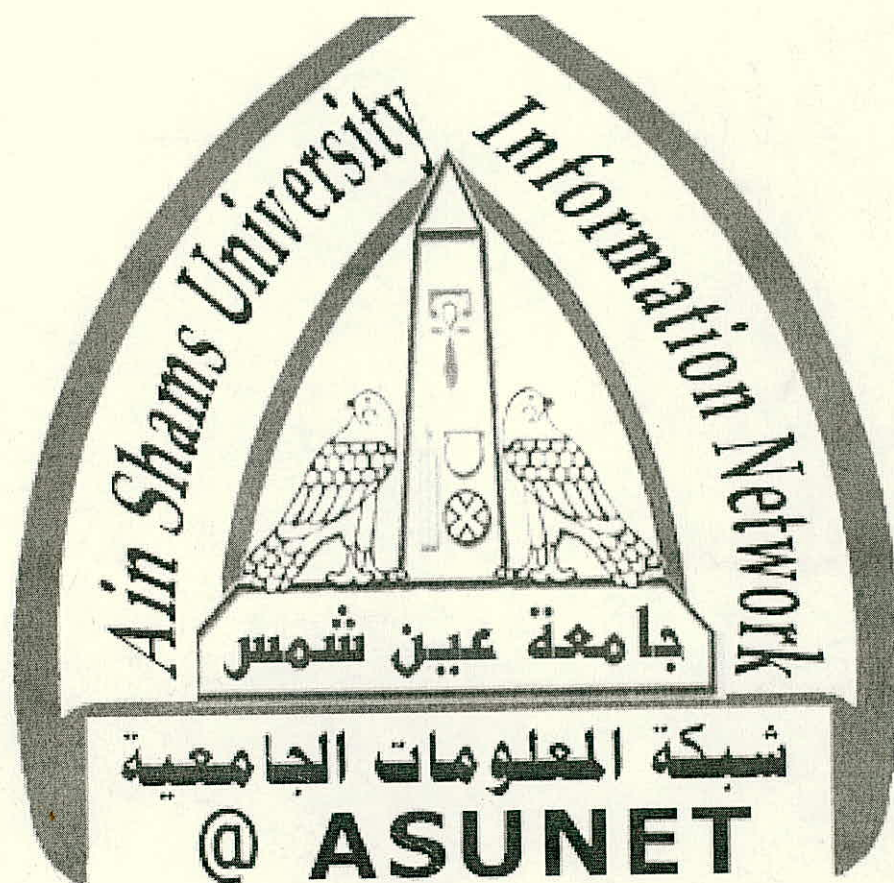




شبكة المعلومات الجامعية

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شبكة المعلومات الجامعية



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بعض الوثائق الأصلية تالفة

EFFECT OF METFORMIN ON GLUCAGON IN NON-INSULIN DEPENDENT DIABETES MELLITUS

**A Thesis Submitted For Partial Fulfilment
of Master Degree in
Internal Medicine**

By

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الْحَمْدُ لِلَّهِ الَّذِي هَدَانَا لِهَذَا
وَمَا كُنَّا لِنَهْتَدِيَ لَوْلَا أَنْ هَدَانَا اللَّهُ
صَدَقَ اللَّهُ الْعَظِيمُ

« سورة الأعراف الآية (٤٣) »

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***INTRODUCTION
AND
AIM OF THE WORK***

INTRODUCTION and THE AIM OF THE WORK

Diabetes mellitus is a common metabolic disorder characterized by hyperglycemia and chronic complications affecting one or more vital organs.

Many attempts have been carried out to understand the pathogenesis of this disease and to treat or at least control its manifestations and complications.

Pharmacologic therapy plays an important role in controlling hyperglycemia not responding to other dietary regimens. One member of this therapy is metformin which belongs to the biguanide group of drugs.

The aim of this work is to study the effect of metformin on plasma level of glucagon hormone which seems to play an important role in the pathogenesis of hyperglycemia characterizing diabetes mellitus. The study will also include the effect of metformin on blood glucose and on body mass index in obese non-insulin dependent diabetic patients.

***REVIEW
OF
LITERATURE***

DIABETES MELLITUS

Diabetes mellitus is the most common endocrine disease. The frequency of this disease is probably between 5-6%. The disease is characterized by metabolic abnormalities, by long-term complications involving the eyes, kidney, nerves and blood vessels and by the lesion of the basement membranes demonstrable by electron microscopy. (Unger; 1990).

Diagnosis :

When a patient presents with signs and symptoms attributable to an osmotic diuresis and is found to have hyperglycemia, the diagnosis of diabetes mellitus in this patients could be made easily. The problem arises with the asymptomatic patient who, for one reason or another, is considered to be a potential diabetic but has a normal fasting glucose concentration in plasma. Such patients are often given an oral glucose tolerance test, and, if abnormal values are found, diagnosed as having "chemical diabetes". The National Diabetes Data Group of the National Institutes of Health in 1979 provided revised criteria for the diagnosis of diabetes following a challenge with oral glucose:

- (1) Fasting (overnight): Venous plasma glucose ≥ 140 mg/dl on at least two separate occasions.
- (2) Following ingestion of 75 g. of glucose: venous plasma glucose concentration 200 mg/dl at 2h. and on at least one

other occasion during the 2-h test i.e. two values ≥ 200 mg/d must be obtained for diagnosis. (Foster et al (1990).

Classification :

Diabetes mellitus is classified into primary and secondary types. The primary type implies that no associated disease is present while in the secondary category some other identifiable causes allow a diabetic syndrome to develop. Insulin dependence in this classification is not equivalent to insulin therapy. Rather, the term means that the patient is at risk for ketoacidosis in the absence of insulin. Many patients classified as non-insulin-dependent require insulin for control of hyperglycemia although they do not become ketoacidotic if insulin is withdrawn. (Foster et al; 1990).

The term type I is often used as a synonym for insulin-dependent diabetes (IDDM), and type II has been considered equivalent to non-insulin-dependent disease (NIDDM). This is not ideal since some patients with apparent non-insulin-dependent are prone to ketoacidosis. The subset of patients in this category are non-obese subjects who usually express HLA antigens associated with susceptibility to insulin-dependent diabetes and exhibit islet cell antibodies in the blood. For this reason it has been suggested that the terms insulin-dependent and non-insulin-dependent describe physiologic states (Ketoacidosis-prone and ketoacidosis-resistant, respectively) while the terms type 1 and type 2 refer to pathogenetic mechanisms (immune-mediated and

non-insulin-dependent mediated, respectively). Using such a classification, three major forms of primary diabetes could be recognized (1) type 1 insulin - diabetes (2) type 1 non-insulin-dependent diabetes, and (3) type 2 non-insulin-dependent diabetes (Unger; 1990).

Category 2 can be considered as type 1 insulin-dependent diabetes in evolution i.e. autoimmune beta-cell destruction occurs slowly rather than rapidly with the result that there is a delay in reaching the ketoacidotic threshold of insulin deficiency. (Foster et al; 1990).

Secondary forms of diabetes encompass a lot of conditions. Pancreatic disease, particularly chronic pancreatitis in alcoholics, is a common cause. Destruction of the beta-cell mass is the etiologic mechanism. Hormonal causes include pheochromocytoma, acromegaly, Cushing's syndrome and therapeutic administration of steroid hormones. Stress hyperglycemia associated with severe burns, acute myocardial infarctions, and other life-threatening illnesses. Mechanisms of hormonal hyperglycemia include varying combinations of impairment of insulin release and induction of insulin resistance. (Unger; 1990).

A large number of drugs can lead to hyperglycemia, but most simply produce impaired glucose tolerance. Hyperglycemia and even ketoacidosis may occur as a result