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Study of comparative between insulin ,daonil drugs and effect on immune resistance in diabetes mellitus patients

دراسة مقارنة بين علاج الأنسولين والداؤونيل وتأثيرهما على الاستجابة المناعية لمرضى السكري

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Abstract:

This study was design to explain the action of insulin drug in saving on the normal level of immunoglobulins in diabetes mellitus patients compared with daonil drug .

Fasting venous blood samples were taken from 60 subjects of which 20 patient with type I diabetes mellitus, 20 patient with type II diabetes mellitus and 20 healthy individuals.

All the blood samples were analyzed for C -Reactive Protein and immunoglobulins (immunoglobulin G, immunoglobulin A, immunoglobulin M).

The results detected an increase in CRP in sera of patients with type II group compared for patients with type I and control groups.

Immunoglobulins (IgG,IgA) levels were increased in sera of patients with type II group compared to patients with type I and control groups, while, IgM level was decreased in sera of patients with type II group compared with patients with type I and control groups.

Keywords:Diabetes mellitus,insulin , Daonil.

الملخص:

أقيمت هذه الدراسة لتبين دور علاج الأنسولين في الحفاظ على مستوى الكلوبيولينات المناعية الطبيعي عند مرضى السكري مقارنة بعلاج الداؤونيل. سحبت نماذج عينات الدم الوريدية للصائمين من 60 فردا و التي منها 20 مريضا بالسكري النوع الأول ، 20 مريضا بالسكري النوع الثاني و20 فردا من الأصحاء .

حللت كل نماذج الدم لقياس C- Reactive Protein والكلوبيولينات المناعية (IgA ,IgM ,IgG) , حيث أظهرت نتائج التحليل الاحصائي ارتفاع مستوى C- Reactive Protein عند مرضى السكري النوع الثاني مقارنة بمجاميع مرضى السكري النوع الأول والأصحاء.

وارتفعت كذلك مستويات الكلوبيولينات المناعية IgA , IgG في مصل دم مرضى السكري النوع الثاني مقارنة بمجاميع مرضى السكري النوع الأول والأصحاء بينما قل مستوى IgM في مصل دم مرضى السكري النوع الثاني مقارنة بمجاميع مرضى السكري النوع الأول والأصحاء.

مفتاح الكلمات: مرض السكري , الأنسولين , الداؤونيل .

Introduction

Diabetes mellitus is actually a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both[(1)]. Diabetes mellitus is classified into four broad categories : type 1,type 2, gestational terms ,including childhood-onset diabetes ,juvenile diabetes , insulin-dependent diabetes mellitus (IDDM) . Likewise ,and type 2 diabetes has replaced several former terms ,including adult –onset diabetes ,obesity -related diabetes and , non-insulin-dependent diabetes mellitus (NIDDM).Beyond these two types ,there is no agreed –upon standard nomenclature [(3)]

This disease is usually initiated by an environmental factor of infection (usually a virus) in individuals with a genetic predisposition and causes the immune destruction of the β cells of the pancreas and, therefore, a decreased production of insulin characteristics of type 1 diabetes include abrupt onset, insulin dependence, and ketosis tendency[(4)]. Type II diabetes is most commonly associated with obesity in middle-aged individuals. It is due to reduction in the number or affinity of insulin receptors on the plasma membrane of cells in target tissues, or an abnormal binding of insulin to the receptors[(5)]. Insulin causes most of the body's cells to take up glucose from the blood

(including liver, muscle, and fat tissue cells), storing it as glycogen in the liver and muscle, and stops use of fat as an energy source. When insulin is absent (or low), glucose is not taken up beny most body cells and the body begins to use fat as an energy source (i.e., transfer of lipids from adipose tissue to the liver for mobilization as an energy source) [(6)].

It has several other anabolic effects throughout the body. When control of insulin levels fail, diabetes mellitus results, insulin is used medically to treat some forms of diabetes mellitus. Patients with type I diabetes mellitus depend on external insulin (most commonly injected subcutaneously) for their survival because the hormone is no longer produced internally. Patients with type II diabetes mellitus are insulin resistant, have relatively low insulin production, or both, some patients with type II diabetes may eventually require insulin when other medications fail to control blood glucose levels adequately[(7)].

The Drug (Daonil) is used as a second- generation sulfonylurea antidiabetic agent, appears to lower the blood glucose acutely by stimulating the release of insulin from the pancreas, an effect dependent upon functioning beta cells in the pancreatic islets. With chronic administration in type II diabetic patients, the blood glucose lowering effect persists despite a gradual decline in the insulin secretary response to the drug. Sulfonylurea likely bind to ATP- sensitive potassium- channel receptors on the pancreatic cell surface, reducing potassium conductance and causing depolarization of the membrane. Depolarization stimulates calcium ion influx through voltage – sensitive calcium channels, raising intracellular concentrations of calcium ions, which induces the secretion, or exocytosis, of insulin[(8)] .

C-Reactive protein (CRP) is synthesized in the liver and appears in the blood of patients with diverse inflammatory diseases. It is significantly elevated in acute rheumatic fever, bacterial infections, myocardial infarcts, rheumatoid arthritis, carcinomatosis, gout, and viral infections [(9)].

Immunoglobulins are five major groups in the serum: IgA , IgG, IgM, IgD, and IgE. They are synthesized in plasma cells. Their synthesis is stimulated by an immune response to foreign particles and micro organisms. The Immunoglobulins are not synthesized to any extent by the neonate. IgG crosses the placenta; the IgG present in the newborn's serum is synthesized by the mother. IgM does not cross the placenta but rather is the only Immunoglobulins synthesized by the neonate. The concentration of IgM initially is 0.21 g/L, but this increases rapidly to adult levels by about age 6 months. IgA is virtually lacking at birth (0.003 g/L), increases slowly to reach adult values at puberty, and continues to increase during the life time.[(10)]

Material and methods

Sampling:

The samples were collected. They have been classified into three groups as the following:-

1. Control group:- include (20) healthy individual from both sexes, with age range (25-65) years and no previous disease which may interfere with the parameters analyzed in this study.
2. Type-I- (Insulin Dependent Diabetes Mellitus) IDDM group: include (20) patients from both sexes, with age range (15-65) years.
3. Type- II - (non-Insulin Dependent Diabetes Mellitus) NIDDM group: include (20) patients from both sexes, with age range (35-65) years.

Collection of Blood:

5 ml venous blood was taken from the above groups, left for (15min) at room temperature, then centrifuged (at 2500 rpm from 10min) to get the serum.

Determination of C-reactive protein(CRP)

CRP was measured in serum samples of all studied groups according by[(11)] and [(12)]methods.

Determination of Immunoglobulines (IgG; IgA; IgM)

IgG, IgA and IgM were determined in serum samples of all studied groups according to [(13)] and [(14)] methods**.**

Statistical analysis

Data presented were the means and standard deviations, student -t- test was used to compare the significance of the difference in the mean values of two groups. ($P \leq 0.05$) was considered statistically significant[15].

Results and Discussion

Table (1) and figure (1) showed the results of CRP and in sera of patients with type I, type II Diabetes Mellitus and control groups.

A significant increase in level of CRP in sera of patients with type II Diabetes Mellitus compared with control, while no significant alteration in CRP level in sera of patients with type I Diabetes Mellitus compared with control.

Under physiologic conditions the liver synthesizes mainly constitutive hepatic proteins, such as albumin, prealbumin, or transferring. After trauma the synthesis shifts from constitutive- hepatic proteins to acute phase proteins, such as haptoglobin , α2-macroglobulin, α1-acidglycoprotein, and c-reactive protein (CRP)[16].

This reaction of the liver is called the hepatic acute phase-response. The goal of the hepatic acute-phase response is to restore homeostasis, however, a prolonged and exaggerated response leads to the enhancement of hyper metabolism and catabolism, thus to increase morbidity and mortality[17].

An inflammatory pattern indicating an inflammatory condition is seen when there is a decrease in albumin and an increase in the α_1-globulins (α_1-acid glycoprotein, α_1-antitrypsin), α_2-globulis (Ceruloplasmin and haptoglobin), and β-globulin blood (C-Reactive protein). Although the main physiological abnormalities are insulin resistance and impaired insulin secretion[18].

Inflammation as measured by c-reactive protein (CRP) has been shown to be increased in people with type I and type II diabetes who have macro vascular complications[19-22].

Our results agree with studies claimed that some of these markers are elevated in patients with type II diabetes and insulin resistance, indicating a pivotal role of inflammation in this metabolic disorder [23]. However, The results of present study agree with previous study found a positive correlation between inflammatory markers and type II diabetes[24, 25].

Adipose tissue (body fat) has been lately regarded as a separate body organ which can produce a number of different biologically active molecules-such as cytokine proteins that are associated with inflammation, and the hormone resistance, which is linked to insulin resistance and the development of type two diabetes[26].

In the present study we investigated the effects of insulin hormone and Daonil drug on the systemic inflammatory response in patients with type I and type II Diabetes Mellitus respectively both suffering from the same inflammatory diseases. Without taking any non steroidal anti inflammatory, aspirin and statin drugs, Angiotension Converting Enzyme Inhibitor (ACEI), and Glitazones. Showed that insulin is decreasing pro-inflammatory hepatic acute-phase protein concentrations in sera of patients with type I Diabetes Mellitus group compared with the effects of Daonil drug on the systemic inflammatory response in patients with type II Diabetes Mellitus. Results given the fact that the insulin treat diabetes, also may have potential treatment for inflammatory diseases.

Table (2) and figure (2,3,4) showed the results of IgG, IgM, IgA in sera of patients with type I, type II Diabetes Mellitus and control groups.

A marked significant increase in IgG and IgA (1933.9±303.5) (469.6±194.2) levels respectively and a significant decreased in IgM(48.9±29.36) level in sera of patients with type II DM compared to control, while no significant alteration in IgG, IgM and IgA was found in sera of patients with type I Diabetes Mellitus compared to control group. Also a significant differences in IgG, IgM & IgA levels between both patients groups themselves was found ,These results were consistent with[27].

It has been postulated that type II Diabetes Mellitus may represent a disease of the innate immune system a hypothesis of particular interest because both of these inflammatory biomarkers

also are known to predict the development of cardiovascular disease in otherwise healthy populations[28].

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Table (1) CRP levels in sera of three studied groups

GROUPS	No.	CRP(mg/dl) Mean ± SD
Control	20	0
Type I	20	0
Type II	20	8 ± 1.301

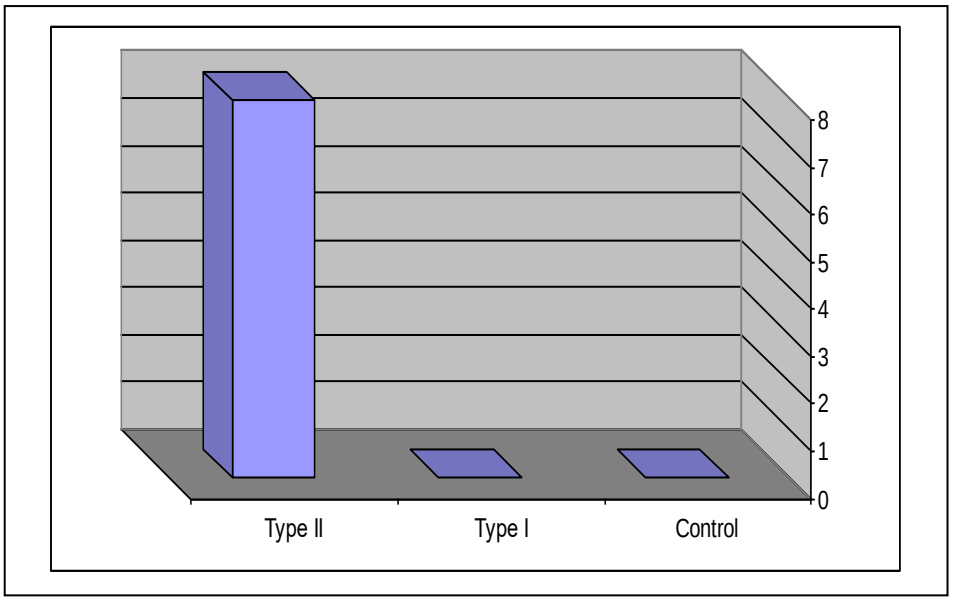
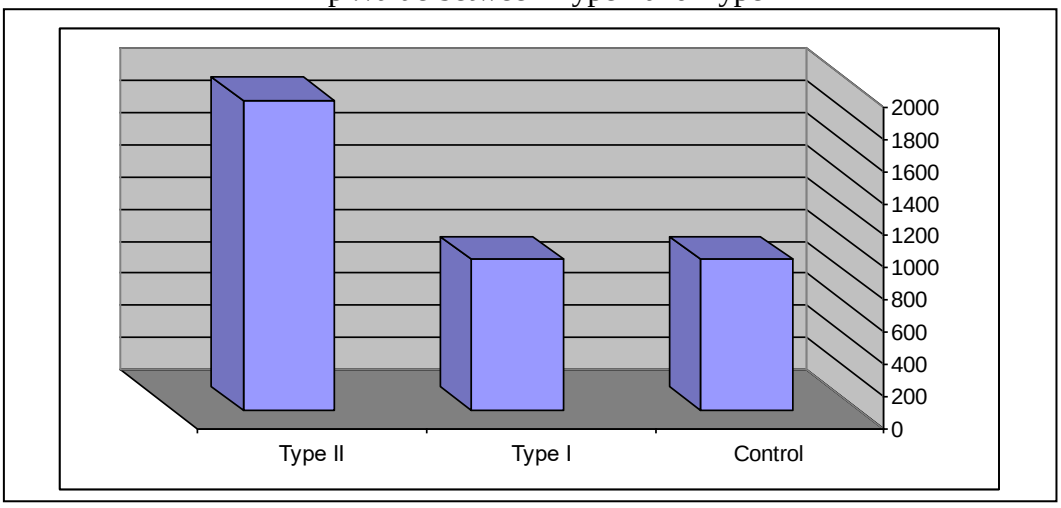


Figure (1) CRP level in sera of three studied groups

Table (2) IgG, IgA, IgM levels in sera of three studied groups

GROUPS	No.	IgG(mg/dl) Mean ± SD	IgA(mg/dl) Mean ± SD	IgM(mg/dl) Mean ± SD	P
Control	20	941.8 ±329.5	180.1±114.3	163.9±107.7	
Type I	20	941.3±390.36	181.5±103.3	155.2±84.5	P>0.05
Type II	20	1933.9±303.5	469.6±194.2	48.9±29.36	P≤0.05
					P*≤0.05

P*= p .value between Type I and Type II



Figure(2) IgG levels in sera of three studied groups

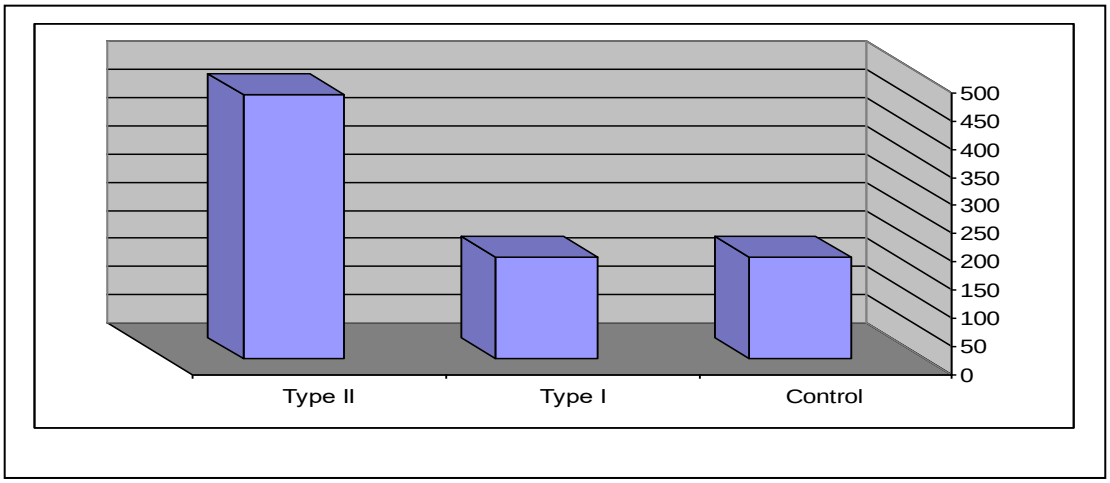
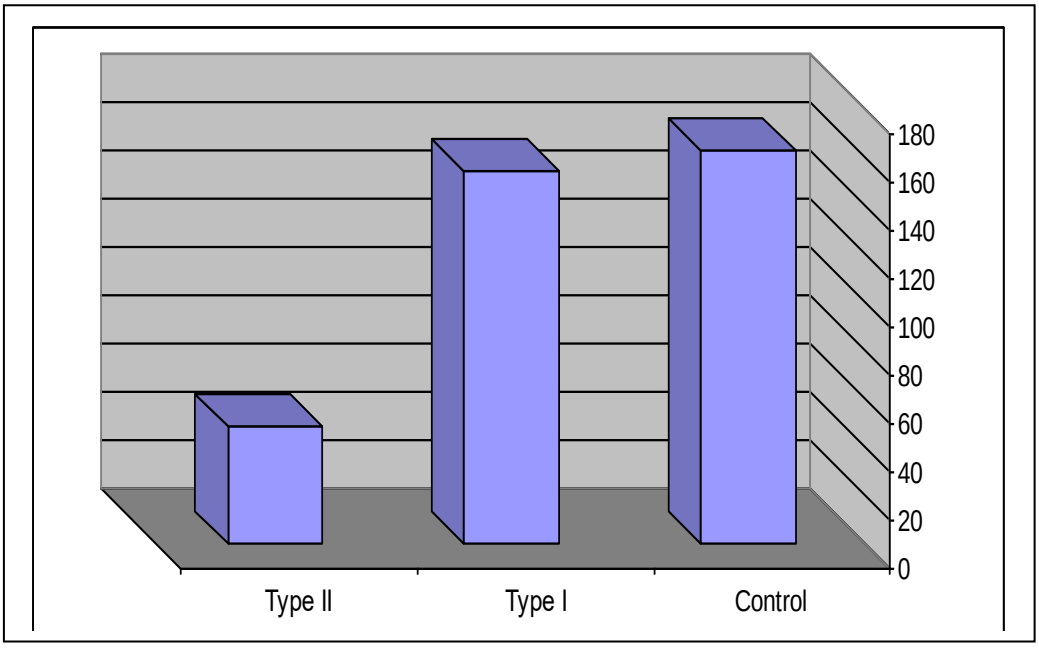


Figure (3) IgA levels in sera of three studied groups



Figure(4) IgM levels in sera of three studied groups