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Effect of Metformin and Glimepiride Treatment on Some Biochemical Parameters in Diabetic Male Patients with Chronic Renal Failure

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Abstract

The present study was included a measurements of fasting serum glucose, total protein, potassium, and calcium levels in the sera of 25 diabetic male patients suffer from chronic renal failure; their ages range were (32-75) and compared them with 25 healthy males as control group. The aim of this study was to study the effects of antidiabetic drugs on some biochemical parameters such as fasting serum glucose, serum total protein, serum potassium and calcium. The current results demonstrated a hyperkalemia in patients and this increasing of potassium is significantly ($p = 0.03$), but calcium level showed no significant variations ($p>0.05$), and serum total protein was significantly decreased in patients as compared to the controls ($p = 0.0002$).

Keywords: Metformin, Glimeperide, Chronic renal failure, Diabetes Mellitus.

1. Introduction

Diabetes mellitus was considered a disease which is chronic progressive, could be diagnostics by control losing of glycaemic over time as the lose capacity of insulin-secreting pancreatic β-cells to amende for the predominant levels of insulin sensitivity [1]. There are numbers of disorders or diseases could cause chronic kidney diseases, that effect on blood delivery to the kidneys via renal arteries. One of these diseases that causing kidney disease and risk on microvascular is diabetes mellitus [2]. and this risk increased with glucose abnormalities [3]**.** The volume and composition of body fluids are tightly regulated by kidney, and the kidneys are largely responsible for maintaining regulatory or homeostasis of electrolytes and fluids in the body [4]. Renal failure is described a reduction of glomerular filtration rate, it can occur abruptly as an acute renal failure or it occurs unexpected rate and a variable [5, 6]. Ca^{+2} is formalizes the most abundant mineral in human body, which has a several important functions [7]. More than 99% of Ca^{++} of total body is stored in the bones and teeth to an assistant and supporting of their composition [8]. The remaining percentage 1% is founded in the muscle and blood. And the fluid between cells, which was needed for muscle contraction, also blood vessel expansion and a contraction, secretion of hormone and enzymes, and sending messages throughout the nervous system so that these biological

processes of body function efficiently [9]. Ca^{+2} have been regulated by calcitonine and parathyroid hormones (PTH) [10]. Extracellular Ca^{+2} decreases it stimulates the secretion of (PTH) that stimulates the reconversion of vitamin D to its active form (calcitriol) in the kidneys [11]. Calcitriol increases intestinal Ca^{+2} absorption. When blood Ca^{+2} returns to normal concentration, the parathyroid glands stop secreting PTH and the kidneys start to excrete may any Ca^{+2} excess in to the urine [7,12]. Potassium (K^{+}) is the major mono charged cation found in the cells or intracellular. Where is 97% founded in the intracellulare fluid and (2-3)% is found in the extracellulare fluid for example intravasculare and fluids of intestinal alsosmall amount in the bone and blood.Which is damaged cells lead to releasing of K^{+} into the blood [13]. The normal of K^{+} concentration in the cell water is 145.0 mEq/L, that (1.0 mEq of K^{+} is equal to 39 mg). While the normal serum K^{+} range is (3.5-5.5 mEq) .These ranges is regulated by kidneys . Recently researches in the United States of America have been demonstrated that a low K^{+} intake, which is thoroughly common and tends to hypertension [14, 13]. The total serum protein consists of both globulins 40% and albumin (60%). All they are share some parts to the coiled oncotic pressure (COP) of the Plasma, which is essential for normal hemodynamics. Unlike that salts of sodium and glucose, the movement of protein from plasma into the interstitial fluid is limited. A total protein is attended by changing of fluid balance. Thereby dehydration causes a proportional increasing in all of the serum protein [15]. Glimepiride is a sulfonylurea and one of the drugs was used by patient with diabetes mellitus, which is classified either second generation or first third generation as sulfonylureas [16-18]. Where the mechanism of action in a first stimulation and secretatory of insulin releasing from the ß-cell of pancreas and increased of intracellular insulin receptors, in the second way reduction of serum glucagon level, and the third pathway increasing binding of insulin to receptor of target tissue cell. Which these drugs were metabolized via the liver and excreted by liver or kidney [18, 19]. Metformin is another drug which is used as hypoglycemic agent from obese individuals, to prevention of diabetes and widely regarded for the treatment of two type diabetes [20, 21]. By decreasing hepatic glucose output and inhibiting gluconeogenesis. This drug may be used alone or in combination with glimepiride [18].

2. Samples and Methods

2.1. Samples Collection

The blood samples were taken from 25 diabetic male patients with CRF that are took anti diabetic drugs such as Glimepiride and Metformin; their ages ranged from (32-75) years in Al-Kindy hospital/ Baghdad-Iraq during the period from January until the end of April 2018 and compared them with 25 healthy males as control group; their ages ranged from (20-64) years. Five milliliters of venous blood samples and allowed to clot for 20 min at room temperature, centrifuged at 3000xgfor 4 minutes, and then sera were collected was stored at -17C$^{\circ}$ until to use. The serum was utilized for the estimations of serum glucose, total protein, Ca^{+2} and K^{+} ions.

2.2. Determination of Fasting Serum Glucose

Colorimetric method was used to determine of glucose in the sera was achieved by using Linear kit. The determination of glucose level done by enzymatic oxidation of glucose by glucose oxidase to produce hydrogen peroxide, and in the presence of peroxidase and 4-aminoantipyrine is oxidized by hydrogen peroxide then produce quinoneimine as colored compound red dye read at (500 nm), proportional to the concentration of glucose [22].

2.3. Determination of Serum Total Protein

Colorimetric method was used to determine of total protein in the sera of patient and control groups, by using Linear kit. The principle of this method is Biuret reaction, when a cleating compound formation between the Cu^{+2} ion and the peptide bond in alkaline media to give a violet colored complex, and read at 540 nm. The density of color is proportional to the concentration of total protein in the serum [23].

2.4. Determination of Serum Potassium

Colorimetric method was used to determine of K^{+} ion in the sera of patient and control, by using Agape kit. The principle of this method was depending on reaction between K^{+} that presence in the serum with sodium tetraphenyl borate, to give K^{+} tetra phenyl borate read at 578nm [24]. This procedure was carried out on the patient and control groups.

2.5. Determination of Serum Calcium

Colorimetric method was used to determine of total Ca^{+2} in sera without deproteinization was achieved by using Human kit. The principle of this method depending on Ca^{+2} ion reacts with the 8-hydroxy quinoline in an alkaline media. The color density of the Ca-8-HQ complex, read at wave length (540 nm), is proportional to the quantity of calcium presence in the sample. 8-hydroxyquinoline reacts with calcium to formation color complex. And Cresophthalein expunges interferences from proteins [25]. this procedure was carried out on the patient and control groups.

3. Results

Biochemical parameters in patients and controls are listed in tables. Glucose has been determined. The mean value in **Table 1.** showed hyperglycemia., increased highly significant (p = 0.004) of Glucose level in the sera of patients in comparision with that of the control group.

Table 1. Glucose mean level in the sera of control and patients as test group with statistical analysis value.

Groups	N (Numbers)	Age/year	Mean (mg/dL)	SD	P-Value
Test	25	32-75	189.2	42.23	P= 0.004
Control	25	20-64	110.5	27.95	

Total protein has been determined and mean value showed in **Table 2.** that demonstrated decreased highly significant (p = 0.0002) in total protein level in the sera of patients in comparision with that of the control group.

Table 2. Total protein in the sera of control and patients as test group with statistical analysis value.

Groups	N (Numbers)	Age/year	Mean (g/dL)	SD	P-Value
Test	25	32-75	5.354	0.91	P= 0.0002
Control	25	20-64	7.484	0.46	

Potassium (K^{+1}) was measurment have been a results that obtained from this work, and showed in the **Table 3.** The mean value manifested hyperkalaemia where potassium level in the sera of patient group increased significantly with variations ($p = 0.03$) in comparision with that of the control group.

Table 3. Potassium mean level in the sera of control and patients as test group with statistical analysis value.

Groups	N (Numbers)	Age/year	Mean of (mmol/L)	SD	P-Value
Test	25	32-75	5.272	0.94	P= 0.03
Control	25	20-64	4.308	0.44	

Calcium measurement results demonstrated the mean value in **Table 4,** showed non significant variations ($p>0.05$) in calcium level in the sera of patients, in comparision with control group.

Table 4. Calcium mean level in the sera of control and patients as test group with statistical analysis value.

Groups	N (Numbers)	Age/year	Mean (mmol/L)	SD	P-Value
Test	25	32-75	8.94	1.36	P >0.05
Control	25	20-64	9.112	0.62	

4. Discussion

Chronic renal failure (CRF) indicated to to an irreversible deterioration in kidney function which developes over of many years., or function and physiological state regarded abnormal of kidney that appear for at least three months or achronic significantly decreasing in kidney function [26]. Total protein measurement was regarded very important in the present study at end stage of chronic renal failure. There are many physiological and diseases were recorded lead to decreasing in sera of total protein [27]. Hypoproteinaemia in diabetic patients as listed

in **Table 2.** Attributed to increasing of protein excretion with urine as well as albumin, in the same time the liver cannot be able to substitution this protein loos [28]. On the other hand, K^+ was regarded a major important cation in cells metabolism of nerve and muscles. It's mainly located intracellular [29]. In the present study hyperkalemia is a clear, was presented in **Table 3.** and its metabolism related with endocrine and some other drugs., which was recorded and proved in many researches. The patient's group with CRF in the present study was administrated sulfonyl urea drug that affected on the endocrine system and related with K^+ metabolism. Hyperkalemia that showed in our study may be due to inhibition of aldosterone, which is found in other metabolic pathways, as well as metformin inhibits aldosterone-induced cardio fibroblast activation [30]. Aldosterone induced K^+ potassium excretion in the renal distal tubule, and colonic epithelium [31]. Glimepiride can effect on the surface of intracellular membrane which caulked all three types of K_{ATP} channel [32]. Therefore, can patients with CRF and diabetic patients who had low insulin levels may be have hyperkalemia. Elevated level of the ultimate hormone is an unnecessarily by feedback inhibition so many of intermediate hormone inhibits the release of earlier hormones in the cascade, therefore Cortisol signal stress including, blood glucose with diabetes mellitus by cortisol counter-balances those of insulin [33].

5. Conclusion

We concluded any patient that undergoing from chronic renal failure and diabetes mellitus suffer from high level in sera potassium when administration metformin and glimepiride. Due to these drugs affected on the potassium metabolism. And don't eating any dietary which containing on high level of potassium or moderating the dose of these drugs to less dose.

6. Recommendation

Further studies were characterization of these drugs on other metal ions metabolism.

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