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ORIGINAL ARTICLE

Prospects of Drug Interaction of Metformin with Lifesaving Hypertensive Drugs in Type2 Diabetic Patients. A Clinical Comparative Study

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ABSTRACT

The aims and objectives of current study was to check and concluded the chances of any drug interaction of metformin with hypertensive treatment with beta- blockers and calcium channel blockers in type 2 diabetic patients. During study diabetic patients with type 2 were treated with metformin and hypertensive drugs i.e. beta- blockers and calcium channel blockers. There is no any drug interaction in both gender has seen (1.00± 00.01, 1.00± 00.01). while Significant change ($p<0.05$) regarding glucose levels, systolic and diastolic blood pressure were seen in group B and group C as compared to the group A i.e. control group.

Keyword: Drug interaction, Metformin, Beta- blockers, Calcium channel blockers

INTRODUCTION

Different clinical studies concluded that about fifty percent diabetic patients are hypertensive [1]. Diabetes mellitus and hypertensive complications are correlated with each other. Many researchers find out in their studies that there is a significant correlation between both micro and macro vascular heart diseases and in diabetes mellitus [2, 1]. Therefore it is so important to clearly describe the drug interaction in between those drugs which are used for diabetes mellitus and hypertension because both are life threatening diseases [11].

Biguanide is a class of anti-diabetics drugs and metformin belong to this family which perform anti-hyperglycemic activities [2]. It is a first line therapy for the diabetic patients by its recommend quantity, type 2 diabetes can treat and control. Metformin can be given alone or in combine with any other agents like incretin-based drugs, sodium glucose cotransporter-2 inhibitors, sulfonylureas and thiazolidinedione etc. [1, 3]. The linkages of metformin with serum enzyme elevations during treatment is negligible and it has not any toxicity in liver. It has seen in different studies that metformin has very low chances of lactic acidosis. Different studies concluded that metformin reduces the low density lipoprotein, cholesterol and triglycerides in the human biological system and this is a reason it is used as weight reducing agent in all over the world [4, 13].

The mode of action of metformin is electron transport chain related in which it inhibits the NADPH: ubiquinone oxidoreductase, i.e. complex-I by increasing the AMP to ATP cellular ratio and stimulating the activation of AMP-activation of protein kinase and regulation of AMP-activate of protein kinase enzyme for transcription of target genes [5, 14]. In a study it was concluded that metformin inhabits liver gluconeogenesis and increase the sensitivity of insulin oxidation of fatty acid during all these metabolic pathways changes in the body the levels of glucose become decreased [16]. Many studies also claimed that metformin has antineoplastic effects and cannot allow many cancer tissues to develop and grow. In hypertensive conditions doctors prescribed calcium channel blockers and beta-blockers for proper oxygen intake and normal supply of blood to the heart [17].

Calcium is very important constituent of human body which play an important role in the muscle contractions which is so important for the maintenance of body movement. Calcium also function as a secondary messenger in the human body [11, 13]. The entrance of calcium into the muscles of heart and blood vessels inhabited by the action of calcium channel blockers. Stress on heart and blood vessels can lower down by the applications of beta-blockers. Mainly doctors recommend beta-blockers for the maintenance of high blood pressure and cardiovascular problems [7]. The mode of action of beta-blockers is related with the blockage of certain hormones in the nervous system like adrenaline by which deactivation of "fight-or-flight" mechanism occurred in the system. Beta-blockers reduces the secretion of adrenaline and noradrenaline due to which stress on the heart decreased and in this way the contraction of heart muscles become low and ultimately high blood pressure come down [12].

MATERIALS AND METHODS

In this study 200 individuals were selected and divided them into three different groups. In Group A, 50 healthy individuals were placed which is control group whereas 75 diabetic type 2 patients with high blood pressure were in Group B, and treated with metformin and beta-blockers while 75 diabetic type 2 with high blood pressure patients were in Group C, they were treated with metformin and calcium channel blockers. Gender wise 20 female and 30 male was in Group A, their age was in between 40-60 years. Similarly 20 female and 55 male of age in between 40- 60 years were in both Group B and Group C respectively. Random glucose levels, systolic and diastolic blood pressure and drug interaction between their treatments were concluded. The descriptive statistics model of 2000 for logistic regression of dependent and independent variables for different treatment protocol were implemented and significant statistical levels were considered as $p < 0.05$. Mean standard deviation (Mean±SD) of each parameter was measured under one way NOVA.

RESULTS

Table 1: Normal individuals (Control) n=50, age= 40-60 years

Biomarkers	Female Dosage (Mean±SD)	Female Dosage (Mean±SD)	Drug interaction (Mean±SD)
Glucose (R) levels mg/dl	140.21± 13.21	142.20± 21.20	
Systolic(B.P)	120.11± 1.01	120.31± 21.12	
Diastolic (B.P)	80.01± 01.02	80.01± 02.03	

($p<0.05$)

It has seen that the trend of random glucose levels, systolic and diastolic blood pressure is directly correlated with each other for both group B and group C in male and female (206.21± 13.21, 202.20± 21.20)(130.11± 1.01, 135.31± 21.12),(150.11± 1.01, 155.31± 21.12)(130.11± 1.01, 135.31± 21.12),(90.01± 01.02, 89.01± 02.03)(85.01± 01.02, 84.01± 02.03). Individuals of both groups B and Group C taking same treatment of metformin (2.00± 00.01, 2.00± 00.01) (2.00± 00.01, 2.00± 00.01) but different hypertension resisting compound, Beta- blockers in (1.00± 00.01,

1.00± 00.01) group B and Calcium channel blockers (1.00± 00.01, 1.00± 00.01) in group C. Significant change (p<0.05) regarding glucose levels, systolic and diastolic blood pressure were seen in group B and group C as compared to the group A i.e. control. All the significant changes (p<0.05) regarding variable and non-variable parameters represented in the Fig 1 graphically.

Table 2: Diabetic with high blood pressure individuals (Metformin + Beta-blockers) n=75, age= 40-60 years

Biomarkers	Female Dosage (Mean±SD)	Male Dosage (Mean±SD)	Drug interaction (Mean±SD)
Glucose (R) levels mg/dl	206.21± 13.21	202.20± 21.20	
Systolic (B.P)	150.11± 1.01	155.31± 21.12	
Diastolic (B.P)	90.01± 01.02	89.01± 02.03	
Metformin (750mg)	2.00± 00.01	2.00± 00.01	No
Beta blockers	1.00± 00.01	1.00± 00.01	No

(p<0.05)

Table 3: Diabetic with high blood pressure individuals (Metformin + calcium channel blockers) n=75, age= 40-60 years

Biomarkers	Female Dosage (Mean±SD)	Male Dosage (Mean±SD)	Drug interaction (Mean±SD)
Glucose (R) levels mg/dl	190.21± 13.21	187.20± 21.20	
Systolic (B.P)	130.11± 1.01	135.31± 21.12	
Diastolic (B.P)	85.01± 01.02	84.01± 02.03	
Metformin (750mg)	2.00± 00.01	2.00± 00.01	No
Calcium channel blockers	1.00± 00.01	1.00± 00.01	No

(p<0.05)

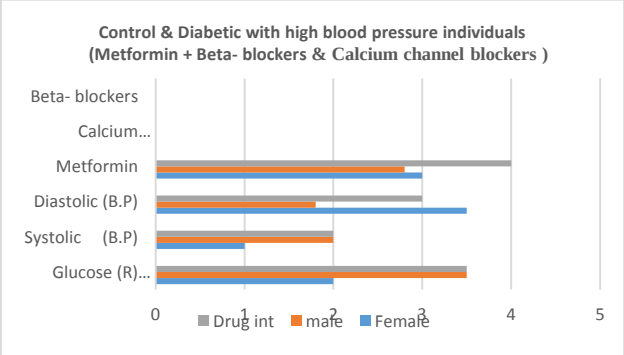

Fig 1:

DISCUSSION

A reaction between within two or more than two drugs or food nutrients is referred as drug interaction [5]. There are three different classes of drug interaction, reaction between two or more drugs, reaction between food and drug, reaction of a drug with conditions of a disease. All drugs are known by their proper generic name even these contain one or more generic compounds. Researchers are indicating very clearly in their research that the rate of diabetes mellitus type 2 is increasing very fast in all over the world [6]. Those drugs which resist the renin-angiotensin system by inhabiting the conversion of angiotensin enzyme and angiotensin receptors are used and very effective line of treatment for hypertension cardiac failure etc. [7].

Different studies elaborated that the management of type 2 diabetes mellitus mostly managed with combination of therapy by different compounds [9]. It has concluded that dyslipidemia and arterial hypertensive complications originated by hyperglycemic syndrome [8]. Different case reports described the pharmacokinetic interference of metformin in hyperglycemia and high blood pressure. It is very difficult to treat effectively the diabetes mellitus Type 2 in the long term. Still there is no any drug which can used in case of pre-diabetic persons [10].

In current study 200 diabetic individuals with high blood pressure were treated through anti-diabetic agent metformin, beta- blockers and calcium channel blockers. It has seen that the trend of random glucose levels, systolic and diastolic blood pressure is directly correlated with each other of group B and group C in male and female. There is no any drug interaction in both gender has seen (1.00± 00.01, 1.00± 00.01). while Significant change (p<0.05) regarding glucose levels, systolic and diastolic blood pressure were seen in group B and group C as compared to the group A i.e. control were noted.

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