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Original Research Article

Effect of Sitagliptin and Combination of Sitagliptin and Metformin on Triglyceride Levels in Diabetic Albino Wistar Rats

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Abstract

Diabetes mellitus is a multi-system disease with multiple complications. Dyslipidemia is one of the, most important event which plays major role in these complications. There is usually high triglycerides level in most diabetic dyslipidemia. Hence ideal management of diabetes should include management of dyslipidemia & hence increased levels of triglycerides and the. This study is carried out to evaluate the effect of Sitagliptin and combination of sitagliptin and metformin on triglyceride level in diabetic rats.

Type-2 diabetes was induced in Albino Wister Rats by using high fat-low Streptozotocin method. Rats were fed with coconut oil and vanaspathi ghee for 6 weeks followed by a low dose Streptozotocin. Rats were treated with Sitagliptin, Metformin and combination of Metformin and Sitagliptin for 21 days. Triglyceride levels were analysed after induction of diabetes and after completion of treatment.

Results: Groups treated with Sitagliptin and combination of Sitagliptin and Metformin showed significant reduction in triglyceride level.

Conclusion: It can be concluded that Sitagliptin and combination of Sitagliptin and Metformin reduces the triglyceride level in diabetic Albino Wister rats.

Keywords: Sitagliptin, Streptozotocin, Dyslipidemia.

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Introduction

Diabetes Mellitus is a syndrome caused by deficiency in production of insulin, or by the ineffectiveness of the insulin produced. Such a deficiency results in increased concentrations of glucose in the blood, which in turn affects multiple systems, in particular the blood vessels and nerves [1]. It's a chronic disease with myriad of complications. Diabetes mellitus is one the leading non communicable disease globally.

Diabetes because of its multisytemic involvement also causes spectrum of complications affecting most tissues. Most important event which plays catalyst to this is dyslipidemia. Plays an important role in microvascular complications. Elevated triglyceride levels is one of the common findings in diabetes along with elevated LDL and cholesterol. Hypertriglyceridemia typically occurs in conjunction with low HDL levels and atherogenic small dense LDL particles and is associated with increased cardiovascular risk Postprandial hypertriglyceridemia also is a common feature of insulin resistance. Small dense LDL that coexist with decreased HDL particles in hypertriglyceridemic states are highly pro-atherogenic due to their enhanced endothelial permeability, proteoglycan binding abilities and susceptibility to oxidation [2].

The management of dyslipidemia hence plays an important role along with management of hyperglycaemia. Metformin, has been the mainstay of treating Type-2 DM for many years. Evidences prove effectiveness of metformin therapy in lowering of HbA1C {1.12%} used as monotherapy and in combination with other therapeutic agents [3].

Sitagliptin is an inhibitor of the enzyme dipeptidylpeptidase-4, an enzyme responsible, among other roles, for the degradation of the incretin hormone glucagon-like peptide-1 (GLP-1; insulinotropin), which plays a role in regulating insulin secretion. It is used in the treatment of type 2 diabetes mellitus, as monotherapy or as dual therapy with metformin [4].

Role of metformin and sitagliptin in management of hyperglycaemia is well established. Through this

study attempt has been made to evaluate the effect of Sitagliptin on triglyceride levels and effect of combination therapy of Sitagliptin and Metformin on triglyceride levels in diabetic Albino Wistar rats.

Methodology

Albino Wistar rats were used in this study.Rats were divided into 4 groups.

- Group 1: control. Diabetes induced rats given normal saline
- Group 2: Diabetes induced rats treated with Metformin 100mg/body wt [5]
- Group 3: Diabetes induced rats treated with Sitagliptin 10mg/kg body wt [5]
- Group 4: Diabetes induced rats treated with combination of Metformin and Sitagliptin

Induction of diabetes**:** Diabetes was induced by High fat diet - Low dose streptozotocin method.

Preparation of high fat diet [6]**:** High fat diet was prepared by mixing edible coconut oil and Vanaspathi ghee, mixed in clean beaker at a proportion of 2 volume of edible coconut oil and 3 volumes of Vanaspathi ghee. It was administered at a dose of 10ml/kg body weight by oral feeding. Care was taken to prevent contamination at each step. Feeding was carried for duration of 6 weeks.

Streptozotocin [7] was given after 6weeks of high fat diet. Streptozotocin was stored at 0-4 degrees and care was taken to maintain the temperature by using ice placed in a beaker whenever it was used Buffer was prepared by using 0.1M citric acid monohydrate and 0.1M trisodium citrate dehydrate [8]. After overnight fasting STZ was administered at a dose of 35mg/kg [7] intraperitoneally.

The animals were observed for adverse effects Blood samples were collected before and after induction of diabetes RBS and triglyceride level were noted. Animals with RBS more than 200md/dl were considered diabetic.

Drug Administration: All the drugs were given for a duration of 21 days. After completion of drug therapy for 21 days [5], blood sample were sent for evaluation of triglyceride levels

Results

Table 1: Change in Mean Triglycerides by Days among Study Groups

Groups		Triglycerides (Mean±Sem)			Anova P Value
		Day 0	After 6 Weeks	After 21 Days	
Group I		83.1±4	210.7±6.8	196.2±10	<0.001*
Group II		88.6±3.3	201.5±7.3	106±1.9	<0.001*
Group III		93±3.3	196±3.9	108±2.8	<0.001*
Group IV		92.7±2.8	208.9±6.7	102±2.3	<0.001*

Triglyceride levels of group 2,3,4 increased significantly following the induction of Diabetes. After the treatment for 21 days, Group 3 animals treated with Metformin triglyceride levels decreased from201.5mg/dl to 106mg/dl showing significant reduction [p<.001]. Group 4 animals, treated with Sitagliptin the triglyceride levels decreased from 196mg/dl to 108.2mg/dl. Showing significant reduction [p<0.001]. Similarly in the animals of group 5 receiving combination therapy of Metformin and Sitagliptin the triglyceride reduced from 208.9mg/dl to 102mg/dl Showing significant reduction[p<0.001].

Conclusion and Discussion

From above results it can be concluded that rats treated with Sitagliptin and combination of Sitagliptin and Metformin showed significant reduction in Triglyceride levels, compared to control. Metformin has been the most commonly indicated drug in the management of diabetes, which also has is effective in managing dyslipidemia. Metformin exerts a beneficial effect on triglycerides metabolism by improving intrahepatic glucose metabolism and reducing extrahepatic insulin resistance. Metformin exerts a beneficial effect on triglycerides metabolism by improving intrahepatic glucose metabolism and reducing extrahepatic insulin resistance [9]. Sitagliptin mainly acts by targeting DPP4 receptors. Further studies have been made on these receptors. DPP-4 receptors are found in many location in human body. There strong expression of a gene in human white preadipocytes and adipocytes with possible contribution of DPP4 to the adipocyte differentiation process [10]. Studies also suggests that Sitagliptin, acutely Inhibits Intestinal Lipoprotein Particle Secretion in non-diabetic healthy Humans [11] hence Sitagliptin used as a monotherapy or in combination with metformin can be a promising therapy not only in treating hyperglycaemia but also hypertriglycer idaemia in management of Diabetes.

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