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Type II Diabetes Mellitus Drug Comparison Study Involving Several Different Anti-Diabetic Oral Medications

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ABSTRACT

Dental hypoglycemic agents are among the drugs used to treat diabetes mellitus (DM) by lowering blood sugar levels. Following the diabetic condition, dental hypoglycemic agents are used singly or even in combination to lower blood sugar levels and balance-related DM issues. The same procedure is frequently used to lower blood glucose levels in type II diabetic animals who are otherwise healthy. Nevertheless, DM management with a risk of other conditions or cardiovascular issues would not be possible with a single therapy. Therefore, in situations like this, combination treatment is typically employed for much better management of DM. After eight and six days of treatment, metformin alone shows a significant reduction in LDL-c and TC levels and an increase in HDL-c levels compared to the starting values. In contrast, Glimepiride individual treatment shows a significant increase in LDL-c and HDL-c levels after the eighth week of treatment. Additionally, the Glimepiride shows virtually no significant TG changes. This particular result might reflect Glimepiride's ability to stimulate the appetite. According to this investigation, metformin was incredibly effective in lowering HbA1c. When compared to the baseline values from the first and second weeks of treatment, the combination of Metformin and Glimepiride therapy also resulted in significant increases in HDL c levels at the eight and six-week mark. Consequently, the combination therapy shows good lipid management profiles.

INTRODUCTION:

Diabetic issues mellitus is a metabolic condition recognized by hyperglycemia with a hampered metabolic process of essential natural ingredients such as carbs, lipids, and protein. The results are generally due to defective insulin secretion, and loss in insulin receptors. Preceding hundreds of years in India, 2 doctors "Charaka as well as Susruta" noted the illness. The etiology of the diabetes type has already been identified or even partly developed also 12% of the affected person public is impacted. The etiologic element might be a hereditary defect changing the β-cell performance or maybe insulin action, pancreatic diseases, endocrinopathies, toxic chemicals or xenobiotics provoked pancreatic harm, along with the pathological condition that causes hyperglycemia.[1,2]

Based on Diabetes Atlas posted in 2007, at this time there are 246 thousand diabetes patients throughout the planet, with eighty percent of them within the developing as well as placed under evolved places. Kancheepuram and Chennai exhibit an increased occurrence of forty% wearing areas that are urban inside 6 yrs, along with forty nine% wearing outlying parts inside 3 seasons. The preclinical phase of sort II DM is specified as damaged sugar tolerance (IGT). The classical glycemic profile of sort II DM is made up of heightened basal or even fasting amounts in which postprandial glycemic trips are superimposed. The beta cellular dysfunction of diabetes patients goes down in 2 unique types.[3,4]

The loss in compensatory systems, including elevated beta cellular mass, quantitative insulin result as well as optimum secretory electrical capacity. The standard fasting insulin amount is somewhere between five as well as fifteen mu/ml. Usually, insulin is released in a pulsatile manner within the beta cells. Ultradian pulses of insulin secretion happen each ninety to 120 mins and are exaggerated after the ingestion of meals. In type II DM subjects the ultradian oscillations of insulin delivery are no longer present and the first phase of insulin release is lost (Chen et al., 1995).[5-7]

In sort II DM, reduced basal as well as insulin-stimulated *glycogen synthetase* within the muscle groups and also to prevent sugar-activated insulin secretion. You will find evidence of a damaged beta cellular reaction to sugar (blindness of beta cells to sugar) however the intense insulin reaction to nonsugar stimulus as hormones, neurotransmitters, and arginine persist. This insulin opposition can happen within several tissue cells, muscles, liver, splanchnic, and so on. Disappointment in the liver to perceive the signal leads to the improved hepatic sugar result and it is manifested as elevated bloodstream sugar amounts in

sort II DM. Impaired sugar tolerance (IGT) belongs to a transient phase between regular sugar tolerance and also the advancement of sort II diabetic issues. Inside subject matter with damaged sugar tolerance, the defect might be on insulin binding to the receptor of its.[8-9]

The indicators of the sort I diabetic issues often show themselves in kids within months or weeks. Irreducible exhaustion as well as a fast fat loss might additionally be triggered by sort I diabetes. Within diabetic issues sort II, nonetheless, the signs and symptoms generally build a lot more gradually. When quick perspective switches happen, the kind I ought to regularly be suspected, while sort II should be suspected. Diabetic issues individuals of the sort I might also provide with diabetic issues ketoacidosis (DKA), a serious type of metabolic deregulation recognized through the smell of acetone over the inhale.[10]

Persistent elevation of bloodstream sugar in diabetic issues plays a crucial job in the growth as well as the advancement of significant diabetic complications. The injurious negative effects of hyperglycemia are characteristically noticed around tissue cells that aren't influenced by insulin for sugar entry directly into the cellular (e.g., brain, kidney, nerve, retina, eye lens, intestine, and red-colored bloodstream cells). The individuals ought to have fasted for ten to fourteen Hours and also really should have stopped sugar-altering medicines three times before the examination working day.[11-12]

MATERIAL AND METHODOLOGY

This study was carried out in both genders of diabetic animals. Animals were distributed into three groups (Group I, Group II, Group III) with 40 animals. All the adverse drug reactions that were invented were noted in the case sheet. The blood glucose level of the diabetic patient sample was measured by self-monitoring. Venous blood is mixed with lysing reagent for the preparation of hemolysate.[13-14]

Elimination of the labile Schiff's base is achieved during Haemolysis. The resin is then mixed with a weakly binding cation-exchange resin. The non-glycated hemoglobin binds to the resin leaving glycated Hb free in the supernatant. Total cholesterol was estimated by CHOD-PAP (Cholesterol Oxidase– Peroxidase 4- amino antipyrine) method. Serum Triglycerides were estimated by the GPO-PAP method (Jacobs and VanDenmark, 1960).

The increase in absorbance is directly proportional to the concentration of triglycerides. 1ml of working reagent was taken in a test tube and to this 10 µl of serum sample was added. The contents were mixed well and incubated at 37°C for 5 min. After zeroing the instrument with

blank, the absorbance of the standard followed by the test sample was measured at 500 nm.[15-16]

RESULT AND DISCUSSION

A total of 40 type-II DM animals were enrolled in the study. Of these, 23 (57.5%) were males and 17 (42.5%) were females Further, the mean body mass index (BMI) of the animals was found to be 0.45 ± 0.02.

Table 1-: Gender distribution of the animals enrolled in the study

Gender	Number of Animals	Percentage (%)
Male	23	57.5
Female	17	42.5
Body mass index (Mean ± **SD)**	0.45 ± 0.02	ND

Table-2: Age wise distribution of animals used in the study

Age Groups	Male Female		Total Number of animals	
30-40 days	3	3	6	2.4
41-50	6	6	12	4.8
51-60	4	6	10	4.0
61-70	6	6	12	4.8

Table-3: Duration of diabetes among the study

Duration	Number of Animals	Percentage (%)
>5 months	11	4.4
6 -10 months	21	8.4
11- 15 months	8	3.2

The duration of diabetes of the Animals recruited in the present study were as follows, 11 animals (4.4%) presented for less than 5 months. 21 (8.4 %) animals elicited for 6-10 months, and 8 animals (3.2%) showed that 11-15 months.

Table-4: Co- Morbid condition among the animals in the study

Diseases	Number of Animals	Percentage (%)
Hypertension	13	5.2
Peripheral neuropathy	11	4.4
Gastritis	6	2.4
UTI	7	2.8
Parkinson's	3	1.2

Among the 40 types II diabetic animals recruited for the study, 13 animals were without any co-morbid condition, while remaining 27 animals had one of the 6 co-morbid conditions. co-morbid condition were (1) Hypertension, (2) Peripheral neuropathy, (3) Gastritis, (4) Urinary tract infection (UTI), (5) Parkinson's diseases and (6).

The animals suffering from co-morbid conditions included; 13 animals with hypertension, which were males 7 animals and females 6, 11with peripheral neuropathy, 6 animals in males and 5 animals were in females. 7 with urinary tract infection, which is only, affected female groups. 6 with gastritis 4 animals with males, and 2 animals were in females, and 3 with Parkinson's which is affected only male group.

Diabetes, the most common metabolic disease, is associated with major micro and macro vascular complications**. (Stratton *et al.*, 2000).** Many recent studies have demonstrated that elevated postprandial plasma glucose effects the diabetes complications, primarily in macro vascular complications more severely than elevated fasting plasma glucose**. (Erlinger TP, *et al.*, 2001, Parkin CG, *et al.*, 2001)** Since fluctuations of fasting plasma glucose and postprandial could affect HbA1c, this study was to assess the treatment goal was to bring the blood glucose level close to normal values.

Effect of Metformin treatment on blood glucose level (Group - I):

In the present study, the fasting and postprandial blood glucose level was estimated at the following time points 0 week, 4th weeks, 6thweeks and 8th weeks. There was a significant (P< 0.001) decrease in the blood glucose level were observed at the 8th week of treatment in fasting condition as compared to the 0 weeks (168.05 ±23. 81 vs 145.11 ±13. 36) and the 99% confidential intervals (CI) found to be 9.707 to 36.17. Similarly, in the case of postprandial blood glucose level the significant level of reduction in blood glucose was found at 4th, 6th and 8th weeks of treatment as compared to the 0 week (248.10 vs 232.68 ± 32.66; 248.10 ±31.78 vs 212.43 ± 21.42; 248.10±31.78 vs 190.10 ±13. 85). The 99% CI was found to be 1.170 to 33.37, 18.40 to 52.94 and 40.73 to 75.27 respectively.

Table 5: Effect of Metformin treatment on blood glucose level

Treatment	Blood Glucose level (mg/dl)							
	Fasting	Post Prandial						
Time points (in weeks)	0	4	6	8	0	4	6	8
Group-I (Type II diabetic animals treated with Metformin)	168.05 ± 23.81	162.42 ± 21.10	160.61 ± 20.10	145.11 ± 13.36***	248.10 ± 31.78	232.68 ± 32.66*	212.43 ± 21.42***	190.10 ± 13.85***

Data were represented Mean ± SD, N=40; One way ANOVA, repeated measures using Dunnett's posttest all values were compared with 0 week. Where, *** P< 0.001- Extremely significant; ** p<0.01 - Highly significant; * p< 0.05 – significant.

a. Effect of Glimepiride treatment on blood glucose level (Group- II):

In the present study, the fasting and postprandial blood glucose level was estimated at the following time points 0 week, 4th weeks, 6thweeks and 8th weeks. There was a significant (P< 0.01) decrease in the blood glucose level were observed at the 8th week of treatment in fasting condition as compared to the 0 week (158.16 ±12.81vs 142.79 ± 18.66**) and the 99% confidential intervals (CI) found to be 1.114 to 29.63. Similarly, in the case of postprandial blood glucose level the significant level of reduction in blood glucose was found at 6th and 8th weeks of treatment as compared to the 0 week (272.49 ± 19.89 vs 249.13 ±39.62; 272.49 ± 19.89 vs 200.47 ± 24.59). The 99% CI was found to be 4.123 to 42.60 and 52.78 to 91.26 respectively (Table-6).

Table-6: Effect of Glimepiride treatment on blood glucose level

Treatment	Blood Glucose level (mg/dl)							
	Fasting				Post Prandial			
Time points (in weeks)	0	4	6	8	0	4	6	8
Group- II (Type II diabetic animals treated with Glimepiride)	158.16 ± 12.81	154.02 ± 19.31	150.09 ± 31.11	142.79 ± 18.66**	272.49 ± 19.89	263.89 ± 28.99	249.13 ± 39.62**	200.47 ± 24.59***

Data were represented Mean ± SD, N=40; One way ANOVA, repeated measures using Dunnett's post test all values were compared with 0 week. Where, *** P< 0.001- Extremely significant; ** p<0.01 - Highly significant; * p< 0.05 – significant.

Table 7: Effect of Metformin, Glimepiride single and its combination treatment on Glycosylated hemoglobin level

Timeline (In weeks)	Metformin	Glimepiride	Glimepiride+ Metformin
0	9.47±0.78	8.89±0.28	11.76±0.58
6	6.92±0.52*	6.14±0.16*	7.85±0.26*
8	6.07±0.45*	5.85±0.54*	6.52±0.42*

All values are expressed as Mean ± SD, N=40, One way ANOVA, repeated measures using Dunnett's post test. All the values are compared with 0 week.* denotes statistically significant ($p<0.05$).

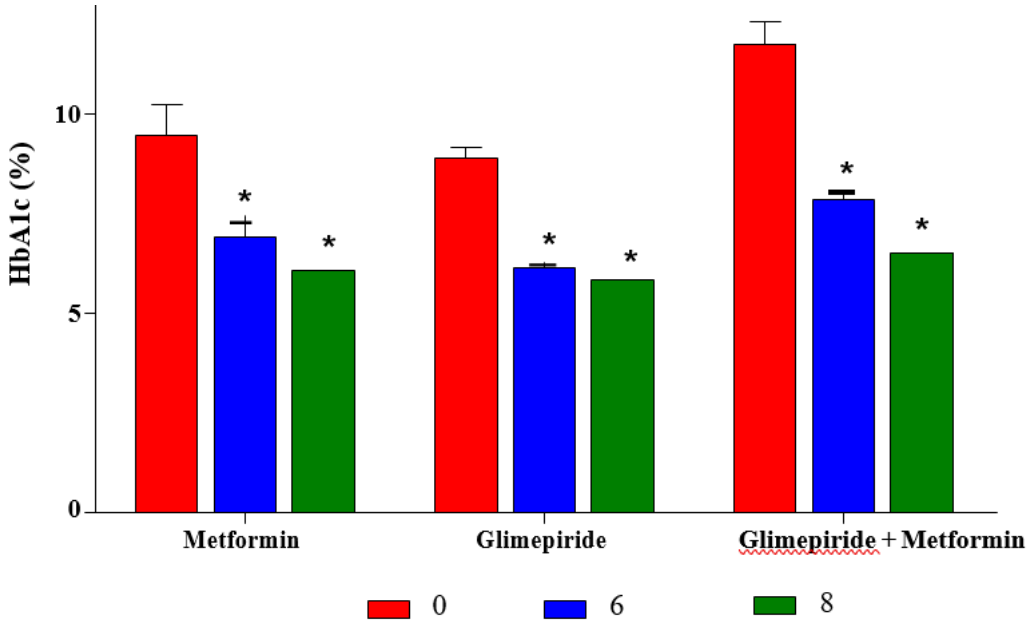

Fig-1: Effect of Metformin, Glimepiride single and its combination treatment on Glycosylated hemoglobin level

CONCLUSION

The advancement of diabetic issues outcomes from a vicious cycle of insulin opposition as well as β-cell disaster. Dental hypoglycemic representatives are definitely the number of medications is consumed to deal with the DM by turning down sugar amounts within the bloodstream. The one treatment is often used to lessen bloodstream glucose degree in type II

diabetic issues creatures, not having virtually any problems. Glimepiride and Metformin individual or maybe mixture treatment demonstrates considerable decrease of HbA1c amounts subsequent to 6th & 8 the week therapy when compared with baseline. Nausea as well as vomiting had been noticed.

Gentle abdominal disturbance (diarrhea) was noticed with Metformin medicated creatures. Nevertheless, it disappeared after a preliminary program on the treatment method at three to six times. Many creatures are encouraged to grab the antidiabetic medication together with ideal treatment as an H2 or vitamin sublimation receptor antagonist to stay away from gastric irritation.

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