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COMPARATIVE EFFICACY OF ORAL ANTI-DIABETIC DRUGS IN DIABETES MELLITUS TYPE 2 PATIENTS

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ABSTRACT Diabetes mellitus is a chronic illness that results from defects in insulin secretion and/or insulin response that requires life – long medical care. Currently, various classes of anti-diabetic drugs are used in the treatment of diabetes. Only 50 % of patients were controlled by monotherapy, as the disease advances combination therapy with a complementary mechanism of action is more logical. The study aimed to evaluate the comparative efficacy of anti-diabetic drugs for the best management of type 2 diabetes mellitus. In this study after 36 weeks of metformin and group 2 (metformin + glimepiride) therapy a significant decrease of mean FPS, PPS, and HBA1c ($p < 0.05$*) occurred. There was a significant decline in mean FPS, PPS, and HBA1c from baseline ($p < 0.05$* to $p < 0.01$**) observed after 24 weeks and 36 weeks with metformin + sitagliptin and metformin + vildagliptin combinations. It was found that effective glycemic controls were achieved better with combination therapy and Biguanides - Dipeptidyl peptidase inhibitors - 4 inhibitors combination therapy is better for their effectiveness.

KEYWORDS : Anti-diabetic agents, monotherapy, combination therapy, type 2 diabetes mellitus.

INTRODUCTION:

Diabetes mellitus is a chronic illness that results from defects in insulin secretion and/or insulin response that requires life–long medical care to prevent acute complications and reduce the risk of morbidity and mortality.[1] The prevalence of diabetes mellitus is increasing globally and more than 90 % of cases of diabetes mellitus belong to type 2 diabetes mellitus.[2] currently various classes of anti-diabetic drugs are used in the treatment of diabetes, which acts by different mechanisms to maintain optimal glycemic control.[3]

Due to functional decline in beta cells after 3 years of diagnosis, only 50 % of patients were controlled by monotherapy. As the disease advances combination therapy with a complementary mechanism of action is more logical.[4] Lack of patient compliance, clinical inertia, insulin resistance, and lack of dietary control are the reasons for poor glycemic control.[3] More than half of all patients of diabetes fail to achieve glycemic control, have dyslipidemia and a large percentage have diabetic vascular complications.[5,6]

Improved short and intermediate-term glycemic control is probably attained by diabetes self-management education (DSME) to promote higher physical activity levels, dietary modifications, and optimizing drug therapy.[7] Hence the study aimed to evaluate the comparative efficacy of anti-diabetic drugs for the best management of type 2 diabetes mellitus. The objectives are to compare fasting plasma sugar (FPS), postprandial plasma sugar (PPS), and glycosylated hemoglobin (HbA1c) levels in all groups.

Material and methods: It was a prospective, observational study performed at Santosh Medical College in collaboration with AIIMS Bhopal. A sample of 120 patients was used for this study, patients with type 2 diabetes mellitus of both sexes and age 18 years or above and who receiving antidiabetic therapy for more than 1 year were included in the study.

Patients who meet our study criteria were selected for participation. After receiving informed consent, demographics details, past medication history, and current treatment charts were recorded in the data collection form. Initially fasting plasma sugar (FPS), postprandial plasma sugar (PPS), and glycosylated hemoglobin (HbA1c) were noted and compared to FPS, PPS, AND HBA1c in every visit.

Patients were divided into four groups according to the oral anti-diabetic agents in prescription. In Group 1 patients on metformin, group 2 patients on metformin + glimepiride, group 3 patients on metformin + sitagliptin, and group 4 patients on metformin + vildagliptin were included.

STATISTICAL ANALYSIS:

Data collected for this study was analyzed on excel 2007 and SPSS 20, data are presented as mean with standard deviation and percentage. Results are assessed by using a t-test with $p < 0.05$ was considered to be statistically significant.

RESULTS:

Data collected from one hundred and twenty (n = 120) patients of type 2 diabetes mellitus were analyzed. Out of 120 subjects 53.33% (n=64) were male, 46.66% (n=56) were female with age ranging from 24 to 77 years with a mean of 53.14 ± 11.64 years. In this study initial FPS is higher in group 3 compared to all groups. The mean FPS decreased by 13.8 mg/dl (8.72 %) after 24 weeks and 26.3 mg/dl (16.62 %) after 36 weeks in group 1 was statistically significant ($p < 0.05$*). In group 2 the decrease in FPS 12.55 % (19.9 mg/ dl) was statistically significant after 36 weeks ($p < 0.05$*).

In group 3 the mean FPS decreased by 18.7 mg/dl (11.6 %; $p < 0.05$*) after 24 weeks and 31.4 mg/dl (19.60 %; $p < 0.01$**) after 36 weeks. Similarly, the decrease of mean FPS was Statistically significant in group 4 after 24 weeks 14.6 mg/dl (9.24 %; $p < 0.05$*) and after 36 weeks 28.3 mg/dl (17.91%; $p < 0.01$**).(Table 1)

Table 1: Impacts of oral anti diabetic drugs on mean fasting plasma sugar

Blood sugar FPS (mg/dl)	Group 1		Group 2		Group 3		Group 4	
Initial	158.2		158.6		160.2		158	
After 12 Weeks	149		157.76		152.2		154	
Decrease in %	-9.2	5.80%	-0.84	0.53%	-8	4.99%	-4	2.50%
After 24 Weeks	144.4		154.2		141.5		143.4	
Decrease in %	-13.8	8.72%	-4.4	2.77%	-18.7	11.67%	-14.6	9.24%
	P < 0.05*				p < 0.05*		p < 0.05*	
After 36 Weeks	131.9		138.7		128.8		129.7	
Decrease in %	-26.3	16.62%	-19.9	12.55%	-31.4	19.60%	-28.3	17.91%
	P < 0.05*		p < 0.05*		p < 0.01**		p < 0.01**	

*Statistically Significant

In this study the initial PPS is higher in group 3 compared to all groups. The mean PPS decreased by 19.1 mg/dl (7.35 %) after 24 weeks and 25.4 mg/dl (9.77 %) after 36 weeks in group 1 was statistically significant ($p<0.05$*). In group 2 the decrease in PPS 16.43% (19.9 mg/dl) was statistically significant after 36 weeks ($p<0.05$*).

In group 3 the mean PPS decreased by 49.4 mg/dl (18.53 %; $p < 0.05$*) after 24 weeks and 69.6 mg/dl (26.17 %; $p < 0.01$**) after 36 weeks. Similarly, the decrease of mean PPS was statistically significant in group 4 after 24 weeks 26.7 mg/dl (10.16%; $p < 0.05$*) and after 36 weeks 42.2 mg/dl (16.06 %; $p < .05$*). (Table 2)

Table 2: Impacts of oral antidiabetic drugs on mean postprandial plasma sugar

Blood sugar PPS (mg/dl)	Group 1		Group 2		Group 3		Group 4	
Initial	260		263		266		262.7	
After 12 Weeks	257.2		256.1		234.2		252.2	
Decrease in %	-2.8	1.07%	-6.9	2.62%	-31.8	11.95%	-10.5	3.99%
After 24 Weeks	240.9		238.9		216.7		236	
Decrease in %	-19.1	7.35%	-24.1	9.16%	-49.3	18.53%	-26.7	10.16%
	P < 0.05*				p < 0.05*		p < 0.05*	
After 36 Weeks	234.6		219.8		196.4		220.5	
Decrease in %	-25.4	9.77%	-43.2	16.43%	-69.6	26.17%	-42.2	16.06%
	P < 0.05*		p < 0.05*		p < 0.01**		p < 0.05*	

* Statistically significant

In this study, the initial HBA1c is higher in group 3 compared to all groups. The mean HBA1c decreased by 7.24 % after 36 weeks in group 1 was statistically significant ($p < 0.05$*). In group 2 the decrease in HBA1c 6.32 % was statistical significance after 36 weeks ($p < 0.05$*).

In group 3 the mean HBA1c decreased by 13.26 % ($p < 0.01$**) after 24 weeks and 21.26 % ($p < 0.01$**) after 36 weeks. Similarly, the decrease of mean HBA1c was statistically significant in group 4 after 24 weeks 10.79 % ($p < 0.05$*) and after 36 weeks 17.70 % ($p < 0.01$**). (Table 3)

Table 3: Impacts of oral ant diabetic drugs on mean HBA1c

HBA1c (%)	Group 1		Group 2		Group 3		Group 4	
Initial	8.15		8.23		8.75		8.53	
After 12 Weeks	7.87		8.07		8.24		8.12	
Decrease in %	-0.28	3.44%	-0.16	1.94%	-0.51	5.83%	-0.41	4.81%
After 24 Weeks	7.76		7.86		7.59		7.61	
Decrease in %	-0.39	4.79%	-0.37	4.50%	-1.16	13.26%	-0.92	10.79%
					p < 0.01**		p < 0.05*	
After 36 Weeks	7.56		7.71		6.89		7.02	
Decrease in %	-0.59	7.24%	-0.52	6.32%	-1.86	21.26%	-1.51	17.70%
	p < 0.05*		p < 0.05*		p < 0.01**		p < 0.01**	

* Statistically significant

DISCUSSION:

Among 120 patients included in the study majority of them were male, which is similar to the studies done in India.[1, 8,9,10] The mean age of patients was 53.14 ± 11.64 years, a contrast to that obtained in a study conducted in Karnataka reported the mean age of patients as 59.6 years.[1]

This study was carried out to describe the efficacy of anti-diabetic drug therapy to achieve optimal glycemic levels; we find the improved glycemic level in all the groups. In this study, patients were divided in to four groups based on anti-diabetic drug therapy.

Metformin inhibits hepatic gluconeogenesis, increases peripheral insulin sensitivity, and decrease intestinal glucose absorption. In this study after 36 weeks of metformin therapy a significant decrease of mean FPS, PPS, and HBA1c ($p < 0.05$*) occurred. A similar result was found by shashikala et al after 24 weeks.[11]

The study demonstrates that there was a significant decline in mean FPS, PPS, and HBA1c from baseline in group 2 (metformin + glimepiride) after 36 weeks of therapy ($p < 0.05$*). A similar result was found in a study by Konuru and Reedy.[12] Glimepiride has a dual mode of action, it reduces insulin resistance and improves glucose utilization results in a potent glycemic reduction.[13]

The dipeptidyl peptidase inhibitors - 4 inhibitors have been recommended for therapy due to their superior efficacy, weight neutrality, low risk of hypoglycemia, and excellent tolerability.[14] There was a significant decline in mean FPS, PPS, and HBA1c from baseline ($p < 0.05$* to $p < 0.01$**) observed after 24 weeks and 36 weeks with metformin + sitagliptin and metformin + vildagliptin combinations. Similarly, metformin + sitagliptin and metformin + vildagliptin combinations were reported to be effective hypoglycemic agents by different studies.[15,16]

CONCLUSION:

Findings of this study concluded that a significant reduction in mean FPS, PPS, and HBA1c from baseline was seen in all groups of patients. It was found that effective glycemic controls were achieved better with combination therapy and Biguanides - Dipeptidyl peptidase inhibitors - 4 inhibitors combination therapy is better for their effectiveness. The choice of therapy depends on various co-factors that need a detailed investigation in a larger diabetic population.

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