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Research Article

COMPARATIVE STUDY OF EFFICACY AND SAFETY OF METFORMIN+GLIMEPIRIDEVSMETFORMIN +GLIMEPIRIDE+VOGLIBOSE IN TYPE 2 DIABETES MELLITUS PATIENTS AT TERTIARY CARE CENTRE, KANPUR

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ABSTRACT

The present study was aimed to compare the efficacy of metformin 500mg + glimepiride 1mg combination with metformin 500mg+ glimepiride 1mg+ voglibose 0.2mg combination in type 2 diabetes mellitus patients. The primary objective of the study is to compare the efficacy of double drug (metformin & glimepiride) versus triple drug therapy (metformin, glimepiride and voglibose) in type 2 diabetes mellitus subjects and secondary objective is to quantify their effect on glycated haemoglobin (HbA1c) levels in diabetic patient. A total of 100 type-2 diabetic patients were included in the study after obtaining the patient's consent and institutional ethics approval. The study was designed as prospective, nonrandomized, two-arm trial. One hundred type 2 diabetic patients after satisfying the inclusion criteria were included in the study and divided in two groups of 50 each as Group A and Group B. Group A patients received metformin 500mg + glimepiride 1mg, and Group B patients received metformin 500mg + glimepiride 1mg + voglibose 0.2mg. The patient blood samples were analysed for HBA1c, blood sugar levels, serum urea and creatinine during the trial initiation and other follow-ups in 3 months (day0, day15, day30, day45, day60, day75, day90). The obtained data was analysed using chi-square test for non-parametric data and student t-test for parametric data. A significant change in mean HbA1c levels (p value- 0.0001) were observed in Group A and Group B patients between the baseline values (7.3±1.4 & 9.7±1.2) and after 3 months treatment values (6.9±1.4 & 7.8±1.1). While comparing the mean HbA1c levels between Group A and Group B after three months of treatment, it was >7.5% in group B patients. No significant effect was seen on serum blood urea of group A and B patients. Triple drug intensification of metformin 500mg with glimepiride 1mg and voglibose 0.2mg showed significant decrease in HbA1c levels during three months of treatment. Further observational studies may be required to provide prolonged treatment data of this combination.

Keywords: Diabetes mellitus, HbA1c, Voglibose, Triple drug therapy.

1. INTRODUCTION

Diabetes Mellitus (DM) is a complex metabolic disorder characterized by hyperglycemia followed by abnormalities in carbohydrate, fat and protein metabolism producing chronic complications [1]. Worldwide DM is highly prevalent and economically devastating illness. The level of morbidity and mortality due to diabetes and its potential complications are enormous, and pose significant healthcare burdens on both families and society. India, the second most populous country of the world, has been severely affected by the global diabetes epidemic [2]. Globally, 422 million populations were affected with diabetes during 2016 and estimated to double by 2030 [3, 4]. Type 2 diabetes mellitus (t2DM) is characterised by the presence of insulin resistance with concomitant or eventual beta cell dysfunction. Resistance to insulin- stimulated glucose uptake is present in most of the patients with this disease [5]. The

multifactor etiology of DM in India includes genetic and environmental causes including obesity, urban migration, and economic boom and lifestyle changes associated with increased living standards [6]. A major problem in the management of t2DM is that glycemic control with diet and/or drug treatment declines as the disease progresses [7]. The basic principle of combination therapy is that with small doses of two drugs, there is greater efficiency and fewer side effects than with a large dose of either drug used as mono therapy [12]. Some physicians now advocate the therapy combining three oral agents (sulfonylurea, metformin, alpha-glucosidase inhibitor or sulfonylurea, metformin, thiazolidinedione) in the management of type 2 DM [8].

This study was aimed to evaluate the efficacy of triple drug combination (*i.e.* voglibose, metformin and glimepiride) and its impact on Glucose Triad *i.e.* HbA1c, FPG and PPHG. The primary objective of the study is to compare the efficacy of double drug (metformin & glimepiride) versus triple drug therapy (metformin, glimepiride & voglibose) in type 2 diabetes mellitus subjects and secondary objective is to study their effect on glycatedhemoglobin (HbA1c) levels in diabetic patient.

2. MATERIAL AND METHOD

This prospective, nonrandomised, open-label study was conducted in the Department of Pharmacology and Department of Medicine, at tertiary care hospital, Kanpur during 12/07/2017 to13/7/2018. The patients attending Medicine OPD were recruited after taking the institutional ethics committee approval and informed consent. A total of 100 t2DM patients, identified from the outpatient clinic and satisfying the inclusion criteria were selected for the study. For the research, t2DM patients aged 18-70 years who were prescribed metformin, glimepiride and voglibose were selected. The study excluded t2DM patients newly diagnosed, not prescribed with the above drugs or combinations, pregnancy, chronic co-morbidities, and not willing to provide consent.

The selected patients were allocated in to two groups. Group A included 50 patients receiving metfomin+ glimepiride and Group B included 50 patients receiving metformin 500mg + glimepiride 1mg + voglibose 0.2mg. The patients were followed for a period of three months (6 follow-ups) during which their vitals and blood sugars were evaluated. The 5ml venous blood sample was obtained from the patients in clear vacutainers under the standard protocol for sample collection and was sent to the laboratory for investigation (blood glucose, HbA1c, serum urea, serum creatinine levels) [9].

2.1. Statistical Analysis

The SPSS windows version 16.0 programme was used to analyse the results. The percentage changes were determined after tabulating the values in the data. Student's t-tests and Chi-square test were used to analyse the data. Statistical significance was described as a P value of less than 0.05.

3. RESULTS

This prospective, observational study included 50 patients in group A and group B each. Among them there were 2 dropouts from each group. The analysis was performed for the data available from the participated patients. The age distribution among the groups was comparable (χ^2p-0.77) (Table 1). The gender distribution among the groups did not show any statistical significance (χ^2p-0.27) (Fig. 1).

Group A was having average fasting blood glucose (FBG) 166.4±11.5 mg /dl before treatment and was having 127.7±11.2 mg/dl at the end of treatment, indicates significant decrease. Group B was having average fasting blood glucose 161.8±14.03mg/dl before treatment and was having 119.3±14.4 mg/dl at the end of the treatment. The $p<0.001$ is considered significant. Group A was having average post prandial blood glucose (PPG) 260.06 ± 27.1 mg/dl before treatment and was having 214.7 ± 26.8mg/dl at the end of treatment. The $p<0.001$ is considered significant. Group B was having average post prandial glucose 261.2±23.08mg/dl before treatment and was having 167.1±20.9 mg/dl at the end of treatment. The $p<0.001$ is considered significant.

Group A was having average HbA1c 7.3±1.4% before treatment and was having 6.9±1.4 % at the end of treatment. The $p<0.001$, which is considered significant. GroupB was having average HbA1c 9.7±1.2 %before treatment and was having 6.9±1.01 % at the end of treatment. The $p<0.001$ is considered significant.

Group A was having mean serum blood creatinine 0.9mg/dl before treatment and 1.04mg/dl at the end of treatment ($p<0.001$). Group B was having average serum blood creatinine0. 98mg/dl before treatment and 0.98mg/dl at the end of treatment ($p<0.3$). No significant effect seen on serum blood creatinine in group B (Table 3).

Group A was having average serum blood urea 29.64 mg/dl before treatment and 27.01mg/dl at the end of treatment (p=0.22). Group B was having average serum blood urea 28.6 mg/dl before treatment and 26.7mg/dl at the end of treatment (p=0.24). No significant effect seen on serum blood urea in group A and B (Table 3).

Table 1: Age distribution of study participants

AGEGROUP	GROUP A		GROUP B	
	Patients (N=48)	Percentage (%)	Patients (N=48)	Percentage(%)
30-40	9	18.75	7	14.58
41-50	10	20.83	13	27.08
51-60	15	31.25	12	25
61-70	14	29.16	16	33.33

Pearson Chisquarep-value is 0.77, N=48.

Table 2: Glucose triad

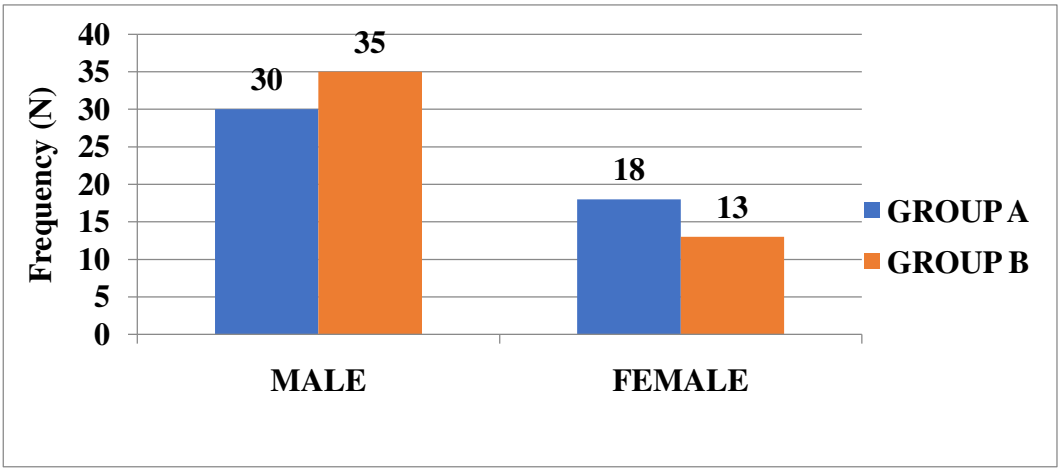
S.No		Group A			Group B		
		FBS mg/dl (Mean±SD)	PPBSmg/dl (Mean±SD)	HBA1c% (Mean±SD)	FBSmg/dl (Mean±SD)	PPBSmg/dl (Mean±SD)	HBA1c% (Mean±SD)
1	Baseline	171.6±8.12	260.06±27.1	7.3±1.4	175±10.6	261.2±23.08	9.7±1.2
2	DAY 15	164.9±8.41	251.3±25.4		170±10.4	247.2±22.1	
3	DAY 30	158.1±7.76	243.7±25.01		164±10.08	233.4±22.6	
4	DAY 45	152.1±8.13	236.1±24.5		157±10.27	216.6±22.5	
5	DAY 60	145±8.18	229.1±24.6		150±10.7	197.8±22.2	
6	DAY 75	138±8.74	221.2±25.4		142±11.66	182.1±21.5	
7	DAY 90	133±9.59*	214.7±26.8*	6.9±1.4*	135±12.5*	167.1±20.9*#	7.8±1.1*#

Student's t-test, N=48

Table 3: Renal parameters

		Group A	Group B
S. creatine	BASELINE	0.91±0.38	0.98±0.53
	DAY 90	1.04±0.38*	0.98±0.52
S. urea	BASELINE	29.64±9.8	27.01±8.3
	DAY 90	28.6±9.7*	26.7±8.3*

Student's t-test, N=48



Pearson chi-square p-value is 0.27, N=48

Fig. 1: Gender distribution among the study participants

4. DISCUSSION

In our study, the glucose triad showed a very satisfactory result. The male to female ratio is 2.09:1 which shows higher prevalence of diabetes mellitus type 2 in males 67.7 % as compared to females 32.2 %. The fasting blood sugars and post-prandial blood sugars have significantly decreased in both groups in comparison to before treatment mean values. Between group FBS and PPBS mean values were comparable (p value 0.8) at baseline. After three months treatment, PPBS mean values were significantly lower than in group A (p value 0.0001). The HBA1c values were comparable at baseline between groups, and their statistical significance in comparison to baseline within groups and also between groups after treatment. There were no significant changes in serum creatinine and blood urea.In modern clinical approach, it is now recommended that for optimal management of type 2 diabetes, there is the requirement to understand the relationship between HbA1C, FBS and PPBS (the glucose triad). When antidiabetic therapy is initiated, physicians may need to consider selection of agents that target both fasting & post-prandial hyperglycemia.

The study results of age distribution were in line with results of Krishna Murti*et al.*, which also showed a significant decrease in FBS and PPBS in both treatment groups. HbA1c reduction was more in case of triple drug therapy which supports our study. According to CRao etal, The FPG level was 137±17.64 mg/dl at baseline. The Fasting plasma glucose level was significantly reduced just after 1month of the treatment from the baseline value [10]. Arif A Faruqui*et al.*, (2016) study of safety and efficacy offixed dose combination of voglibose, Glimepiride and Metformin in Indian type 2 diabetes mellitus patients observed 62% males and 38 % females near about similar with our study [11]. Significant differences were found in the value of HbA1c from baseline to the value observed after completion of treatment, whichis also near about similar to our study.Jindal *et al*,also found significant differences in the value of HbA1c from baseline to the after completion of treatment, which is similar to the present study [12]. According to Derosa*et al*, after 15 weeks of therapy, the acarbose-treated patients exhibited a significant decrease in HbA1c (-1.4%, $p < 0.05$), FPG (-10.7%, $p < 0.05$), PPG (-16.2%, $p < 0.05$) [13].

There were no adverse events observed during this study.

The serum creatinine and serum urea of study participants were in normal reference ranges during this study [11]. The limitations of this include shorter duration of the study and was carried out in 98 study population. Further studies may be required with prolonged study duration and larger effective sample size.

5. CONCLUSION

Triple drug therapy showed significant reduction in glucose triad levels. The add on therapy using voglibose in dual therapy including glimepiride and metformin showed a very significant benefit in controlling the glucose triad levels when compared to dual therapy.

Conflict of interest

None

6. REFERENCES

1. American Diabetes Association. *Diabetes care,* 2010; **33(1):**S62-S69.
2. Kaveeshwar SA, Cornwall J. *The Australasian medical journal*, 2014; **7(1):**45.
3. Roglic G, editor. Global report on diabetes. World Health Organization; 2016.
4. Wild S, Roglic G, Green A, Sicree R, King H. *Diabetes care*, 2004; **27(5):**1047-1053.
5. Armstrong C. *American family physician*, 2017; **95(1):**40-43.
6. Unnikrishnan R, Rema M, Pradeepa R, Deepa M, Shanthirani CS, Deepa R, et al. *Diabetes care*., 2007; **30(8)**:2019-2024.
7. Bharti SK, Srivastava A, Singh R. *Population*, 2014; **5(10):**90.
8. Ovalle F, Bell DS. *Endocrine Practice*, 1998; **4(3)**:146-147.
9. Parial CH, Islam M, Ahmad M, Kasru A. *Journal of Scientific Research*, 2013; **16(11)**:1508-1511.
10. Murti K, Sethi MK, Dey A, Lal CS, Pandey K, Das P. *International Journal of Pharmacology*, 2016; **12(4):**422-428.
11. Faruqui AA, Nulwala H, Pmn P, Rane PS. *Pacific Journal of Medical Sciences*, 2015; **15(1):**24-33.
12. Jindal A, Jindal M, Kaur M, Kumar R, Brar RS. *Indian J Basic Appl Med Res*., 2014; **3(3)**:111-116.
13. Derosa G, Salvadeo SA, D'Angelo A, Ferrari I, Mereu R, Palumbo I, et al. *Current medical research and opinion*. 2009; **25(3):**607-615.