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Research article

A COMPARATIVE STUDY ON COMBINATIONAL DRUG APPROACH IN TYPE II DIABETES MELLITUS PATIENTS

Komati Siva Rama Krishna[1]*, CH Manikanta Rajesh Kumar[1], Bade Raveena Reddy[1], K Venu Priya Bharathi[1], Kurapati Raviteja[1], Dr D Curie[2]

[1,*]Pharm D students, Vishwa Bharathi College of Pharmaceutical Sciences, Perecherla, Guntur, Andhra Pradesh, India, 522005.
[2]Assistant Professor, Pharm D, Vishwa Bharathi College of Pharmaceutical Sciences, Perecherla, Guntur, Andhra Pradesh, India, 522005.

ABSTRACT

Introduction: Diabetes mellitus (DM) is a metabolic disorder characterized by hyperglycemia which is mainly due to the disturbances in carbohydrate, protein and fat metabolism leading to the dysfunction and failure of various organs. Aims and Objective: To compare the behavior of anti-diabetic drugs given in two combinations in patients with diabetes mellitus type II and compare the drug reliability. To assess the safety and efficacy of metformin plus glimepiride in patients with type II diabetes mellitus. To study the safety and efficacy of metformin plus voglibose in diabetes mellitus type II patients. Methods: One Hundred and eight patients who met the inclusion criteria were enrolled into the study. A total of 100 patients completed all the follow up visits. Patients enrolled were known case of diabetes mellitus type II, with no co morbid conditions and have been administered with either of the drug combinations of our study. The mean ±SD age of patients in the study was 53.51±9.4920795. The mean age of Group-A patients is 52.5 while it is 54.5 in Group-B patients. The percentage of male patients is higher in group-B whereas it is vice versa in case of female patients. The baseline demographic parameters of Group -B (Metformin +Voglibose) patients have been given. Conclusion: Diabetes mellitus has been alarming globally with 1.2million of new patients in south Asian continents. Altered Quality of Life (QOL) is the major consequence of it, crippling the public health. To treat diabetes mellitus type II, proper assessment of patient's glucose profile is key to start treating the diabetes. When compared between metformin plus glimepiride and metformin plus voglibose, the former combination is better in terms of efficacy.

Key Words:- Diabetes mellitus, Metformin, Voglibose.

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Corresponding Author

Komati Siva Rama Krishna
Vishwa Bharathi College of Pharmaceutical Sciences, Perecherla, Guntur, Andhra Pradesh, India, 522005.

E-mail: sivaram.komati831@gmail.com

INTRODUCTION

The key factors to promote and maintain good health throughout the life are diet and nutrition. Chronic diseases that are related to imbalance in the diet and nutrition are diabetes mellitus, cardiovascular disease, stroke, obesity, cancer, osteoporosis and dental diseases (K.G.M.M.Alberti, P.Z. Zimmet ; Ramachandran, 2014). In 2001, 60% of the total deaths among 56.5 million people is mainly due to chronic diseases contributed approximately 46% of the global burden of disease (Miriam Cnop *et al*., 2005). The global burden of chronic diseases is expected to increase to 57% by 2020. The incidences of chronic disease are high in developing countries like India when compared to developed countries. It has been projected that, by 2025, chronic disease like Diabetes Mellitus will account for almost three-quarters of all deaths, and 70% of deaths due to diabetes will occur in developing countries (Hans K.A

Kerblom et al., 2002; Ravindranath Aathira and Vandana Jain, 2014, and Mohan V et al, 2003).

Diabetes mellitus (DM) is a hyperglycemia metabolic condition predominantly caused by the carbohydrate, protein and fatty metabolism disruption that leads to disorder and failure in the different organs. (Abdulfatai B. Olokoba *et al*., 2012). Diabetes mellitus signs and symptoms are:

- Polyuria
- Polydipsia
- Polyphagia
- Blurring vision and
- Weight loss (David M. Nathan *et al*., 2006).

It was predicted that India has 65.1 million adult diabetes mellitus patients by the year 2015 carrying 2nd position among the top 10 countries with high number of diabetes mellitus and this number is expected to increase up to 109 million by 2035[Daniele Sola et al., 2015]. Based on the etiology, WHO has classified DM as TYPE1 DIABETES MELLITUS (insulin dependent diabetes mellitus)and TYPE2 DIABETES MELLITUS (Non insulin dependent diabetes mellitus) (Floris Alexander van de Laar, 2008). However, this classification has disappeared, and new classification has been proposed which explains four types of DM: TYPE I, TYPE II, other specific types and gestational diabetes (Campbell LK et al., 1996). Type1 DM mainly targets pancreatic beta cells by the invasion of mononuclear cells into the islets of pancreas. This inflammatory reaction can be termed as insulitis; death of beta cells in the period of insulitis is mainly due to direct contact with macrophages and T cells which may cause initial loss of first phase insulin secretion to glucose (Wachters-Hagedoorn RE et al., 2007; Ulrike Gottwald-Hostalek *et al*., 2016).

Diabetes mellitus type I:

The major cause of type I DM includes

- Dietary factors,
- Genetics,
- Anti and perinatal risk factors,
- Stress full life events and
- Environmental risk factors (Giuseppe Derosa and Salvadeo Sibilla, 2007).

As Type 1 DM is mainly due to insulin deficiency, rapid acting insulin can be used when the patient requires rapid onset and short duration, and the clinical presentation of type 1 DM include Polyuria, hyperglycemia, polyphagia, polydipsia (Rendell M, 2004).

Diabetes mellitus type II:

Type II DM is a chronic metabolic disorder which is otherwise called as non-insulin dependent diabetes mellitus (NIDDM). Type 2 DM is characterized by insulin resistance and its deficiency, hyperglycemia. Despite of adequate production of insulin, the cells do not have the ability to uptake that insulin due to the resistance. The major causes of type 2 DM include:

Type II pharmacology has altered substantially throughout the last 10 years, offering improved medication use and classes of medications. These medicines enable oral therapy to be combined, typically with increased glucose control that is previously beyond medical treatment's reach. (Evans JM *et al*., 2006).

Diabetic modification was traditionally the cornerstone of the therapy of diabetes. If the diet is modified, weight reduction in patients with new illness beginnings is more likely to regulate glycemia than in patients who are considerable insulinogenic (Riveline JP *et al*., 2003). Medicines which encourage weight loss can be useful for highly chosen people but are not normally advised for the ordinary Type 2 diabetes mellitus patient (Geisen K *et al*., 1996).

AIMS:

To compare the behavior of anti-diabetic drugs given in two combinations in patients with diabetes mellitus type II.

OBJECTIVES:

- To assess the safety and efficacy of metformin plus glimepiride in patients with type II diabetes mellitus.
- To study the safety and efficacy of metformin plus Voglibose in diabetes mellitus type II patients.
- To compare the drug reliability.

METHODOLOGY

Study site and duration:

This study has been conducted in a Government General Hospital, Guntur, Andhra Pradesh, India for a period of 5 months between December to May 2021.

IEC Approval:

Our study has been approved by the institutional Ethics Committee.

Subject recruitment and confidentiality:

Patients of Diabetes mellitus type II of both genders have been recruited for the study. Prior information regarding the structure of study has been given to the subjects before carrying out the same. For the purpose of confidentiality of subjects involved in the study, Sensitive information of the subjects has been secured. Informed consent forms were obtained from the patients after explaining the risks and benefits of the study.

Sample size:

100 Subjects have been recruited for the current study.

Study design:

100 Subjects have been grouped into two and studied Under Prospective cohort study.

Inclusion Criteria:

- Patients with type II Diabetes mellitus have been recruited into the study
- Both the genders are involved
- There is no age disparity while choosing the patients

Exclusion criteria:

- Diabetes mellitus patients who are on therapy of other than metformin, Glimepiride, and Voglibose are excluded from the study.
- Renal failure and Congestive Heart failure patients are not allowed into the study since they are contraindicated with drugs of our choice.
- Patients with underlying medical conditions that compromise their safety or warrant their participation in the study
- Patients who have adverse social habits like alcohol consumption during and 6 months prior to the study have been excluded from the study.
- Pregnant and Lactating mothers will be excluded in the study.
- Subjects with historical amphetamin, cocaine, tetra cannabinoids benzodiazepine, barbiturate, and opioid misuse were excluded within one year of the study.
- Subjects having a substantial history of hypersensitivity to metformin, glimepiride, and voglibose.

Results:

One Hundred and eight patients who met the inclusion criteria were enrolled into the study. A total of 100 patients completed all the follow up visits. Patients enrolled were known case of diabetes mellitus type II, with no co morbid conditions and have been administered with either of the drug combinations of our study. The mean ±SD age of patients in the study was 53.51±9.4920795. The mean ±SD age of females are higher than that of males in group 1 where as in group 2 the mean ±SD of males is higher than that of females. Baseline demographic characteristics of the studied population are shown in **Table 1.**

The mean age of Group-A patients is 52.5 while it is 54.5 in Group-B patients. The percentage of male patients is higher in group-B whereas it is vice versa in case of female patients. The mean age and gender wise allocation of patients in group-A and group-B is shown in table 1**.**

The mean age of Group-A patients is 52.5 while it is 54.5 in Group-B patients. The percentage of male patients is higher in group-B whereas it is vice versa in case of female patients. The mean age and gender wise allocation of patients in group-B is shown in Table 2.

The baseline demographic parameters of Group -B (Metformin +Voglibose) patients have been given in the **Table 3.** The mean age of Group-B patients is higher than Group-A patients but it has no significance.

The mean PPBS of group-B patients at the baseline is 256.54±82.30 while at the end of final review (R3) it is116.26±15.21 Inspite being controlled in both the groups, the ppbs levels of group-A is better controlled than group –B. The cumulative analysis of PPBS is shown in **fig 1.**

Fasting blood glucose levels has been controlled well in Group-A than in Group-B. There is significant difference between mean FBS levels of Group-A and Group-B patients ($P<0.0001$) at the end of review (R3). However, there is no significant difference between the groups during first (R1) and second (R2) review whose P value is 0.2450 and 0.5738 respectively. Mean± SD of FBS of both groups is given in **table 4.**

The mean base line of FBS of Group A patients is159.04±43.97 , and the mean baseline Fasting blood sugar of GROUP B patients is 171.56±60.67 that is higher than group –A. whereas, the mean baseline PPBS in group A is206.58±76.93 and the mean baseline PPBS in group B is 171.56±60.67. The mean ± SD of group A and group B FBS is 107.92±8.38and 110.52±7.62 respectively. The fasting blood glucose levels are better controlled in R_1 when compared to R_1*.

The mean ± SD of fasting blood glucose in R_2 group A is 99.04±4.19 and mean ± SD of fasting blood glucose in R2 of group is98.02±11.93. The fasting blood glucose level is better controlled in R2 of group A when compared to R2 of group B.

The mean ±SD of PPBS in R2 group A is 115.64±7.24and mean ±SD of PPBS inR2 group B is130.72±4.47The PPBS level is better controlled inR2 group A when compared to R2 group B.

The mean ± SD of fasting blood glucose in R_3 group A is 72.68±12.09 and mean ± SD of fasting blood glucose in $R_3$of group B is 92.82±12.85.The fasting blood glucose level is better controlled in $R_3$of group A when compared to R_3 of group B.

The mean ±SD of PPBS in R_3 group A is 104.22±11.22and mean ±SD of PPBS in R_3 group B is116.26±15.21.The PPBS level is better controlled in R_3group A when compared to R_3 group B.

Table 1 : Basic demographic parameters of type 2 diabetes mellitus patients using combination of metformin plus glimepiride versus metformin plus voglibose

S.NO	CLASS	PARAMETERS	GENDER (%)	
		AGE	MALES	FEMALES
1	Metformin plus Glimepiride	52.5± 9.05	42	58
2	Metformin plus Vegliote	54.52± 9.92	58	42

Table 2: Baseline demographic parameters for metformin plus glimepiride.

S.NO	Parameter	Frequency		Mean ±SD
		Range	Number (%)	
1	Age(years)	35-55 55-75	68 32	47.35±5.56 63.43±3.82
2	Height (Cm)	110-140 140-170	30 70	126.33±6.70 153.31±7.00
3	Mass (Kg)	50-75 75-100	58 42	61.85±6.28 83.66±8.01
4	BMI(Kg/m^2)	20-30 30-40	58 42	25.95±2.56 36.97±3.52

Table 3: Baseline demographic characteristics for metformin plus voglibose.

S.NO	Parameter	Frequency		Mean ±SD
		Range	Number (%)	
1	Age(years)	35-55 55-75	58 42	47.68±6.53 63.95±5.25
2	Height (Cm)	140-150 150-160	32 68	144.93±2.10 154.55±2.78
3	Mass (Kg)	50-75 75-100	80 20	62.12±7.42 81.8±5.32
4	BMI(Kg/m^2)	20-30 30-40	66 34	26.25±3.54 33.78±2.62

Table 4: Comparision Of Fasting Blood Sugar Reviews Betwwen And With In Groups.

	R0	R1	R2	R3	P
GROUP 1	159.04± 43.97	99.04± 4.19	105.92± 15.80	72.68± 12.09	**<0.0001**
GROUP 2	171.56± 60.67987	98.02± 11.93732	110.52± 7.629522	92.82± 12.85876	**<0.0001**
P	0.2450	0.5738	0.0696	**<0.0001**	

Figure 1: Post parandreal blood glucose levels in group-b patients

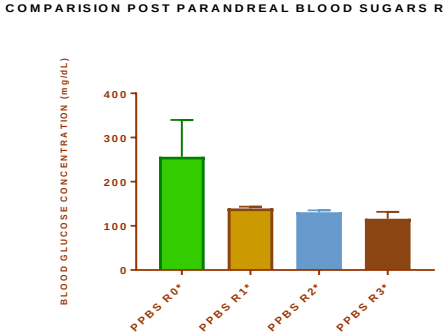


Figure 4: Comparison of HBA1C Reviews within Groups

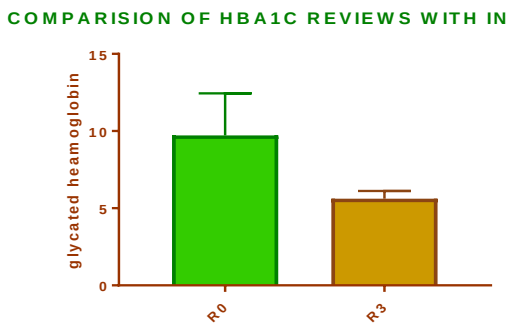


Figure 2: Comparison of Blood glucose parameters between groups

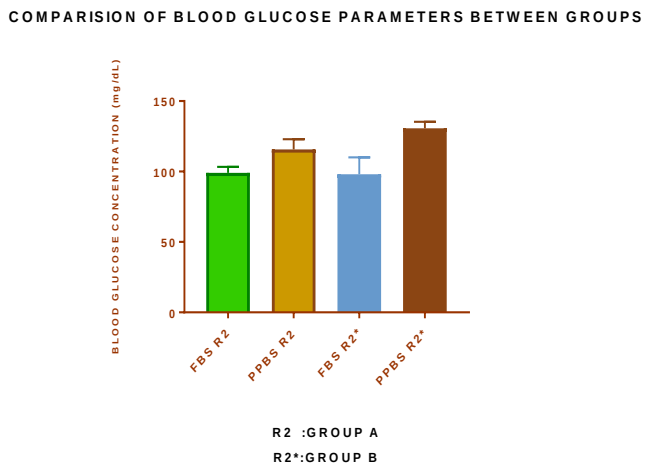


Figure 3: Comparison of Blood glucose parameters between groups

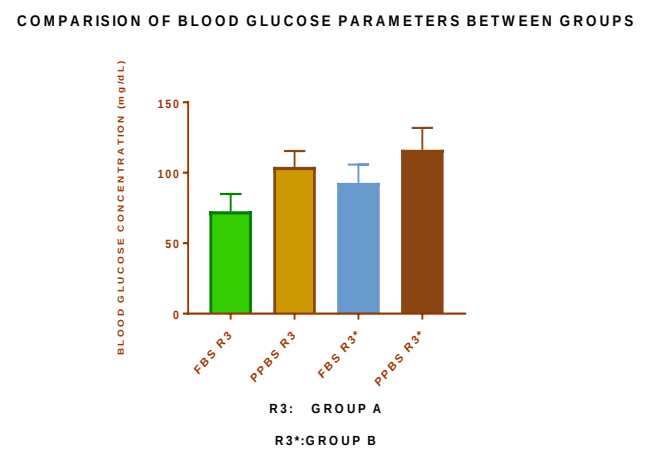


Figure 5: Comparison of HBA1C Reviews within groups

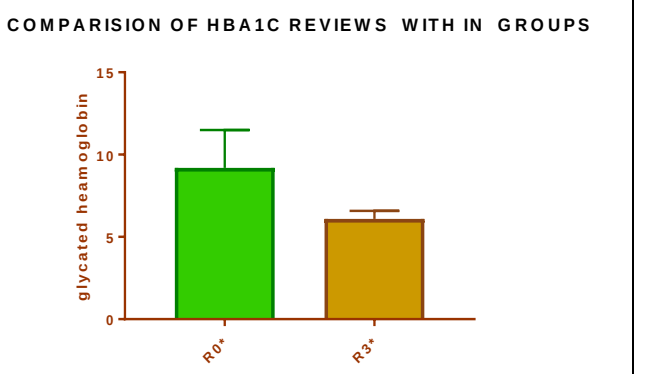
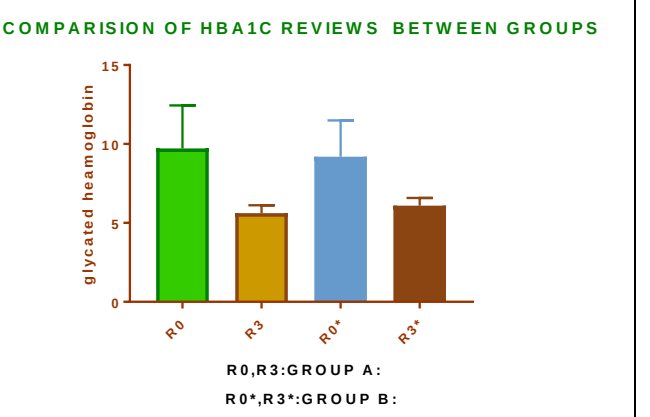


Figure 6: Comparison of HBA1C Reviews between groups



DISCUSSION:

Hyperglycemia caused by abnormalities in insulin production, insulin action, or both characterizes diabetes mellitus. Diabetes' persistent hyperglycemia is linked to long-term impairment, malfunction, and malfunction of a variety of organs, including the eyes, kidneys, nerves, heart, and blood vessels. Despite having numerous evidences about various co morbid conditions causing diabetes mellitus, Relationship between hypertension and diabetes mellitus seems bidirectional. In spite of patients with chronic diabetes mellitus developing hypertension, patients with a strong history of hypertension must be cautious about developing diabetes mellitus. Based on the intensity of the underlying illness condition, the degree of hyperglycemia may alter over time. More than the symptoms of the illness, the intensity of hyperglycemia indicates the complexity of the underlying metabolic processes and its therapy. Hence legible assessment of treatment regimen is must for a patient to yield optimistic efficacy and to have controlled glycemic levels. When treated with metformin plus glimepiride, there has been a better result in the patients when compared with metformin plus voglibose. Although both combinations' mode of action is different, there seems no special credibility to any group in lowering the glucose levels based on the mechanism of action. Irrespective of gender, Metformin plus glimepiride showed better control over the hyperglycemia when compared with the other combination. Initially upto one to two months of therapy, there exist no significant difference between the two groups whereas a noticeable difference can be seen on longer periods of use. on chronic use, patients under metformin plus glimepiride showed better blood glucose levels than the other group of patients on metformin plus voglibose combination. Body Mass Index of group A

patients (Metformin glimepiride) is markedly higher than Group B (Metformin voglibose). Metformin glimepiride combination has lowered blood glucose levels optimistically in over weight and obese patients than the other group. Hence, for treating type II diabetes mellitus, metformin along with glimepiride is better in aspects of efficacy than metformin plus voglibose. However, in terms of drug safety and short-term usage, studies reveal equal efficacy in both the groups. For better reliable and evident data, studies have to be conducted in more sample size focusing geriatrics and obese patients.

CONCLUSION:

Diabetes mellitus has been alarming globally with 1.2million of new patients in south Asian continents. Altered Quality of Life (QOL) is the major consequence of it, crippling the public health. To treat diabetes mellitus type II, proper assessment of patient's glucose profile is key to start treating the diabetes. When compared between metformin plus glimepiride and metformin plus Vegliote, the former combination is better in terms of efficacy. Irrespective of the therapy regimen, proper monitoring is needed to check the patient for not being hypoglycemic especially in cases of sulfonylureas.

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