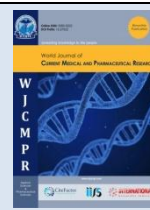




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A PROSPECTIVE OBSERVATIONAL STUDY ON SAFETY AND EFFICACY OF METFORMIN AND ITS COMBINATION USED IN TYPE-II DM PATIENTS

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Article History	Abstract
Received on: 02-11-2023 Revised on: 03-12-2023 Accepted on: 17-12-2023	Diabetes is due to either the pancreas not producing enough insulin, or the cells of the body not responding properly to the insulin produced. This study was carried out with an objective to determine the efficacy of Metformin with other oral hypoglycemic agents, to educate the patients about the disease and use of drugs in diabetes mellitus and to evaluate which class of drugs in oral hypoglycemic agents with Metformin shows more effectiveness. The patients in each group received the medication for 8 weeks duration. A study was carried out about the comparative, efficacy of glimepiride and metformin in type-2 DM which was a meta-analysis of randomized controlled trials. The results of the study were that metformin alone does not show the efficacy than with Metformin+ Tenueligliptin and Metformin + Glimepiride in overall efficacy of controlling FBS and PPBS. Combination of Metformin+ Glimepiride is more effective than Metformin+ Tenueligliptin and Metformin alone. The findings from the study observed the combination of metformin efficacy to some extent. Keywords: Metformin, Glimepiride, Tenueligliptin, diabetes mellitus, randomized controlled trials.
	

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Introduction

Diabetes is due to either the pancreas not producing enough insulin, or the cells of the body not responding properly to the insulin produced [1, 2]. Diabetes mellitus (DM also known as simply diabetes, is a group of metabolic disorders in which there are high blood sugar levels over a prolonged period. This high blood sugar produces the symptoms of frequent urination, increased thirst, and increased hunger [3]. The goals of therapy for diabetes are to alleviate the symptoms related to hyperglycemia (fatigue, polyuria, etc.) and to prevent or reduce the acute and chronic complications of diabetes [4].

The choice of antidiabetic agents is based on efficacy along with drug safety. Metformin has been the most recommended monotherapy for the initial treatment of T2DM [5-7]. However, majority of patients have advocated combined therapy in the long run to maintain glycemic control. The combined regimens

are effective to minimize the dosage of antihyperglycemic agents and thereby their unwanted effects. A combination of glimepiride plus metformin is widely used in Indian clinical settings due to its cost-effectiveness and efficacy in improving glycemic control [8,9]. However, a combination of glimepiride and metformin is frequently associated with side effects such as weight gain and hypoglycemic events [10,11]. Hence, physicians and researchers are in search of a combination having better efficacy and minimal side effects as compared to the present antidiabetic formulation available in the market.

This study was carried out with an objective to determine the efficacy of Metformin with other oral hypoglycemic agents, to educate the patients about the disease and use of drugs in diabetes mellitus and to evaluate which class of drugs in oral hypoglycemic agents with Metformin shows more effectiveness. The study was conducted in the endocrinology department of the Queen's NRI Hospital. A prospective observational study on safety and efficacy of metformin and its combination uses in type-2 diabetes mellitus patients.

Materials and Methods

Study site: The study was conducted in the endocrinology department of the Queen's NRI Hospital.

Study design: A prospective observational study on safety and efficacy of metformin and its combination uses in type-2 diabetes mellitus patients.

Study population: 70-90 populations attending OPD & IPD in Queen's NRI Hospital were recruited into the study with their informed consent.

Patient selection: The selection of patients was carried out with the help of physician who has the knowledge of patient's medical history.

- The subjects selected are the patients who referred to the department of endocrinology at queen's NRI hospital.
- Diagnosis of diabetes mellitus was based on clinical examination by physician and confirmed by lab reports (FBS, PPBS)
- The study procedure was completely explained to the patients and patient consent form was collected from them.
- The study method involves selection of patients based on inclusion and exclusion criteria.

I. Inclusion criteria:

- Patients who are diagnosed with Diabetes recruited from OPD & IPD were included in the study.
- Patients of both genders are considered.
- Patients with co-morbidities are also included in this study.
- Patients with 30-80 years of age are considered.

II. Exclusion criteria:

- Pregnancy women and terminally ill are excluded.
- Alcoholics and smokers are excluded.
- Patients who are not willing to participate in our study.
- Seriously and mentally ill patients.

Study period: The study was conducted in the Queen's NRI Hospital, Visakhapatnam, for a period of six months.

Group-1 patients were given Metformin (500mg) alone and followed up for 8 weeks.

Group-2 patients were given Metformin (500mg) + Teneligliptin (20mg) and followed up for 8 weeks.

Group-3 patients were given Metformin (500mg) + Glimepiride (2mg) and followed up for 8 weeks.

Data collection: A specially designed data collection format was used to collect all the details of information like Age, Gender, IP/OP Number, Date of admission, Date of discharge, Reason for admission, H/o Past medical, H/o Past medication/o Laboratory tests, diagnosis and Treatment. In addition to data collection, we are also going to collect answers for questionnaires regarding adverse effects of oral hypoglycaemic agents.

Methodology

Obtaining the permission of ethics committee at Queen's NRI Hospital. Enlisting patients into the study as per inclusion criteria. Study will be carried out in 90 diabetic patients. Details of information like Patient name, Age, Gender, IP NO., OP NO., Date of admission, Date of discharge, blood glucose values. Prescriptions were evaluated for prevalence of risk factors and complications.

Other indicators measured are Adverse effects caused by each hypoglycemic drug, Prevalence of diabetes, Common adverse effects are observed, Medication adherence of diabetes patients

was assessed by using the questionnaires. All the case records were analysed accordingly and results were tabulated using simple statistical measures.

Results and Discussion

The early combination therapy with glimepiride and metformin is the most commonly used combination, whereas DPP-4 inhibition is the new approach of treatment for T2DM which has the potential to reduce and may even normalize both FPG and PPG concentrations without adverse effects such as weight gain and hypoglycemia. Few studies have reported conflicting results of both teneligliptin and glimepiride added to metformin regarding the efficacy of antidiabetic agents and safety outcomes [12-15].

Among 90 patients participated in the study the age ranged between > 30 to <80 maximum were from adulthood (51-60) age group.

The present study was conducted in the Queen's NRI hospital from August 17th 2022 to Jan 31st 2023. In this study, we compared the efficacy of combination Metformin + Teneligliptin and Metformin + Glimepiride in the treatment of type-2 DM patients. 90 patients of Type-2 DM were included in the study and were divided into 3 groups of medication received patients.

Table 1. Age and Gender Distribution of Metformin + Teneligliptin given patients

Frequency	Male	Female
31-40	2	1
41-50	1	4
51-60	5	4
61-70	3	2
71-80	2	2

Table 2. Age and Gender distribution of Metformin + Glimepiride given patients

Frequency	Male	Female
31-40	2	2
41-50	3	3
51-60	6	9
61-70	11	3
71-80	5	4

Table 3. The comparison of Fasting Blood Glucose (FBS) level in different study groups

Groups	Baseline (mg/dL) Mean $\pm$ SEM	After 4 Weeks (mg/dL) Mean $\pm$ SEM	After 8 Weeks (mg/dL) Mean $\pm$ SEM
Group 1 (n=16)	125.6 $\pm$ 3.522	117 $\pm$ 3.593	109.6 $\pm$ 3.276
Group 2 (n=26)	140.9 $\pm$ 2.711	124.1 $\pm$ 2.113	108.3 $\pm$ 1.847

Table 4. The comparison of Post- prandial Blood Glucose (PPBS) level in different study groups

Groups	Baseline (mg/dL) Mean±SEM	After 4 Weeks (mg/dL) Mean± SEM	After 8 Weeks (mg/dL) Mean±SEM
Group-1 (n=16)	222.8± 12.79	213.0±12.09	195.8±11.25
Group- 2 (n=26)	270.7±13.40	255.6±13.51	240.9±13.80
Group-3 (n=48)	313.8±.483	272.1±9.171	223.6±8.244

Table 5. The comparison of FBS changes caused by different study drugs

Group s	Changes (mg/dL) Mean±SEM	P- value	Significanc e	Summar y
Group- 1 0-4 weeks	80.00±5.031	0.1223	No	NS
Group- 1 0-8 weeks	16.00±4.810	0.0023	Yes	**
Group- 2 0-4 weeks	6.962±6.357	0.2787	No	NS
Group- 2 0-8 weeks	16.15±6.091	0.0107	Yes	*
Group- 3 0-4 weeks	16.75±3.437	<0.001	Yes	****
Group- 3 0-8 weeks	32.56±3.280	<0.0001	Yes	****

Table 6. The comparison of PPBS changes caused by different study drugs

Groups	Changes (mg/dL) Mean ± SEM	P- Value	Significance	Summary
Group- 1 0-4 weeks	9.813±17.60	0.5812	No	NS
Group- 1 0- 8 weeks	27.00±17.03	0.1234	No	NS
Group- 2 0-4 weeks	15.08±19.03	0.4321	No	NS
Group- 2 0-8 weeks	29.81±19.24	0.1276	No	NS
Group- 3 0-4 weeks	41.67±12.49	0.0012	Yes	**
Group- 3 0-8 weeks	90.23±11.83	<0.0001	Yes	****

Table 7. The Multiple comparison of FBS changes in the study groups by 2- way ANOVA

Multiple comparisons of druggroups	Summary	P-Value
Group 1(0-4) vs (0-8)	NS	0.9489
Group 2(0-4) vs(0-8)	NS	0.784
Group 3(0-4) vs (0-8)	*	0.0321
(0-4 WEEKS) Group-1 vs Group-2	NS	>0.9999
Group-1 vs Group-3	NS	0.8413
Group-2 vs Group-3	NS	0.6143
(0-8 WEEKS) Group-1 vs Group-2	NS	>0.9999
Group-1 vs Group-3	NS	0.2199
Group-2 vs Group-3	NS	0.0921

Table 8. The Multiple comparison of PPBS changes in the study groups by 2- way ANOVA

Multiple Comparison of drug groups	Significance	P- value
Group 1(0-4) vs (0-8)	NS	0.9931
Group 2(0-4) vs(0-8)	NS	0.9896
Group 3(0-4) vs (0-8)	NS	0.0680
(0-4 WEEKS) Group-1 vs Group-2	NS	>0.9999
Group-1 vs Group-3	NS	0.7941
Group-2 vs Group-3	NS	0.8013
(0-8 WEEKS) Group-1 vs Group-2	NS	>0.9999
Group-1 vs Group-3	NS	0.1167
Group-2 vs Group-3	*	0.0496

However, different dosages are suggested for their respective groups. The patients in each group received the medication for 8 weeks duration. A study was carried out by Zhu *et al.* in May 2013 about the comparative, efficacy of glimepiride and metformin in type-2 DM which was a meta-analysis of randomized controlled trials. The results of the study were that metformin alone does not show the efficacy than with Metformin+ Teneligliptin and Metformin + Glimepiride in overall efficacy of controlling FBS and PPBS. Combination of Metformin+ Glimepiride is more effective than Metformin+ Teneligliptin and Metformin alone.

Conclusion

In the present study, the number of people affected with diabetes in males was more than females. It was also found that combination therapy of Metformin (500mg) + Glimepiride (2mg) for Type-II diabetes mellitus is better for its

effectiveness. Numerically visible and statistically non-significant and improved the glycemic levels of the Type-2 diabetes mellitus patients with better safety and tolerability as compared to metformin and metformin + teneligliptin.

Although some patients glycemic levels were controlled by providing the patient education about the medication adherence, life-style modifications (exercise, diet) thereby patient had an understanding of their disease and role of medication in treatment, about medication adherence and good health outcomes. Hence, patients should have information on prescribed medication or combinations of medications by this type of studies might help patients to cope with unpleasant reactions and enhance adherence. The findings from the study observed the combination of metformin efficacy to some extent.

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Informed Consent and Ethical statement

Not Declared

Conflicts of interest

The authors declare no conflicts of interest.

Author Contribution

M Ganesh Kumar - Supervision of work
S Jahnvi - Design & carrying out study
G Reena Priyadarshini - Literature collection
K Swathi Priya - Evaluation & supervision
D Niveditha - Manuscript preparation

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