

Original Research Article

A Comparative Assessment of Safety, Efficacy And Cost Effectiveness Of Glipizide-Metformin And Glimepiride-Metformin Combination Therapy In Type-2 Diabetes Mellitus

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ABSTRACT

Diabetes mellitus (DM) is defined as a chronic and metabolic disorder. It was approximated about 77 million Indians suffer from DM and it will be increased to 134 million by 2045. Diabetic mellitus can be treated by close control of glucose level which is main aim and target in management of this condition. Management of DM can be done by non-pharmacological and pharmacological approaches. The aim of this study is to compare the safety, efficacy and cost effectiveness of Glipizide-Metformin and Glimepiride-Metformin combination therapy in type 2 diabetes mellitus. In current research by use of prospective method in the cardiology department of Kongunad Multi-speciality Hospital, Coimbatore, in a period of six months from February 2021 to August 2021 we did research according to our aim and used ANOVA statistical test whenever it needed. Our study results demonstrate, the improvement in the addition of glimepiride 2mg to metformin 500 mg has modest beneficial then glipizide 5 mg in terms of efficacy and cost. In terms of safety, both drugs are having similar safety profiles. Current research also assessed the medication safety by using the Naranjo scale.

Keywords: Diabetes mellitus, anti-diabetic medication, hyperglycemia, medication safety.

INTRODUCTION

Diabetes mellitus (DM) is defined as a chronic and metabolic disorder. It was approximated about 77 million Indians suffer from DM and it will be increased to 134 million by 2045. [1] Base on some reports, Tamil Nadu and Kerala had highest prevalence of DM in India. [2] It indicates several metabolic disorders which all are common in increase level of blood sugar or hyperglycaemia. Mainly it is cause by deficiency of insulin (secretion or synthesis) or reducing in sensitivity of tissues against insulin. Type 1 diabetes mellitus (T1DM), Type 2 diabetes mellitus (T2DM), Gestational DM, and DM secondary to other diseases are different type of this metabolic condition in which type 2 DM is most common. [3] All type of DM if not controlled lead to macro vascular and micro vascular complications. [4]

Diabetic mellitus can be treated by close control of glucose level which is main aim and target in management of this condition. Management of DM can be done by non-pharmacological and pharmacological approaches. [5] Metformin is the most popular and first drug for pharmacological intervention for managing T2DM. [6] Metformin increases sugar tolerance in patients. It acts by reducing production of glucose in liver, absorption of sugar in intestine and increasing sensitivity to

insulin. [7] Metformin also works on glycogen synthetase enzyme and activates synthesis of glycogen. It improves the capacity of glucose transporters (GLUT). [8]

Commonly if goal of therapy not covered by metformin alone, adding second agent which can be and preferred to be Sulphonylurea (SU) as add-on therapy will be considered to achieve therapeutic goal. [6]

Sulphonylureas have two generations. Tolbutamide as first generation and glibenclamide, glipizide, glimepiride (newest drug in class) as second generation can be listed. [9] This class can reduce HbA1c by 1.25%. [10]

Sulphonylureas act by blocking the ATP-sensitive potassium channels (K) on the beta cells of pancreas. It leads to depolarization of cells and entering of Ca to cells. Increase calcium level results in insulin secretion. [11] They also reduce metabolism of insulin in liver, glucagon secretion and increase sensitivity of tissue to insulin. [12] These are contraindicated in elder patients with renal or hepatic failure. [13] SU can be given with any other DM medications except meglitinides.[14]

The aim of this study is to compare the safety, efficacy and cost effectiveness of glipizide-metformin and glimepiride-getformin combination therapy in type 2 diabetes mellitus.

METHOD:

Current research was a prospective study conducted in the cardiology department of Kongunad Multi-speciality Hospital, Coimbatore, in a period of six months from February 2021 to August 2021. Study population comprised of a total 500 patient's medical records and 200 patient records from 2020-2021 were sampled based on the inclusion and exclusion criteria. Patient with type 2 diabetes mellitus with age above 18 years old were included in research. Patients with current insulin therapy and hepatic dysfunction, pregnant and breast feeding patients and those who were taking other oral hypoglycaemic drugs were excluded from sampling.

A sample of 200 patients was divided equally into two treatment groups. One group was given Metformin500mg/ Glimepiride2mg and other one, given Metformin 500mg/ Glipizide5mg. During 6 months of study period blood sugar level of all collected. The entire collected and documented patient's data was analysed and the efficacy was assessed by using blood sugar level data.

We noted the RBS, FBS and PBS value of all the 200 patients of A group during their first visit to the hospital. Then blood glucose level (RBS, FBS and PBS) of Group (A) patients again monitored after 30, 60 and 90 days. The percentage reduction in Glucose level (RBS, FBS and PBS) in Group (A) patients individually recorded and entered in MS Excel sheets and statistical analysis was done by using ANOVA test.

$$\text{Percentage Reduction in Glucose level of Group (A) Patients} = \left(\frac{G_1 - G_2}{G_1} \right)$$

- G1= Glucose level (RBS, FBS and FBS) noted during initial visit to the hospital.

- G2= Glucose level (RBS, FBS and FBS) noted after 90 days of initial hospital visit.

Same procedure followed for group B. Only difference was about medication given. As mentioned before, they were given with Metformin/ Glipizide. Other steps were same. The mean percentage reduction of glucose level (RBS, FBS and PBS) obtained for Group (A) and Group (B) was compared. The group which showed more percentage reduction in RBS, FBS and PBS level was determined and the drug given to that group is supposed to be more efficient than the other.

COST AND SAFETY ANALYSIS

The cost required for getting one percentage reduction in Glucose level (RBS, FBS and PBS) was calculated for Group (A) and Group (B) respectively.

$$\text{Cost for getting 1\% reduction in Glucose level} = \frac{\text{Total cost of therapy (90 days)}}{\text{percentage reduction in Glucose level}}$$

The group with lower value is said to be more cost effective than the other.

Safety profile also was assessed based on adverse drug reactions produced and causality was estimated by using Naranjo's scale

RESULTS AND FINDINGS

In the present study, a total of 200 medical records from the General Medicine ward were reviewed and 200 DM cases were included in the study. On comparing both the group of subjects given with different drugs, Group A which was provided with Glimipride with Metformin involved 51 male and 49 female subjects and Group B which was provided with Glipizide- Metformin includes 46 male and 54 female subjects.

Most of the patients in Group A belonged to the age group of 51-60 years (38%) followed by age group of 41-50 years (28%) and (22%) of subjects in the age group of 61-70 years and (12%) of subjects in the age group of 30-40 years.

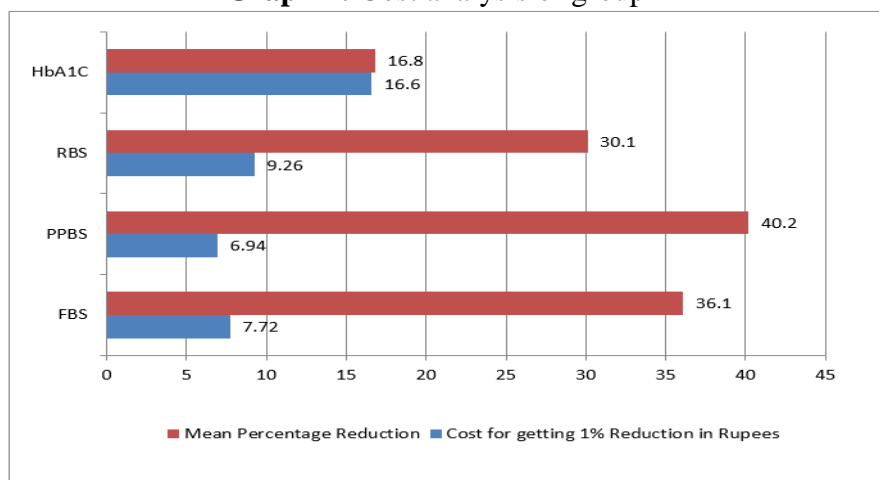
Similarly, in the age wise distribution of Group (B), 39% of the subjects belonged to the age group of 41-50 years, 26% to 41-50 years, 24% to the age group of 61-70 years and 11% belonged to 30-40 years of age.

The mean percentage of reduction achieved in Group (A) from first follow up to final follow up (90 days after initial hospital visit) was 36.1 % (FBS), 40.2 % (PBS), 30.1 % (RBS), 16.8 % (HbA1c). The mean percentage of reduction achieved in Group (B) from first follow up to final follow up (90 days after initial hospital visit) was 28.2 % (FBS), 32.4 % (PBS), 26.6 % (RBS), 15.2% (HbA1c). Statistical calculations were also conducted by using ANOVA. A p-value <0.05 was considered significant.

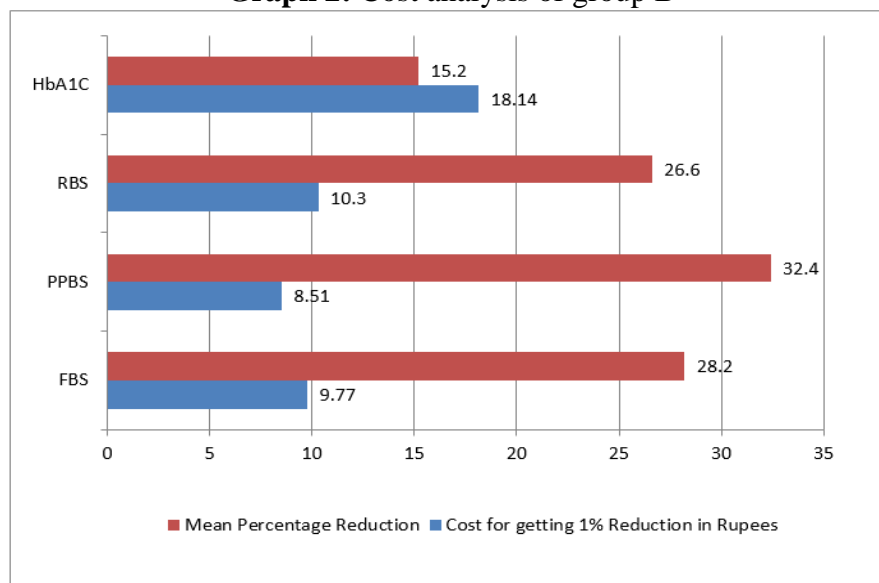
The total cost of Glimipiride therapy for 90 days was 279 INR. We used Isryl-M tablets containing 2mg Glimepiride and 500mg Metformin for our study. The price of 1 pack of Isryl-M containing 10 tablet units was 15.50 INR.

The total cost of Glipizidetherapy was 275.76 INR. We used Glynase-MF tablets containing 5mg Glipizide and 500mg Metformin for our study. The price of 1 pack of Glynase-MF containing 10 tablets was 15.32 INR.

The cost for getting 1% reduction in FBS for Group (A) is 14.38 INR, 4.63 rupees lesser than Group (B). The cost for getting 1% reduction in PBS for Group (A) is 9.238 INR, 2.2 rupees lesser than Group (B). The cost for getting 1% reduction in RBS for Group (A) is 10.03 INR, 5.63 rupees lesser than Group (B).

Graph 1: Cost analysis of group A

In our study drug safety was assessed by assessing the ADRs which were produced by the antidiabetic medication during the study period and the causality assessment had carried by the Naranjo's causality assessment scale. We did not observe any significant difference in ADR occurrence in two groups.

Graph 2: Cost analysis of group B

DISCUSSION

In our study mean HbA1c reduction in group A and B was 16.8% and 15.2% respectively. In study conducted by Chatterjee [15], 41% of individuals in the glimepiride group and 52% of those in the glipizide group recorded about 7% HbA1c below of our findings after 3 months of therapy. Result of Chatterjee study was somehow similar to Gonzalez in which 44% patients who reported HbA1c <7% after one year of treatment. [16]

The mean percentage reduction of FBS in group A of our research was about 36.1% which is much higher than reduction in group A of Chatterjee study by 28.1%. In group B we recorded 28.2% reduction in FBS after therapy which is comparable and fewer than 36.6% reduction in group B of Chatterjee study.

The average percentage reduction of PPBS in group A of our research was about 40.2% which is slightly higher than reduction in group A of Chatterjee study by 34.67%. In group B we recorded

32.4% reduction in FBS after therapy which is comparable and less than 38.53% reduction in group B of Chatterjee study.

In our research we observed 30.1% and 26.6% reduction in RBS in group A and B respectively. In Kandavalli study it reported 25.13% in group A and 17.6% in group B reduction in random blood sugar. [17]

Safety

As far as adverse reaction is concerned, there is no significant difference in rate between groups A, B. This result was supported by Chatterjee [15], Charpentier [18] and Kandavalli [17] studies.

Cost

In current study, it was found treatment which applied in group A is more cost effective. In another study, cost of reducing 1% in FBS after taking metformin and glimepiride was found to be 7.45 ± 3.95 which is about half of cost of our trial. [19]

CONCLUSION

Our study results demonstrate, the improvement in the addition of Glimipride 2mg to metformin 500 mg has modest beneficial than Glipizide 5 mg in terms of efficacy and cost. In terms of safety, both drugs are having similar safety profiles. Current research also assessed the medication safety by using the Naranjo scale.

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