Research Article

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COMPARISION OF POTENTIALITY OF ORAL HYPO GLYCEMIC COMBINATION THERAPY OVER CONVENTIONAL ONES

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ABSTRACT

Diabetes mellitus type 2 is a metabolic disorder that is characterized by high blood glucose in context of insulin resistance and relative deficiency. Though a number of new drugs (Oral Hypo glycemic agents) have become available for treating Type - 2 diabetes, sulphonyl ureas and biguanides still reign the scenario of therapy. While either glibenclamide or glimepiride is the largely used sulphonyl urea derivative, metformin is the drug of choice from the biguanide group. Therefore a study on "COMPARISION OF POTENTIALITY OF ORAL HYPO GLYCEMIC COMBINATION THERAPY OVER CONVENTIONAL ONES" was carried out including 100 patients of type 2 diabetes mellitus receiving two varied types of combination therapy - one with glimipride plus metformin and another with glibenclamide plus metformin. The aim of the study was to compare efficacy of these two combinations in the type 2 diabetic patients by monitoring Fasting Plasma Glucose (FPG) and Glycosylated Haemoglobin (HbA1c) for achieving good glycemic control and also to find out the effect of these two varied combination therapy on Lipid Profile & Body Mass Index (BMI). Male patients (53%) were observed to be more as compared to female patients (47%). Patients between the age group (40-45) were found more. People taking non-vegetarian (30%) was found more as compared to those taking vegetarian food (27%). Those patients having family history of diabetes (60%) were found more in the study group as compared to non diabetic family history (40%). Diabetic control was determined by studying the fasting plasma glucose (FPG) content and the long term control by determining the glycosylated haemoglobin (HbA1c) level. At the end of study glimipride combination therapy patients with 140mg/dl (FPG) were 56% have significant effective differences as compared to glibenclamide combination therapy showing 44% and patients with ≤8% of HbA1c levels reductions observed. Whole group of this study reduction in total and LDL cholesterol occurred significantly. But the reductions in the variables were relatively small in obese patients having higher BMI at baseline. Finally we concluded that glimipride plus metformin combination can be considered as best combination in patients with type II diabetes as compared to glibenclamide plus metformin.

Key words: Glycosylated Hemoglobin, Combination Therapy, Oral Hypo Glycemic Agents, Fasting Plasma Glucose, Metformin, Glimipride, Glibenclamide, Glycemic Control

INTRODUCTION

Diabetes mellitus is a group of metabolic disorder characterized by hyperglycemia and abnormalities in carbohydrate, fat, protein metabolism, its results from defects in insulin secretions and insulin sensitivity both. Diabetes mellitus is classified in to four types: Type 1 Insulin dependent diabetes mellitus, Type II Non insulin dependent diabetes mellitus, Type III Gestational diabetes mellitus and Type IV Pre-diabetes. The high blood sugar levels produces the classical symptoms of Polyuria (frequent urination), Polydipsia (increased thirst) and Polyphagia (increased hunger) [1].

Type 2 diabetes is also termed as adult onset Diabetes, Obesity related diabetes, Non insulin dependent diabetes mellitus (NIDDM). Pathological changes in Type 2 diabetes mellitus is peripheral insulin resistance, increased hepatic glucose production, impaired pancreatic beta cell function leading to relative deficiency[2]. Type 2 diabetes is usually first treated with medical nutrition therapy, physical activity. Although some patient's early Type 2 diabetes may not need to pharmacotherapy for a while the progressive nature of disease ultimately results in the requirement of drug therapy.

The UKPDS (United Kingdom prospective diabetic study) confirmed that most of patients will not be able to maintain glycemic control with a single agent. According to Indian Council of Medical Research (ICMR) and World Health Organization (WHO), stated that the treatment for Type 2 diabetes followed by oral hypo glycemic agents[3] can be used alone or combination with other OHAs or Insulin. Combination therapy[4] with sulfonylurea and

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metformin is potentially effective in maintaining glycemic control. Sulfonylurea like glibenclamide and glimipride are approved by USFDA in combination with metformin. Untreated hyperglycemia leads to complications. Diabetes is the disorder, which can affect all organs in the body. The organs most commonly affected are eyes, kidneys, nerves, heart and blood vessels.

Sulfonylurea and metformin have different mechanism of action. Sulfonylurea mainly decrease glucose levels by stimulating insulin release from pancreatic cell[5] where a metformin reduces blood glucose levels predominantly by improving hepatic and peripheral tissue sensitivity to insulin. Therefore combining on insulin sensitizing agent will augment the efficacy of current oral hypo glycemic agents. This is the rationale for the development and marketing of sulfonylurea plus metformin combination tablets and anti diabetic potentiality of two most commonly used sulfonylurea. Namely glimipride and glibenclamide in combination with metformin has been taken up for determination in the study[6, 7].

India has dubious distinction of having the largest number of people with diabetes. More than 33 million people know they have diabetes and number is climbing steeply. ICMR and national diabetic study concludes that 62.4 million lives with diabetes in India, 77.2 million people with pre-diabetes.

AIM AND OBJECTIVE OF STUDY:

The aim of the study is to perceive the comparison of potentiality of an oral hypo glycemic combination therapy over conventional ones. The combinations therapy using are Glimipride - metformin (group 1) and glibenclamide - metformin (group 2).

- To verify the good glycemic control by measuring two important parameters fasting plasma glucose (FPG) & glycosylated hemoglobin (HbA1c).
- To find out the effect of these two varied combination therapy on lipid profile & body mass index.

MATERIALS AND METHODS:

Site of the study:

The study site is carried out at Shantiniketan Multi Specialty Hospital & Diabetic Care Center; Located at Madanapalli, Andhra Pradesh. The study was carried out for the period of 4 months.

Study population:

Based on inclusion & exclusion criteria 100 patients were selected for study.

Men and women with uncontrolled type 2 diabetes, obese/overweight were eligible to participate. Patents with FPG level >140 mg/dl and Glycosylated hemoglobin (HbA1c) ≥ 8% from inpatient & outpatient departments of the hospital. Each patient was interviewed, for their past medication history for diabetes during the previous 2 months or > 4 months of participation.

Inclusion Criteria

1. The study is conducted in type-2 diabetes mellitus patient only.
2. Obese and non-obese patients are included in this patients
3. Male and female patients between the ages 25-70 years.
4. Patient data is collecting from the inpatient and outpatients.

Exclusion Criteria

- ✓ Includes a clinically relevant medical or psychological condition
- ✓ History of drug or alcohol abuse,
- ✓ Pregnancy
- ✓ Breast feeding
- ✓ Hepatic insufficiency
- ✓ Renal insufficiency
- ✓ History of adverse reaction to sulfonylurea or metformin.

Study procedure:

Patients were randomly assigned to treatment with combination treatment of Metformin + Glibenclamide (Maximum up to 1500 mg/d = 15 mg/d) or metformin + Glimepiride (Maximum up to 1500 mg/d) & 4mg/d) for 4 months. Doses were titrated to obtain ≤ 7 HbA1c and FBS ≤140 mg/dl.

Data Collection

A specially designed data entry form is used for data collection. The Data is collected from inpatients and out patients. The main

source of data collection is patient case notes, prescriptions and laboratory reports.

Design of Data Entry Format (Proforma)

A separate data entry format (PROFORMA**)** for incorporating inpatients & outpatients details was designed. The proforma is divided in to four types. **Proforma I:** Patients Detail - Name, Address, Age, Sex, Height, Weight, IP number, Body Mass Index, DOA, DOD, Review on, Social status. **Proforma II:** Laboratory investigation - includes blood test, lipid profile, & other investigation if any**. Proforma III:** Other details present complaints, past history, course in hospital. **Proforma IV:** Medication details.

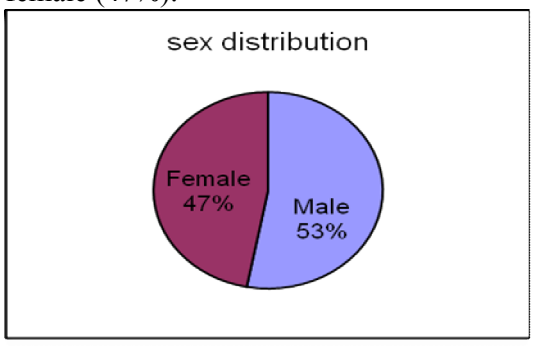
The fasting blood samples reports were collected. The initial data samples were taken as base value and parameters were taken as monthly basis. These lab investigation data obtained after each review is transferred to previously designed proforma.

Analysis of data: The collected data were analyzed for any marked change in fasting blood sugar (FBS) Glycosylated hemoglobin (HbA1c) before in between and at the end of study period and find out effect of these two varied combination therapy on lipid profile & body mass index. All the data have been subjected to T-test and Anova analysis for significance and mean changes.

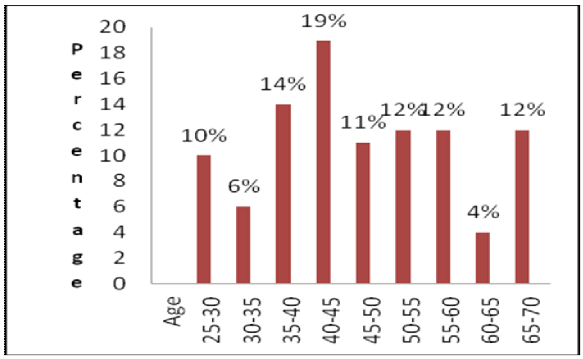
RESULTS AND DISCUSSION

This study included 100 patients receiving two varied oral hypo glycemic combination therapies for 4 months.

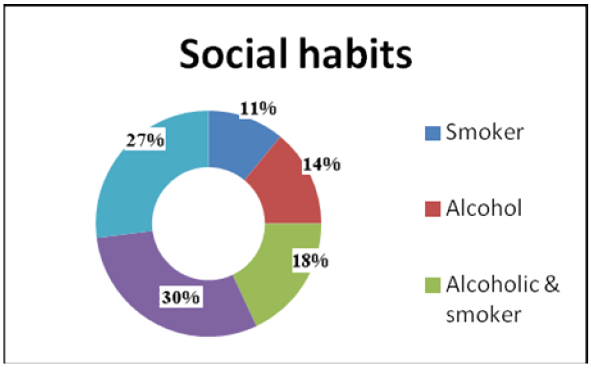
This study include the sex distribution of various patients are categorized followed by 53(53%) patients were males and 47 (47%) patients were females. In this study percentage frequency of male (53%) was higher compared to female (47%).



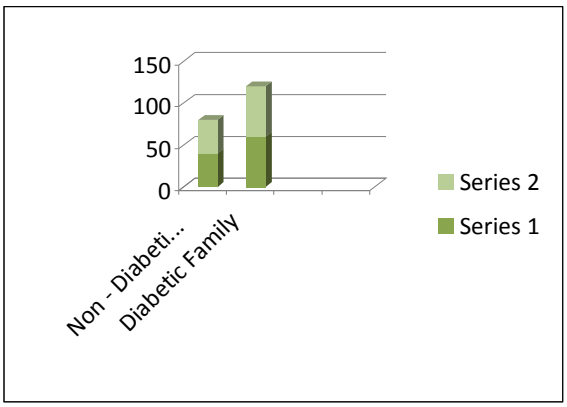
All patients were categorized in to different age groups,10 (10%) patients are found in the age groups between (25-30) years followed by 6 (6%) patients in the age group of (30-35) years,14 (14%) patients in the age group of (35-40) years 19(19%) patients in the age group of (40-45)years, 11 (11%) patients in the age group of (45-50) years,12 (12%) patients in the age group of (50-55)years,12 (12%) patients in the age group of (55-60) years ,4(4%) patients in the age group of (60-65) years, 12 (12%) patients in the age group of (65-70) years. In this study the patients containing age group (40-45) were more prone to disease.



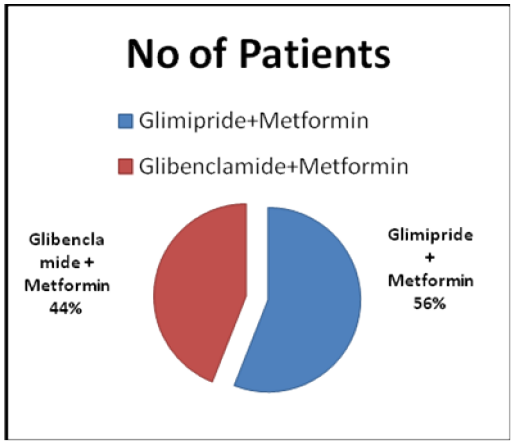
All patients were categorized depending up on their social habits.11 (11%) patients are smokers, 14 (14%) patients are alcoholics,18 (18%) patients are alcoholics & smokers, 30 (30%) patients are non-vegetarian, 27 (27%) patients are vegetarians. In this study non-vegetarians are more prone to diabetes.



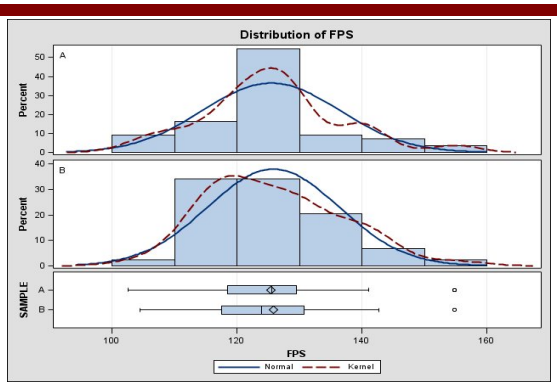
Based on the family history 100 patients are categorized in to two types followed by 40 (40%) patients were found in non-diabetic family, 60 (60%) patients were found in diabetic family.

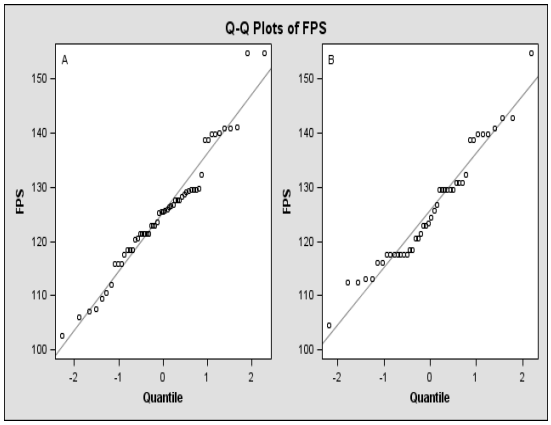


During the study n = 56 (56%) patients were receiving glimipride plus metformin combination therapy (Group A) where as rest of the patients n = 44 (44%) were receiving glibenclamide plus metformin combination therapy (Group B). In group A; mean FBS decreased during the 6 months therapy significantly by 37.164 mg\dl. In group B; mean FBS is decreased by 30.164 mg/dl comparison of mean changes.

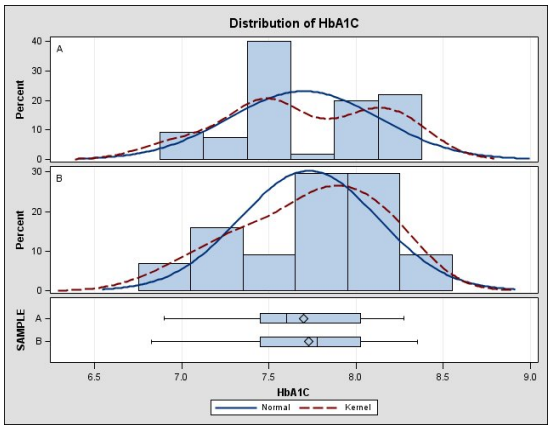


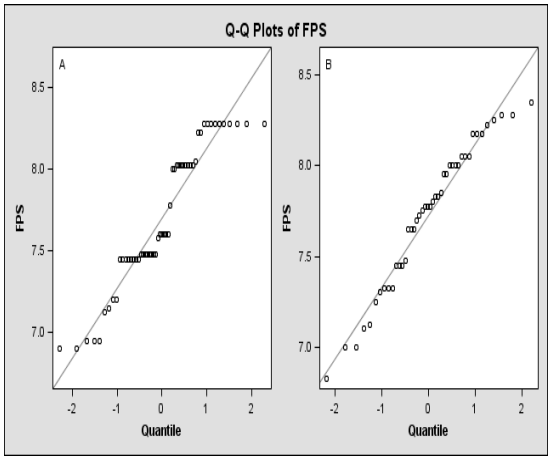
A comparision of two drug combinations (glimipride plus metformin) and (glibenclamide plus metformin) studied using T-test procedure (95% confidence). The study revealed that differences in distribution levels in FBS during the treatment of glimipride plus mettfrmin, glibenclamide plus metformin. A significant effectiveness will be observed in mean levels of FBS during the study. Q-Q plots are represents the mean changes from baseline toword the combination therapy.6e



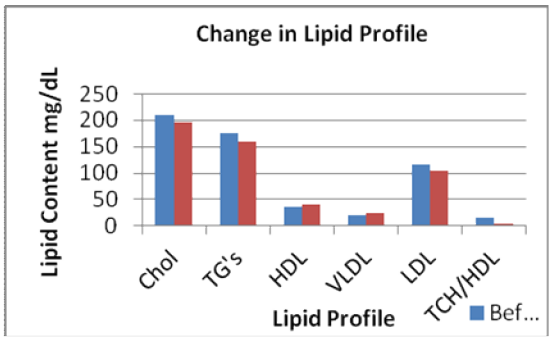


A comparision of two drug combinations (glimipride plus metformin) and (glibenclamide plus metformin) studied using T-test procedure (95% confidence). The study revealed that differences in distribution levels of HbA1c during the treatment of glimipride plus metformin, glibenclamide plus metformin. A significant effectiveness will be observed in mean levels of HbA1c during the study. Q-Q plots are represents the mean changes from baseline toword the combination therapy.

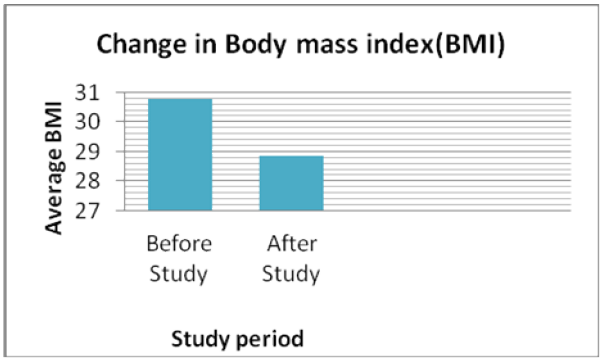




The lipid profile in both groups of patients did not show much change in reduction in cholesterol, TGS, LDL, VLDL, and the TCH/HDL ratio was not significant. As well the increase in HDL value also was not marked.



In the glibenclamide combination therapy means BMI decreased minimally during treatment. In glimipride combination therapy group mean BMI decreased minimally during the treatment.



CONCLUSION:

At the end of study it is concluded that the both combinations such as glimipride plus metformin and glibenclamide plus metformin redused HbA1c and FBS significantly. But the glimipride plus metformin combination provided superior control of glycosinated hemoglobin and fasting blood sugar levels in Type 2 diabetic patients compared to glibenclamide plus metformin in 4 months of study. In both group of study very insignificant reduction occurred in the total and LDL cholesterol levels. The obese patients having higher BMI at base line showed only minimal reduction in BMI at the end of study period.

The findings of the study suggested that glimipride plus metformin therapy is beneficial adjuvant to diet, exercise in management of type 2 diabetes mellitus.

REFERENCES:

1. Joseph T. Dipiro, Robert L. Talbert, Gary C. Yee, 7th edition
2. Henning beck – Nielsen J Pharmacotherapy a Pathophysiologic approach pathophysiology of Non – insulin – dependent diabetes mellitus (NIDDM). Diabetes Research and Clinical Practice 28 suppl. (1995) s13 - s25.
3. Coron Melikian, RN, Adherence to oral anti diabetic therapy in a managed care organization: A comparison of mono therapy, combination therapy, and fixed - dose combination therapy. Clinical therapeutics /vol.24, NO.3, 2002.
4. Tosi, F, Muggeo , M., Burn , E., Spiazzi G., Zonalin, Gori, M., Coppini, A. Combination treatment with metformin and glibenclamide versus single – drug therapy in type 2 diabetes mellitus: a randamised double – blind ,comparative study . Metabolisam; 52(7); 862- 7, July 2003.
5. Kabadi, M.U. and kabadi, U.M. Effects of glimepride on insulin secretion and sensitivity in patients with recently diagnosed type 2 diabetes mellitus. Clinical therapeutics; 26(1): 63-9, Jan 2004
6. Martindale ,j, The complete drug reference 32 edition pharmaceutical press :1999 Page no-313-33
7. Herfindal,agourley Dick R, Loyd Hart, clinical pharmacy and therapeutics 5th addition, Williams and Wilkins; 1992 Page no- 20-23
8. Hamman A Sulfonyl urea plus metformin in over weight individuals with type 2 diabetus inadequately controlled on metformin alone. Exp Clin Endocranial diabetes. 2008 Jan; 116(1); 6-13.
9. Gurrero and Romero J F; efficacy of glimipride metformin combination verses glibenclamide/metformin in patients with un-

controlled type 2 diabetes. Diabetes complications, 2008 Oct 10 related articles.
10. Chipkin,S.R. How to select and combine oral agents for patients with type diabetes mellitus. Am J Med; 118(suppl 5A); 4S-13S; 20 May 2005.
11. D. Dutt G. Roy, Risk Factor Assessment for Type II Diabetes Mellitus in a Tertiary Hospital in Kolkata. Indian Journal of Community Medicine vol.29, No.4 (2004-10-2004-12)
12. Metabolic variations with oral anti diabetic drugs in patients with type 2 diabetes: Comparison between glimepride and metformin Diabetes. Nutr. Metab. 2004 Jun : 143-50
13. Rendell, M .The role of Sulfonyl ureas in the management of type 2 diabetes mellitus. Journal of drugs; 64(12):1338-58, 2004.
14. Gao, Y Efficacy and safety of patients of Asian descent with type 2 diabetes inadequate controlled with metformin or metformin and a sulphonylurea. Diabetes Research and Clinical Practice, 83 (1). pp. 69-76. ISSN 01688227