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Original Article

Drug utilization pattern in patients suffering from type 2 diabetes mellitus visiting medicine department of MMIMSR and the most commonly used anti diabetic drugs

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ABSTRACT

Diabetes mellitus is a condition characterized by chronic hyperglycemia with disturbances of carbohydrate, protein and fat metabolism. This prospective observational study determined the utilization pattern of anti-diabetic drugs and the most commonly used anti-diabetic drug/drugs (with or without insulin) on patients suffering from type 2 diabetes mellitus (newly diagnosed as well as on treatment) attending the Medicine department of MMIMSR, Mullana, Ambala. A total number of 200 patients suffering from type 2 diabetes completed this study of 3 months duration. Utilization pattern of various anti diabetic drugs was determined on the basis of their ability to achieve glycemic targets, measured through the investigations like the fasting blood glucose, postprandial blood glucose (assessed on baseline, 6 weeks, 12 weeks) and HbA1c (assessed on baseline and 12 weeks). The primary end point was mean change in HbA1c from baseline to week 12. Safety was assessed by incidence of hypoglycemia and other adverse events. There was significant reduction in HbA1c, FBS, PPBS levels from baseline to 12 weeks and the p value obtained was highly significant. In conclusion, this study revealed that the combination of metformin and insulin was the most commonly prescribed drugs in type 2 diabetes patients.

Key Words: Type 2 diabetes mellitus, drug utilization, anti-diabetic drugs.

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INTRODUCTION

Diabetes mellitus [1] can be defined as a condition which has multiple etiologies. It is characterized by chronic hyperglycemia with disturbances of three metabolisms i.e. carbohydrate, protein and fat metabolism which occur as a result of various defects in the insulin action, insulin secretion or both. This condition can result in extensive dysfunction, failure and damage of various organs.

Type 2 diabetes mellitus: It ranges from the predominant resistance of insulin with the relative deficiency of insulin to predominant secretory defect with the resistance of insulin

Various approaches for the diagnosis of type 2 diabetes mellitus: The diagnosis of the diabetes mellitus at initial stage is essential to prevent the complications arising from it. The commonly used tests for diagnosis of diabetes mellitus are FBS, PPBS, HbA1c. Latest clinical studies have shown that acute fluctuations in glucose levels along with chronic hyperglycemia may activate the oxidative stress mechanisms in the diabetes mellitus type 2, signifying the value of the therapeutic interventions during the sustained and acute hyperglycemic episodes. [2]

Treatment approach for type 2 diabetes mellitus

Lifestyle modification: Dietary modification, Physical activity/exercise: Diet regulation is foundation of diabetes mellitus treatment, especially in type 2 diabetes mellitus. Dietary control is hard to maintain for prolonged period of time, but dietary control is necessary. [3] The effects of exercise, physical activity on long-term are mainly advantageous for diabetes type 2 patients. On usual basis, aerobic exercise can decrease the fat mass from viscera, can decrease the body weight without lowering the lean body mass, it corrects the deranged glucose levels, insulin sensitivity, blood pressure control, lipid profile as well as decreases the risks for various cardiovascular complications. [4]

Pharmacological therapy:

Glucosidase inhibitors

The alpha- glucosidase inhibitors (AGIs) like voglibose inhibits the hydrolysis of disaccharide in the mucosa of intestines. It decreases the disaccharide hydrolysis to monosaccharides. It decreases the absorption of carbohydrates, thus decreases glucose level in patients of type 2 diabetes. Treatment with voglibose prevents gain in body weight. [5] Alpha- glucosidase inhibitors are largely used in treating type 2 diabetes patients with lowering effect on the insulin levels as well as on postprandial blood glucose. [6]

Biguanides

A biguanide, metformin, is most commonly prescribed first-line anti diabetic drug for treating type 2 diabetes mellitus, it acts mainly by decreasing the glucose production by liver and can produce significant improvement in insulin resistance. [7] Metformin is approved for use in treating type 2 diabetes mellitus in different countries. Different studies have found that it is highly efficacious and safe for treating diabetes mellitus type 2. It has shown to decrease the mortality rate in newly diagnosed patients of diabetes type 2 and is the only known anti diabetic drug which is not associated with chances of increased mortality as well as morbidity in patients of heart disease, also in the heart failure patients. [8]

Third generation sulfonylurea drugs

The sulfonylureas stimulate the release of insulin from the β cells of pancreas, these drugs are in use for type 2 diabetes treatment from more than 50 years. These drugs are efficacious in their anti-hyperglycemic action, the inter individual difference lies in the drug response known as the pharmacodynamics, drug disposition namely the pharmacokinetics and the side effects. [9] The third generation sulfonylurea, glimepiride causes stimulation of nitric oxide production, therefore inhibits nuclear factor which is induced by cytokines (NF)-κB activation in the endothelial cells and thus produces beneficial effects on the vascular endothelial cells. These are preferred for treating type 2 diabetes mellitus as well as various vascular diseases. [10]

Thiazolidinediones

Pioglitazone, a thiazolidinedione, is commonly used for treating type 2 diabetes mellitus. It is selective ligand of peroxisome proliferator-activated receptor. The drugs belonging to this category interact with the PPAR-γ receptors which lie mostly in hepatic, adipose, and cells of skeletal muscles. The modulation of PPAR-γ receptors regulate the genes which are involved in the metabolic control and it also decreases the insulin resistance. Activation of PPAR-γ receptor raises the glucose uptake, lipid uptake, glucose oxidation and decreases the free fatty acid concentration, insulin resistance. Activation PPAR-γ receptor also leads to the activation of adipocyte differentiation resulting in the formation of more fat cells which are smaller in size. The hepatic fat is greatly decreased with improvements in glycemic level and it also causes correction of dyslipidemia.

Insulin action is improved by different mechanisms like synthesis and release of adiponectin from the fat cells, by increasing the expression of genes which increase glucose oxidation and lower plasma free-fatty acid levels. [11]

Dipeptidyl peptidase-4 inhibitors

The DPP-4 inhibitors present different therapy approach in managing patients of diabetes mellitus type2. [12] The drug Sitagliptin is an orally active drug, it is to be taken once daily, it acts by competitively and fully reversibly inhibiting the dipeptidyl peptidase-4 enzyme which degrades incretin hormone known as glucagon-like peptide-1 quickly. It is approved for treating diabetes type2, as mono therapy as well as for the combination therapy for use along with metformin or with a thiazolidinedione. The drug sitagliptin causes considerable improvement in the glycemic control by dropping fasting as well as postprandial blood glucose concentrations, thus, causing meaningful decrease in HbA1c levels.

Insulin

It is major treatment option for patients suffering from type 1 and type 2 diabetes who are not able to control their blood sugar levels adequately by exercise, diet or by taking oral anti diabetic agents. [13]

ADA 2017 Guidelines for Pharmacotherapy of type 2 diabetes mellitus [14]:

If metformin, it is not contraindicated and is well tolerated, then it is preferred as initial pharmacologic agent in treating diabetes mellitus type 2.

Therapy with insulin is considered (without or with extra agents) in the persons who are newly diagnosed with diabetes mellitus type 2 and are markedly symptomatic or those who have raised blood glucose levels of more than 300 mg/dl or HbA1c of more than 10%. Long-term use of the drug metformin may be found to be linked with vitamin B12 deficiency, and thus repeated assessment of vitamin B12 levels should be considered in the patients treated with metformin, especially in persons with peripheral neuropathy or anemia.

If the mono therapy without insulin at the maximal tolerated dose, is not able to achieve or maintain HbA1c target over 3 months period, then a second oral agent, basal insulin or GLP-1 receptor agonist is added. Patient-centered approach to select pharmacologic agents should be used. Insulin initiation in patients who are not able to achieve their glycemic goals should not be delayed.

Progressive nature of the diabetes mellitus type 2 should be routinely explained to the diabetes mellitus type 2 patients. Insulin use as a threat should be avoided, do not describe it as failure or punishment. Self-titration algorithm should be given to the patients. In the patients who have long-standing and sub optimally controlled diabetes mellitus type 2, atherosclerotic cardiovascular disease, the drugs like liraglutide or empagliflozin should be considered as they have proved to reduce the cardiovascular causes and also the other causes of mortality when added to the standard care.

Aim the present work is to determine the utilization pattern of anti-diabetic drugs and the most commonly used anti-diabetic drug/drugs. (with or without insulin)

MATERIALS AND METHODS

Study Design: A prospective observational study was conducted on patients attending the Medicine Department of MMIMSR, Mullana, Ambala, Haryana, India for drug utilization pattern in patients with type 2 diabetes mellitus after obtaining the approval of the institutional ethics committee. Patients fulfilling the inclusion criteria were enrolled for the study. Patients were included after taking their written informed consent.

Study Population: All the patients visiting the Department of Medicine, MMIMSR, Mullana were screened thoroughly and 238 patients of both the sexes suffering from type 2 diabetes mellitus, fulfilling the criteria were selected for the study after taking their written informed consent. Out of these 238 patients, 21 patients were lost in the follow up period of the study and 17 patients did not complete the study. Thus, 38 patients were declared as drop outs from the study and 200 patients completed the study. Duration of study was 3 months. Patients were evaluated at week 0, 6 weeks, 12 weeks.

Study Drugs: Old cases of type 2 diabetes mellitus, those who were already on treatment with oral anti diabetic drugs and insulin were assessed and their treatment was modified on the basis of their glycemic control and newer cases of type 2 diabetes mellitus were put on appropriate treatment with anti-diabetic drugs. If the blood sugar levels were not controlled within normal limits, then the dose escalation was done at 0, 6 and 12 weeks. The efficacy of study drugs were evaluated by measuring the following parameters at week 0, 6 and 12 weeks. The criteria for diagnosis of diabetes fasting blood sugar $\geq$ 126 mg/dl or postprandial blood sugar $\geq$ 200mg/dl or HbA1c $\geq$ 6.5% as per American Diabetes Association and World Health

Organization guidelines. The goals of treatment were to achieve FBS < 100mg/dl, 2hr PPBS < 140mg/dl and HbA1c < 5.6%. The patients were educated to report to the OPD fasting (no solids for last 8 hours). Only water was allowed to be taken during this fasting period. Two hours after breakfast PPBS was taken. Eligibility was ascertained based on inclusion and exclusion criteria.

Inclusion Criteria:

1. Patients diagnosed with type 2 diabetes mellitus.
2. Patients of either sex attending the medicine OPD.
3. Patients of age group 30-70 years.
4. Patients who have given written informed consent.

Exclusion Criteria:

1. Patients with type 1 diabetes mellitus.
2. Pediatric patients.
3. Pregnant and lactating females
4. Unconscious patients.
5. Chronic alcoholics.
6. Patients requiring drugs which interfere with study drugs

eg. NSAIDS, Sulfonamides, Anticoagulants, Beta blockers, Clofibrate etc.

Study Methodology: A detailed medical history of the patient was obtained. General physical examination along with systemic examination was done. Any adverse effects reported by the patient or investigator were recorded and analyzed. Safety and tolerability evaluation was based upon both self-reported adverse effects and also the recorded adverse effects. Statistical data generated was analyzed using IBM-SPSS (International business machines-Statistical Package for the Social Sciences) version 21. Data collected was entered into micro-soft excel worksheet. For qualitative data, proportions were expressed as percentage and for quantitative data, the data was expressed in Mean ±SD, for which paired t test was used and the p values obtained were <0.05, which is considered to be statistically significant.

OBSERVATIONS:

Figure 1:

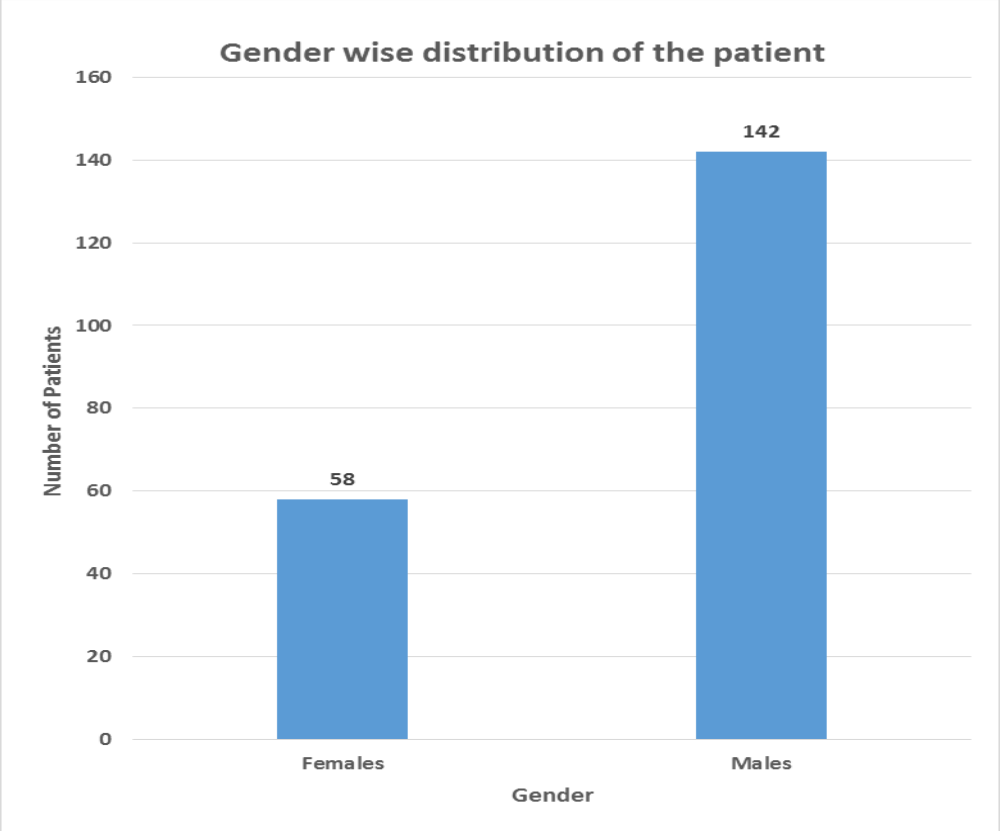
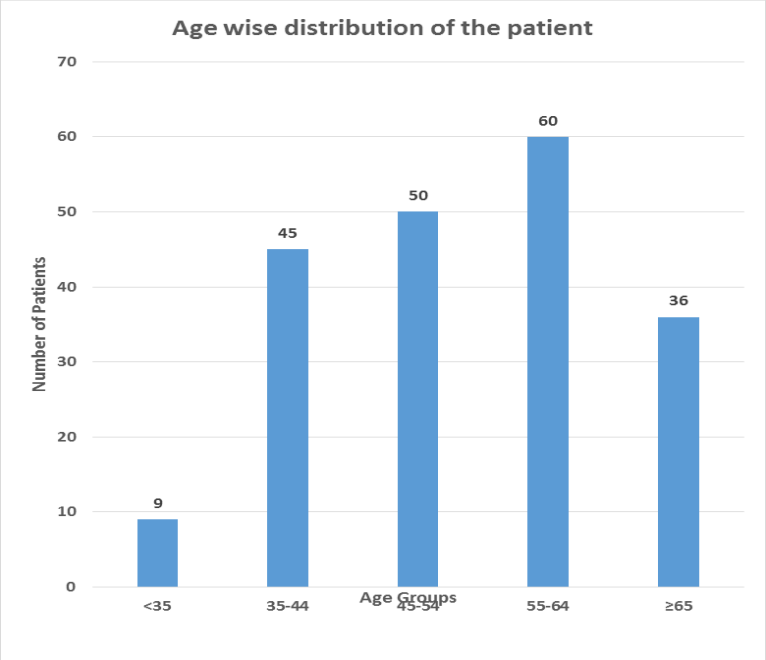


Figure 2:



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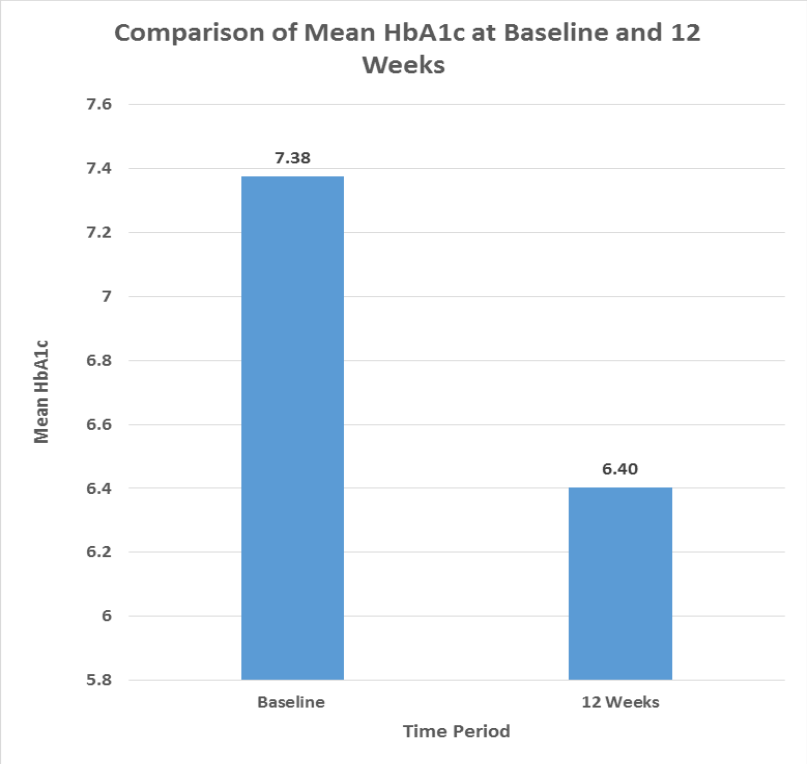

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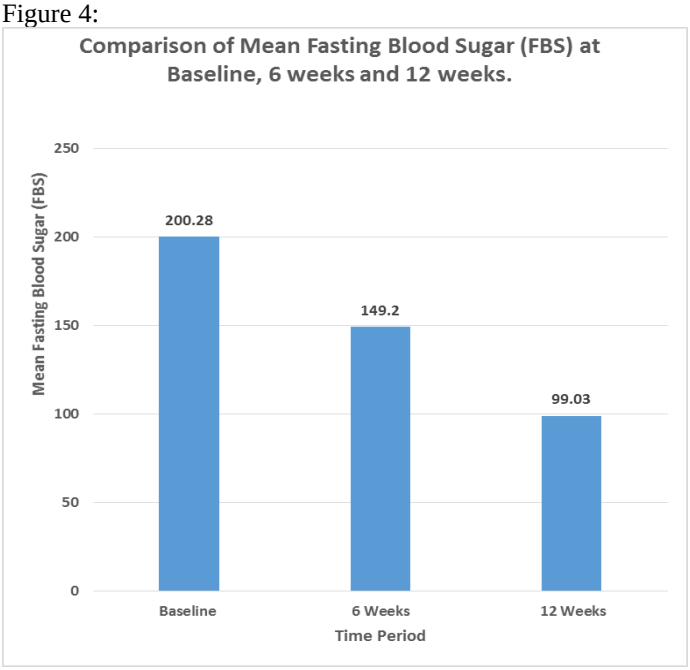


Figure 5:

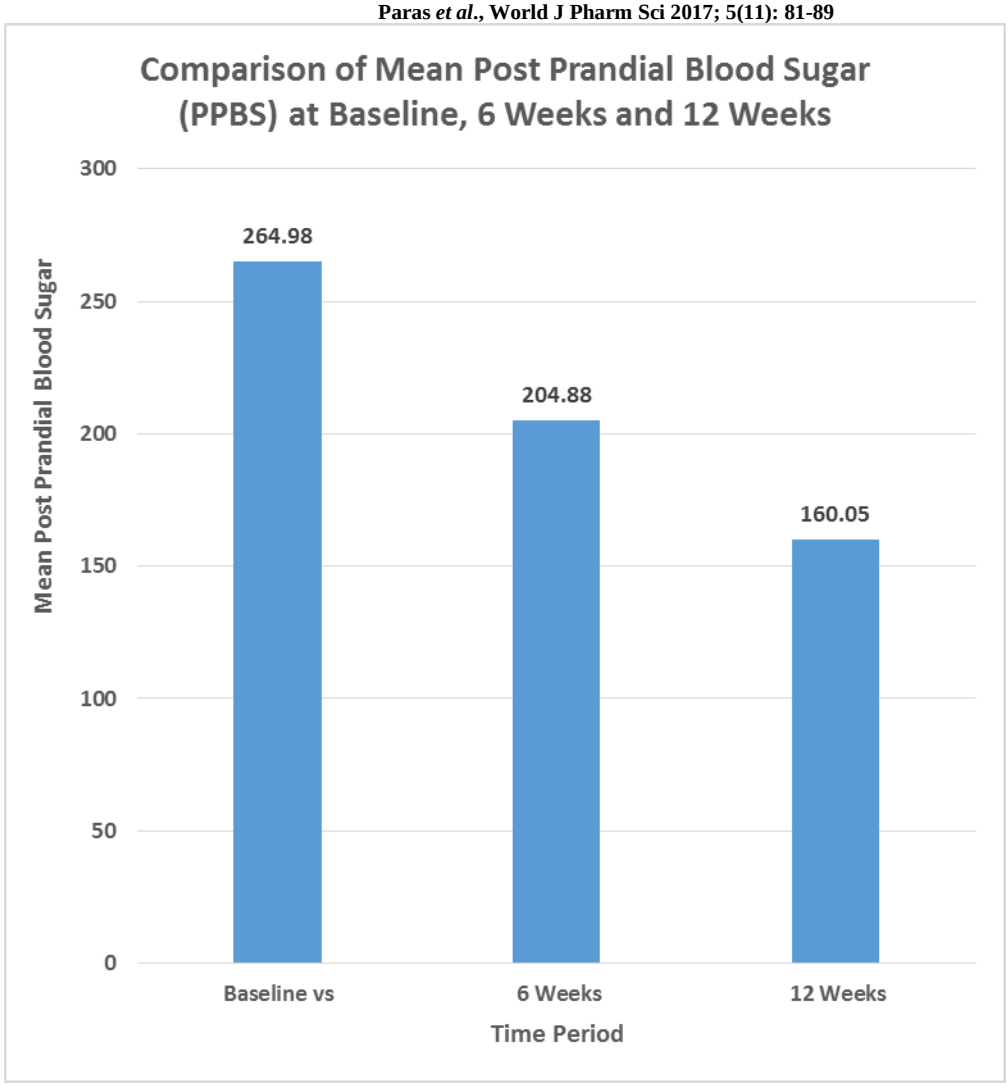
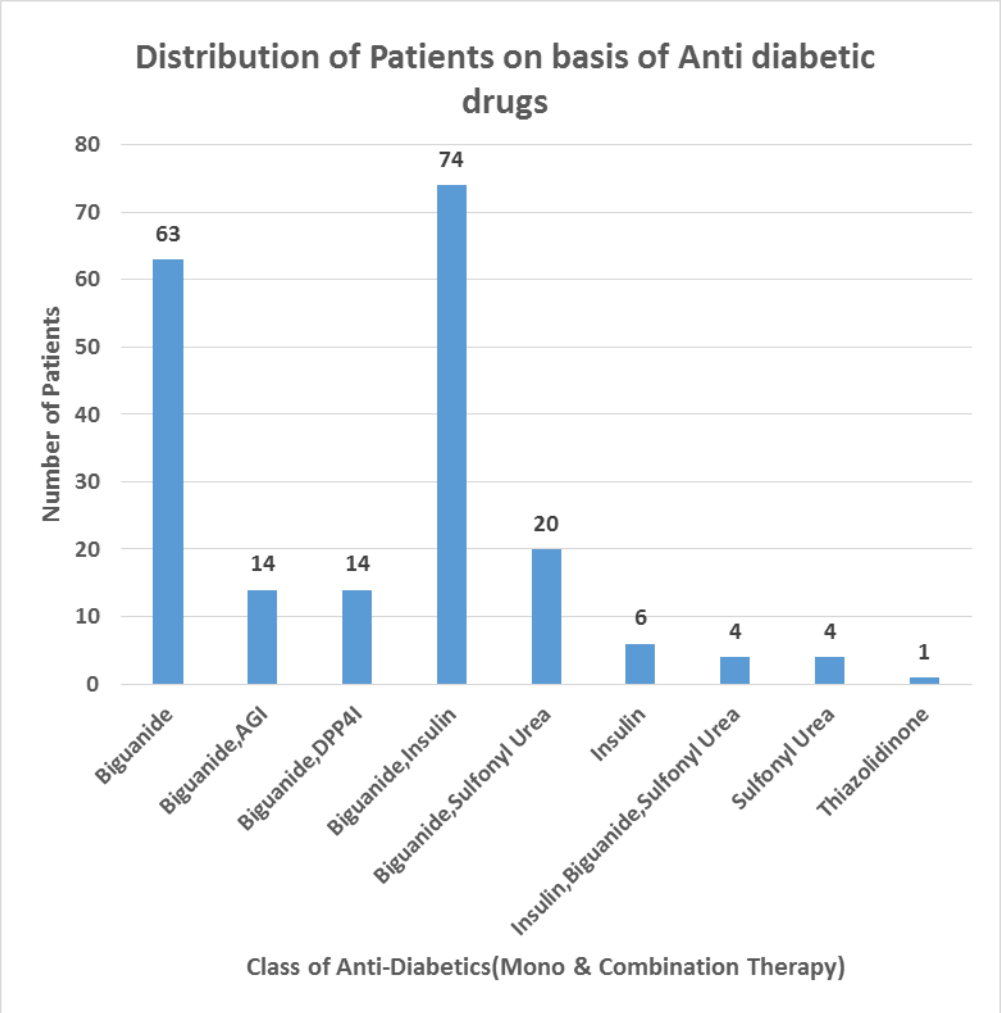

Comparison of Mean Post Prandial Blood Sugar (PPBS) at Baseline, 6 Weeks and 12 Weeks
Mean Post Prandial Blood Sugar
300
250
200
150
100
50
0
264.98
204.88
160.05
Baseline vs
6 Weeks
12 Weeks
Time Period

Figure 6:



DISCUSSION

Out of the total 200 patients in the present study, some patients received mono therapy while some received combination therapy: 63 patients [31.5%] received biguanide (metformin) mono therapy, 6 patients [3%] received insulin mono therapy, 4 patients [2%] received sulfonylureas mono therapy and 1 patient [0.5%] received thiazolidinedione mono therapy.

74 patients [37%] received a combination of biguanide (metformin) and insulin, 20 patients [10%] received combination of biguanide (metformin) and sulfonyl ureas, 14 patients [7%] received a combination of biguanide (metformin) and alpha glucosidase inhibitors, 14 patients [7%] received combination of biguanide (metformin) and di peptidyl peptidase inhibitors, 4 patients [2%] received combination of insulin, biguanide (metformin) and sulfonyl ureas. In the present study, combination therapy with biguanide (metformin) and insulin was the most commonly prescribed treatment, a finding similar to that obtained from a study [15] on the usefulness of the combination therapy with insulin and metformin and it was found that metformin is more effective in conjunction with the insulin for treatment of non-insulin dependent diabetes mellitus. Because of its action on insulin resistance, it might be a more suitable adjunct to insulin than sulfonylurea in obese patients with non-insulin dependent diabetes mellitus who are receiving high insulin doses.

In contrast, some studies favoured the effectiveness of metfomin. In a study [16] titled 'Metformin: A review of its metabolic effects' carried out by K. Cusi, R. A. DeFronzo, it was found that metformin is an effective and safe therapeutic agent for the treatment of type 2 diabetes. Its ability to improve insulin sensitivity and the cardiovascular risk profile of type 2 diabetic patients has enhanced its clinical use as first-line therapy. In this U.K. prospective diabetes study, metformin was the only medication that reduced diabetes-related death, heart attacks, and stroke. In a study [17] titled 'Decreased mortality associated with the use of

metformin compared with sulfonylurea monotherapy in type 2 diabetes', it was found that metformin therapy, alone or in combination with sulfonylurea, was associated with reduced all-cause and cardiovascular mortality compared with sulfonylurea monotherapy among new users of these agents.

CONCLUSION

A total number of 7 classes of anti-diabetic drugs including insulin were prescribed. The common mono therapy prescribed in patients of type 2 diabetes with mild rise in blood glucose levels was metformin and the most common combination therapy prescribed in patients of type 2 diabetes with high blood glucose levels was insulin and metformin. These prescribed drugs achieved good efficacy and safety in this rural population. But studies in larger population and of longer duration are required to confirm the above findings so that the results of this study can be translated for the benefit of patients attending this rural area of Haryana state.

REFERENCES

1. World Health Organization Department of non-communicable disease surveillance. Definition, diagnosis and classification of diabetes mellitus and its complications. Diabetes Mellitus Geneva World Health Organization. 1999; 99.2, 59. http://www.who.Int/iris/handle/10665/66040.
2. Monnier L, Mas E, Ginet C, Michel F, Villon L, Jean-Paul, et al. Activation of oxidative stress by acute glucose fluctuations compared with sustained chronic hyperglycemia in patients with type 2 diabetes. Journal of American Medical Association. 2006; 295: 1681-1687.
3. Shabbidar S, Fathi B, Shirazifard NM. Effects of clinical nutrition education on glycemic control outcomes in type 2 diabetes. International Journal of Diabetes in Developing Countries. 2006; 26: 156-159.
4. Feo P, Loreto C, Ranchelli A, Fatone C, Gambelunghe G, Lucidi P, et al. Exercise and diabetes. Acta Biomedica Journal. 2006; 77: 14-17.
5. Negishi M, Shimomura K, Proks P, Shimomura Y, Mori M. Alpha glucosidase inhibitor voglibose can prevent pioglitazone-induced body weight gain in type 2 diabetic patients. Brazilian Journal of Clinical Pharmacology. 2008; 66: 318–319.
6. Van de Laar FA, Lucassen, Akkermans RP. Alpha- glucosidase inhibitors for type 2 diabetes mellitus. Cochrane Database of Systematic Reviews. 2005; CD003639.
7. Charbonnel B, Karasik A, Liu J, Wu M, Meininger G. Efficacy and safety of the dipeptidyl peptidase-4 inhibitor sitagliptin added to ongoing metformin therapy in patients with type 2 diabetes inadequately controlled with metformin alone. Diabetes Care. 2006; 29: 2638–2643.
8. Eurich DT, Suyuki RTT, Majumdar SR, Alister FAM, Lewanczuk R, Shibata MC,et al. Metformin treatment in diabetes and heart failure: when academic equipoise meets clinical Reality. Trials Journal. 2009; 10: 12.
9. Aquilante CL. Sulfonylurea pharmacogenomics in Type 2 diabetes: the influence of drug target and diabetes risk polymorphisms. Expert Review of Cardiovascular Threapy. 2010; 8: 359-72.
10. Jojima T, Suzuki K, Hirama N, Uchida K, Hattori Y. Glimepiride up regulates eNOS activity and inhibits cytokine-induced NF-κB activation through a phosphoinoside 3-kinase–Akt-dependent pathway. Diabetes, Obesity, Metabolism Journal. 2009: 143–149.
11. Smith S, Jonge L, Volaufova J, Li Y, Xie H, Bray G. Effect of pioglitazone on body composition and energy expendiure: a randomized controlled trial. Metabolism Journal. 2005; 54: 24–32.
12. Deacon CF. Dipeptidyl peptidase 4 inhibition with sitagliptin: a new therapy for type 2 diabetes. Expert Opinion and Investigational Drugs Journal. 2007; 16: 533-45.
13. Nathan DM, Buse JB, Davidson MB, Heine RJ, Holman RR, Sherwin, et al. Management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy. Diabetes Care. 2006; 29: 1963-1972.
14. American Diabetes Association. Diagnostic criteria and Pharmacotherapy in Type 2 Diabetes. Diabetes Care. 2017; 40 (1): S64-S74. http://doi.org/10.2337/dc17-S011.
15. Hermann LS. Combination therapy with insulin and metformin. Endocrinology Practice. 1998; 4(6): 404-12.
16. Cusi K, Defronzo RA. Metformin: A review of its metabolic effects. Journal of Diabetes Reviews. 1998; 6: 89-131.
17. Johnson JA, Majumdar SR, Simpson SH, Toth EL. Decreased mortality associated with the use of metformin compared with sulfonylurea