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Relevance of metformin as a first line in type 2 diabetes mellitus

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Abstract
Background: Metformin is most commonly prescribed drug in the management of diabetes. There is a global increase in the obesity prevalence in children, adolescents and it is accompanied by the appearance and there is increased prevalence of insulin resistance, prediabetes and type 2 diabetes mellitus (T2DM). All Guidelines have recommended Metformin in Type 2 Diabetes Mellitus patient as a first line drug. Metformin acts by inhibiting production of hepatic glucose and increased uptake of glucose in peripheral tissues. In obese patients apart from glycemic control the Metformin have shown additive effects in controlling the lipids and it has been document to also have a Cardio- protective action. Apart from usage of metformin in treating diabetes it can also be used in other conditions like prediabetes, obesity, PCOD (polycystic ovary disease), NASH-non-alcoholic fatty liver disease. It is a drug of choice of physician due to its insulin sensitizing action. It is therefore a primary drug of choice in these conditions for both prevention and treatment.
Methods: 124 patients were selected between the age group of 26 to 40 years whose BMIs was between 28- 35 kg/m 2 who were diagnosed with type 2 diabetes mellitus.
Inclusion criteria: 1) Fasting plasma glucose concentrations more than 126mg/dl but less than 180mg/dl and PPBG more than 200 mg/dl but less than 299mg/dl 2) hemoglobin A1C concentrations 6.5-8.5%.
Excluding criteria: 1) Patient with BMI more than 35 and less than 28were excluded from the study. 2) HB1C more than 8.5 3) Patient with comorbidities were excluded from the study. 4) Elderly patient 5) any other systemic organ dysfunction 6) if FBS>200mg/dl, PPBS >300mg/dl
Results: This study has shown better glycemic level controls when patient were started on medication than compared to placebo group. Fasting Blood glucose level in the Metformin group of patients was significantly reduced than in placebo group. Metformin group of patient had a reduction of BMI by a mean of 1.12 kg/m2 when compared with placebo. Metformin group of patient had significant reduction of HbA1c.This signifies the metformin still holds the good in management of obese diabetic patients.
Conclusions: Metformin is the most commonly prescribed therapy for patients with T2DM. It has a good safety profile and is associated with low cost. The study has confirmed that usage of metformin as an initial drug help in getting the glycemic control unless contraindicated. Patients treated with metformin had weight reduction in obese children and adolescents. Apart from reduction of BMI, metformin also helps in reduction of resistance to insulin in hyperinsulinemia children and adolescents who are obese. Longer-term studies in different populations are required to establish metformin role in the treatment of overweight children.

Keywords: concentrations, populations, children, establish, metformin

Introduction
In 1950 Jean Sterne a French physician discovered metformin importance in humans and it was used in 1957 by France, but it FDA regulatory approval in 1995 as an oral hypoglycemic agent [1-2]. Metformin is grouped in the most essential drugs category by World Health Organization's, and it is termed as most essential drug for the Diabetic Patient. Metformin is recommended as a first line drug in patients with Type 2 Diabetes mellitus by European Association of the Study of Diabetes and American Diabetes Association guidelines [3]. Metformin is a biguanide derivative, by controlling blood glucose level it decreases complications of Diabetes. Metformin works by helping to restore the body's response to insulin. It decreases the amount of blood sugar that the liver produces and that the intestines or stomach absorb [4-5]. Metformin, other than hypoglycemic activity, has been taken with diet and exercise changes to prevent diabetes in people who are at high risk for becoming diabetic. It is also used in women with polycystic ovarian syndrome. Metformin acts by counteracting the resistance of insulin, particularly in liver and skeletal muscle. It suppresses hepatic gluconeogenesis, increases peripheral sensitivity of insulin in tissues like adipose tissue and muscle, and results in peripheral utilization of glucose. Half-life of metformin is nearly five hours and major excretory mode i.e. 90% of the drug is via renal system within 24 hours [6-7].

Methods
124 patients were selected between the age group of 26 to 40 years whose BMIs was between 28- 35 kg/m 2 who were diagnosed with type 2 diabetes mellitus.

Inclusion criteria: 1) Fasting plasma glucose concentrations more than 126mg/dl but less than 180mg/dl and PPBG more than 200 mg/dl but less than 299mg/dl 2) hemoglobin A1C concentrations 6.5-8.5%.

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Selections of Patients were randomized and there were placed on metformin (500 mg twice daily to maximum 2 gm/day) or a placebo for a total of duration of 6 months. The effects of metformin on BMI, glucose tolerance, and lipemic levels were analyzed.

Results

This study has shown better glycemic level controls when patient were started on medication than compared to placebo group. Fasting Blood glucose level in the Metformin group of patient i.e. from a mean of 139 to 100.9mg/dl and In contrast, in placebo group the fasting glucose levels rose slightly from 82.6 to 90.8 mg/dl. In metformin group arm of patients had developed some minor gastrointestinal symptoms like mild abdominal discomfort, nausea and diarrhea occurred in 25% of patients; there were no episodes of vomiting or lactic acidosis reported. Metformin group of patient had a reduction of BMI by a mean of 1.12 kg/m2 when compared with placebo. Metformin group of patient had significant reduction of HbA1c, the mean HbA1c level of reduction was 0.93%.it was interesting to know that the HDL level increased after the metformin treatment from 29.69±9.7 to 34.26± 9.0 when compared to placebo, and Triglyceride level mildly reduced after treatment from 218.10 ± 59.1 to 193.51 ± 54.9; whereas there was mild significant changes in total cholesterol levels 211.15 ± 49.6 to 196.51 ± 64.9 in metformin group than compared to placebo group but it was not statically significant ; whereas there was no significant changes in LDL levels in both the study groups. This signifies the metformin still holds the good in management of obese diabetic patients.

Discussion

It is very well known about the action of Metformin, basically it acts by inhibiting the hepatic glucose production and increased in uptake of glucose in the peripheral tissues. Various studies have shown that metformin in obese patient apart glycemic control have additive effects in controlling the lipids and it has been document to also have a Cardio-protective action. Apart from usage of metformin in treating diabetes it can also be used in various other conditions like prediabetes, obesity, PCOD (polycystic ovary disease), NASH-non-alcoholic fatty liver disease. In many Epidemiological studies it has been shown that when treated with metformin had lower incidence of cancer than those of Non- Metformin-treated patients, hence it was concluded that it has an anti-cancer activity [7-9].

Metformin has several benefits in patients with type 2 diabetes mellitus, which includes decreasing the hyperinsulinemia, weight reduction, surprisingly it can also augmented fibrinolysis, improved lipid profiles and enhanced endothelial function.

Now EASD, ADA consensus guidelines also indicated clearly that the first line drug is Metformin and it has to be initiated in all Type 2 diabetes mellitus patients unless contraindicated.

Our study has also shown that the metformin initiation as the first line in diabetes patient it can have good glycemic control, weight reduction and some benefit on lipemic levels.

Lily et.al 2009 has also shown the beneficial effect of starting metformin in prediabetes. In UKPDS study also it is clearly evident the importance of metformin [10-11].

Ito h et.al 2010, studied the impact of metformin in non-obese individual over long term, it has also shown significant improvement [12].

Scarpello JH *et al* 2008, study has also reemphasized that metformin have cardio protective effects [13]. It is also proven by many prospective and retrospective studies, and it also appear to have glucose-independent effects on the vascular endothelium, suppressant effects on glycation, oxidative stress and formation of adhesion molecules, stimulation of fibrinolysis and have favorable effects on the lipid profile.

Conclusion

Metformin is the most commonly prescribed therapy for patients with T2DM. It has a good safety profile and is associated with low cost. The study has confirmed that usage of metformin as an initial drug help in getting the glycemic control unless contraindicated. Metformin is a good sensitizer of insulin and its effectiveness and efficacy is proved in adolescent and adult patient with type 2 diabetes mellitus. Metformin has been shown to reduce weight gain, hyperinsulinemia, and hyperglycemia in adults with type 2 diabetes and to reduce progression from impaired glucose tolerance to diabetes in those without diabetes.

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