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Original Research Paper

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A STUDY ON SITAGLIPTIN AND REPAGLINIDE IN THE MANAGEMENT OF UNCOMPLICATED TYPE 2 DIABETES MELLITUS

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ABSTRACT

Introduction : GLP-1and GIP stimulates glucose dependent insulin secretion by pancreatic β-cells and GLP-1 also suppressed glucagon release by pancreatic alpha cell in glucose dependent fashion. Through these mechanism, DPP-4 inhibitors improve control of postprandial glucose excursions and lower fasting plasma glucose (FPG) in patient with type-2 diabetes.Aims and Objectives1.To observe the effect of sitagliptin and repaglinide on plasma glucose level fasting and post prandial.2.To observe the effect of sitagliptin and repaglinide on HBA1c.3.To observe the effect of sitagliptin and repaglinide on weight of patient. Materials and MethodThe current study had been designed, single blind, study with two parallel treatment groups. The duration of the study was 24 weeks for each subject from the commencement of study medications. Group A – Sitagliptin 100mg OD: Group B – RepaglinideDiscussionmean glycosylated hemoglobine level in Group A decreased from 9.14 % at 0 week to 6.97 % at 24 week and in Group B decrease from 8.78 % at 0 week to 7.48 % at 24 week

KEYWORDS :

INTRODUCTION

According to "The International Diabetes Federation", the number of people living with diabetes worldwide is expected to rise from 366 million in 2011 to 552 million by 2030. This equates to approximately three new cases every ten seconds or almost ten million cases per year. The International Diabetes Federation (IDF) reports a projected prevalence of 70 million patients in India by the year 2025, and the World Health Organization (WHO) estimates that India will have 80 million cases of diabetes by 2030. This places India second only to China in terms of number of people living with diabetes. Prevalence of Diabetes is increasing day-by-day in our country. The average cost of treating a diabetic in India has been estimated at 575 US Dollars or Rs.28750 annually in terms of direct costs, while, indirect costs like lost work-time, would account for another 100 US Dollars or Rs.5000 annually The greatest number of people with diabetes is between 40-59 years of age. IGT (Impaired Glucose Tolerance) is also a mounting problem in India. The prevalence of IGT is thought to be around 8.7 per cent in urban areas and 7.9 per cent in rural areas, although this estimate may be too high. It is thought that around 35 per cent of IGT sufferers go on to develop type 2 diabetes, so India is genuinely facing a healthcare crisis.

Diabetes mellitus itself was a major cause of morbidity and mortality till a few decades back. Advent of insulin and oral hypoglycemic drugs like sulfonylureas & big uanide sthiazolidinediones were able to control the raised blood sugar level thus giving a longer life to a diabetes patient. Over the last decades, novel breakthroughs in the treatment of type-2 diabetes mellitus have been introduced. New therapeutic classes of antihyperglycaemic agencies (AHAs) targeting the incretin axis, including the dipeptidyl peptidase-4 (DPP4-) inhibitors, in which sitagliptin was the first agent of this class which was approved by the FDA in 2006.

The DPP-4 inhibitor prevents degradation of incretin hormone glucagon like peptide-1 (GLP-1) and glucose dependent insulinotropicpolypeptide (GIP), both of which released by the intestine at very low levels throughout the day and increases significantly in response to a meal.

. Sitagliptin is highly selective DPP-4 inhibitors that provides 24 hr DPP-4 inhibition when dosed once daily .In patient with type-2 diabetes, sitagliptin, both as monotherapy and when given in combination with other AHAs, has been shown to improve glycaemic control and measures of β-cell function and to be well tolerated in large multinational placebo controlled and active controlled trials .

Repaglinide is an antidiabetic drug in the class of medications known as meglitinides, used in addition to diet and exercise for blood sugar control in type 2 diabetes mellitus . Like sulfonylureas, it stimulate insulin released by closing KATP channel in pancreatic β-cell , This depolarizes the beta cells, opening the cells' "calcium channels" and the resulting calcium influx induces insulin secretion. Repaglinide absorbed rapidly from gastrointestinal tract & metabolised rapidly from liver (CYP3A4) to inactive metabolites. The major side effects of repaglinide is hypoglycemia. Safety in pregnant women has not been established . In this study it was planned to compare the efficacy and safety of sitagliptin with repaglinide therapy in Indian patients with type-2 diabetes over a period of 6 month.

Aims and Objectives

- To observe the effect of sitagliptin and repaglinide on plasma glucose level fasting and post prandial.
- To observe the effect of sitagliptin and repaglinide on HBA1c.
- To observe the effect of sitagliptin and repaglinide on weight of patient.

MATERIALS AND METHOD

Rationale of the study:

With the introduction of a number of drugs of this class in quick succession in recent past with widely varying cost, it was decided to compare one of the new introductions to an older Meglinitide.

STUDY DESIGN:

The current study had been designed, single blind, study with two parallel treatment groups.

STUDY DURATION:

The duration of the study was 24 weeks for each subject from the commencement of study medications. No follow up was envisaged after this period. However, serious adverse events coming to the notice of the investigator for one week following termination was documented.

Subject Selection Criteria:
Screening for eligibility of the subject was performed on the very first visit, based on the following criteria.

Inclusion Criteria:
- Age >18 yrs
- Newly diagnosed case of T2DM and impaired tolerance
- Uncomplicated T2DM

Exclusion Criteria:
- Patients of type 1 DM
- Complicated T2DM
- Pt. On insulin therapy
- Pregnancy
- DN
- Infection
- MI or chest pain with ECG abnormality
- Pt.with chronic disease
- Other factors impairing the ability of patients to participate in the study

Study Groups and Medications:
Group A – Sitagliptin 100mg OD
Group B – Repaglinide 2mg TDS before each meal

Results and Analysis

Table 1: Age distribution

Age (yrs)	No. of patients	Percentage
<40 yrs	4	4.8%
41-50	28	33.7%
51-60	34	40.9%
61-70	12	14.4%
>70	5	6%

The table show that max .no of diabetic 40.9 % in 6th decade.

Figure1: Bar diagram showing age distribution of subjects

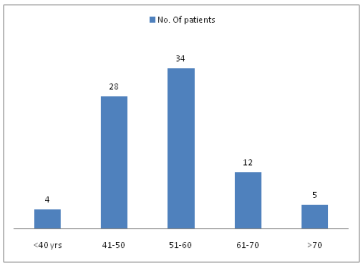

Figure2: Pie diagram showing sex distribution of subjects

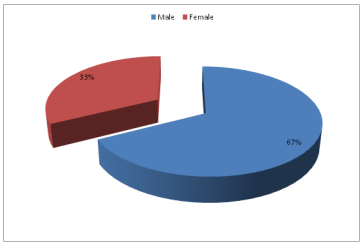

Table 2: Sex Distribution of subjects

Sex	No. of patients	Percentage
Male	56	67.4%
Female	27	32.53%

Among total 83 patients qualified for inclusion into this study 56(67.4%) were male and 27(32.53%) were female.

Table 3: Hemodynamic variables in diabetic patients of both group

VARIABLE	BASELINE	12 WEEK	24 WEEK
SBP (A)	138 ± 7.4	137.1 ± 6.4	134.31 ± 8.4
SBP (B)	134.68±7.6	133.56±6.1	130.06±7.8
DBP (A)	85.96±4.6	85.25± 3.8	84.39±5.2
DBP(B)	83.37±4.5	83.25±4.1	83.06±4.8

Table 4: Fasting blood sugar level before and after therapy in both groups

GROUP	0 week(I)	12 week	24 week(F)	ΔFBS(I-F)	ΔFBS%
A	206.13±39.9	174.66±1.55	123.80±9.53	82.3±3	39.9±6
B	190.75±35.8	158.62±2.81	124.56±8.34	66.1±9	34.6±9

The table 4 shows the man fasting blood sugar level in the both group at 0, 12 and 24 weeks of study.

Figure 3: Bar diagram showing fasting blood sugar level before and after therapy in various groups

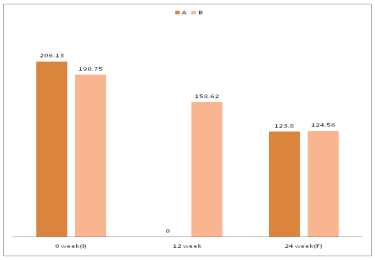

Table 5: Post prandial blood sugar level before and after therapy in both groups

GROUP	0 week(I)	12 week	24 week(F)	ΔFBS(I-F)	ΔFBS%
A	269.96±39.18	212.96±35.48	154.31±16.05	115.65	42.83
B	247.31±41.29	208.03±15.48	158.09±15.45	88.42	35.75

The table 5 shows the mean post prandial blood sugar level in the both group at 0,12 and 24 weeks of study.

Figure4: Bar diagram Showing postprandial blood sugar level before and after therapy in various groups

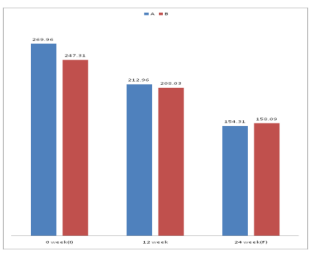

Table 6: Glycosylated haemoglobin level before and after therapy in both groups

GROUP	0 week(I)	12 week	24 week(F)	ΔGHB(I-F)	ΔGHB%
A	9.14±1.24	8.87±1.18	6.97±1.04	2.17	23.74
B	8.78±1.12	8.24±0.96	7.49±0.57	1.29	14.69

The table 6 shows the mean HBA1c level in the both group at 0, 12 and 24 weeks of study.

Figure 5: Bar diagram Showing glycosylated haemoglobin level before and after therapy in various groups

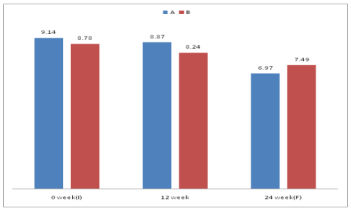

Table 7: Change in mean body weight before and after therapy in both groups

GROUP	0 week(I)	12 week	24 week(F)	Δ weight(I-F)	Δweight%
A	65.37±3.3	64.98±3.18	64.53±2.3	0.84	1.28
B	67.67±4.08	67.20±3.98	66.79±1.68	0.88	1.30

The table 7 shows the mean body weight in the both group at 0,12 and 24 weeks of study.

Table 8: Statistical significance

S.No.	No. of affected patients	P value
1.	Group A- change in FBS before and after treatment	<0.001
2.	Group B- change in FBS before and after treatment	<0.001
3.	Group A- change in PPBS before and after treatment	<0.001
4.	Group B- change in PPBS before and after treatment	<0.001
5.	Group A- change in HBA1c before and after treatment	<0.001
6.	Group B- change in HBA1c before and after treatment	<0.001

DISCUSSION

This study was carried out in patients who attend the indoor and outdoor of dept. of medicine, Anugrah Narayan Maghad Medical College and Hospital, Gaya.

In the present study a total of 123 patients were included. In which only 83 were available for follow up and there data were collected at 12th week and 24thweek follow up period, remaining 40 cases were lost to followup.

In the first group (Group A) newly diagnosed cases of type 2 diabetes mellitus (uncomplicated) were kept on sitagliptin and in second group (Group B) newly diagnosed cases of uncomplicated type 2 diabetes mellitus were kept on Repaglinide

Table 1- Shows the age at which the patients had presented with uncontrolled hyperglycemia at our hospital. Most of the patient belonged to the age group of 51-60 yrs, comprising about 40.9%.The no. of patient below 40 yrs age were 4.8%. 33.7% of the cases belonged to group of 41-50 yrs.

Table 2-Shows the sex distribution of cases. A total of 83 patients were qualified for inclusion in the study, In which 56 (67.4%) were male and 27 (32.53%) were female.

Table 3- shows the mean blood pressure of both groups. The mean systolic blood pressure at 0 week of Group A was 138 (SD 7.4) and at 24 week was 134.31(SD 8.4) and of Group B was 134(SD 7.6) at 0 week and 130.06(SD 7.8) at 24 week.

This study shows that in Group A mean SBP reduced by 2.67% & in Group B mean SBP reduced by 3.44 % but effect on mean DBP is not positive. The relationship is not significant.
Table 4 –shows observation after 24 week of therapy, the mean fasting blood sugar level (FBS) in Group A decreased from 206.13 at 0 week to 123.80 at 24 weeks[a decrease of {ΔFBS(I-F) 82.33mg/dl} about 39.96 %].

The mean FBS level in Group B decreased from 190.75 at 0 week to 124.56mg/dl at 24 week [a decreased of { Δ F BS (I-F) 66.19 mg/dl } about 34.69 %]

Table 5 – shows the mean post prandial blood sugar level (PPBS) of Group A were 269.96 mg/dl at 0 week decreased to 154.31 mg/dl at 24 week [a decreased of {ΔPPBS (I-F) 115.65 mg/dl } about 42.83%] and of Group B were 247.31mg/dl at 0 week decreased to 158.09 mg/dl at 24 week[a decrease of {ΔPPBS(I-F) 88.42 mg/dl } about 35.75 %

Table 6 – shows the mean glycosylated hemoglobine level in Group A decreased from 9.14 % at 0 week to 6.97 % at 24 week [a decrease of {ΔGHB (I-F) 2.17}] and in Group B decrease from 8.78 % at 0 week to 7.48 % at 24 week [a decrease of {ΔGHB (I-F) 1.29.

Table 7- After 24 week of therapy , the mean body weight(MBW) in Group A decrease from 65.37 kg at 0 week to 64.01 kg at 24 week [a decrease of {ΔMBW (I-F) 1.36 kg}]. The mean body weight in Group B decrease from 67.67kg at 0 week to 66.09 kg at 24 week [a decrease of {Δ MBW (I-F) 1.58kg}].

Summary and Conclusion

The data was analysed statistically .The mean FBS sugar and PBPS before and after therapy were compared .Role of sitagliptin and repaglinide was statistically significant in both group .p value was <0.001 in both group.

1. Sitagliptinmonotherapy produced a reduction of 82.33 mg/dl (39.96%) in fasting blood sugar level and 115.65 mg/dl (42.83%) in post prandial blood sugar level at the end of 24 weeks therapy (P value <0.001)

2.Repaglinide monotherapy produced a reduction of 66.19 mg/dl (34.69 %) in fasting blood sugar level and reduction of 88.42 mg/dl (35.57 %) in post prandial blood sugar level at the end of 24 weeks of therapy .(P value <0.001)

3. Sitagliptin showed reduction of 2.17 (23.74% from baseline value) in glycosylated haemoglobin (P<0.001).

Glycosylated haemoglobin decrease by 1.29 (14.69 % from baseline value) in Repaglinide group.(Group B) (P<0.001)

4. Sitagliptin (Group A) showed reduction of 2.08 % (1.36 kg) in mean body weight , mean body weight decreased by 2.33 % (1.58 kg) in Group B .

5. Sitagliptin and Repaglinide have no significant effect on blood pressure of patients.

Hence it is concluded that Sitagliptin and Repaglinide is and overall effective oral hypoglycaemic agent in controlling hyperglycemia, reduction of HbA1c level with neutral effect on mean body weight of the patients.

As above conclusion were drawn from a small sample size, larger sample size and longer follow up will add to the quality and strength of the study.

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