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General Medicine

TO EVALUATE AND COMPARE THE SAFETY AND EFFICACY OF INCRETINS AND SECRETOGOGUES BASED THERAPY IN INADEQUATELY CONTROLLED TYPE 2 DIABETES MELLITUS

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ABSTRACT Type 2 Diabetes Mellitus is a complex group of disorders. Patients with type 2 diabetes has an increased risk of vascular disease which further gives rise to severe complications. The present study was conducted in the medicine department of shri mahant indiresh hospital. The subjects suffering with type 2 diabetes mellitus whose glycemic targets were not achieved (FBS > 126mg/dl and HbAlC>6.5%), and who were enrolled in the study based on the following inclusion and exclusion criteria. Both male and female patients suffering with type 2 diabtes mellitus aged above 18 years and prescribed with incretins and secretogogues and with FBS > 126 mg/dl and HbA1C 6.5% were included in the study. All the subjects were followed for 3 months on monthly basis. Allthe subjects were evaluated for the following parameters at start of the treatment-anthropometry,glycemic parameters, test of pancreas, and lipid parameters. In this study, both treatment groups incretin and secretogoguos based therapy prescribed to inadequately controlled type 2 diabetic patients,produced significant reduction in FBS,PPBS and HbA1c from baseline. The reductions in these values were more in DPP 4 inhibitor group than in sulphonylureas group.

KEYWORDS : Type 2 Diabetes Mellitus, HbA1,Secrretogogues/Sulfonylurease, DDP-4 Inhibitor

INTRODUCTION

Type2 diabetes Mellitus is a complex group of disorders comprised of impaired insulin secretion, insulin resistancbeta cell dysfunction, altered lipid, carbohydrate and protein metabolism, inappropriate, glucose production; and characterized by a common end point i.e hyperglycaemia[.1,2]

Patients with type 2 diabetes has an increased of of vascular disease which further gives rise to severe complications therefore requires multiple anti hyperglycaemic agents to attain glycaemic control[3].

Insulin secretogogues are one of the conventional treatment for type 2 diabetes for many decades due to their reliability, efficacy, decreasing microvascular complications and low cost. Second generations SUs glibenclamide ,glipizide and glimepiride are still the choice of drug for the management of T2DM in India[6].

Whilst usually well tolerated , low costs, minimal side effects, efficacy in attaining glycaemic control and reducing microvascular complications, these agents are also associated with an increased risk of hypoglycaemia and weight gain which may reduce adherence to the treatment[7,8]. Hypoglycaemia is caused due to prolonget stimulation of insulin secretion with fall in the glucose concentrations[9]. Weight gain is another common side effect of sulfonylureas[10]. In addition to this, sulphonylureas are also associated with the development of b-cell apoptosis and b-cell exhaustion, endothelial dysfunction with increased risk for ischemic complications and possibly an increased dysfunction with increased risk for ischemic complications and possibly increased mortality risk.

Glucose-dependent Insulinotropic Polypetide (GIP) and Glucagon-like Peptide-1 (GLP-1) are the two incretin harmones which are released from the intestinal cells in response to the ingestion of food, and plays an important role in glusose homeostasis by stimulating glucose - dependent insulin secretion and inhibiting glucagon secretion[11-13].

The effect in known as the incretin effect. But both these hormones GLP-1 and GIP are rapidly degraded or cleaved by Dipeptidyl peptidase IV (DPP-IV) which is a plasma enzyme, thus to avoid their degradation and to maintain the physiological glucose level, DPP4 inhibitors came into existence. DPP4 inhibitors are also known as gliptins.

The incretin-based drugs glucagon-like peptide 1 (GLP-1) receptor agonists and dipeptidyl peptidase 4 (DPP-4) inhibitors are novel treatment options for the treatment of type-2 diabets. Currently, two GLP-1 analogues (exenatide and liraglutide) and four DPP-4 inhibitors (sitagliptin, vildagliptin, saxagliptin, alogliptin and teneligliptin) are in the market, and many others are under develpment. The DPP4 inhibitors, works by inhibiting the DPP-4 enzyme that degrades GLP-1 and GIP thereby stabilizing the active form of GLP-1 and GIP. Active GLP-1 stimulates glucose-dependent insulin secretion, suppresses glucagon release and delays gastric emptying. In contrast to GLP-1 analogues, DPP-4 inhibitors have no effects on gastric emptying and are weight neutral[11-13]l.

Gliptins can be used as monotherapy or in combination with metformin sulfonylurea or thiazolidinedione. DPP4 inhibitors are also available in fixed dos combination with metformin.[14]

Gliptins offer a good glycemic control, enhanced b-cell function , reductions in blood glucose glycated haemoglobin (HbAlc) levels, as compared to other oral anti hyperglycemic agents as thus making them a suitable treatment option for the patients to maintain sufficient levels of b-cell function and maintainin glycemic levels[11-13].

Gliptins are associated with an acute risk of hypoglycemia, weight neutrality[15].

DPP4 inhibitors have other effects too, studies shows that activation of GLP-1R by DPP4 inhibitors in the kidney results in diuretic and natriuretic effects. This may be possibly through direct actions on renal tubular cells and sodium transporters , Incretin-based therapy also reduces albuminuria, glomerulosclerosis, oxidative stress, and fibrosis in the kidney[16]. DPP4 inhibitors also have lipit lowering actions

In addition to their beneficial effects, DPP4 inhibitors also possess some adverse effects like upper respiratory tract infections, nasopharyngytis and acute pancreatitis.

Thus this study was intended to evaluate and compare the effect of sulphonyiureas and DPP4 inhibitors on glycemic and other related parameters and to observe ne adverse effect of both the therapies among the subjects with type to diabetes mellitus

AIM AND OBJECTIVES

AIM: To evaluate and compares the safety and efficacy of incretin and secretogogues based therapy and subjects with inadequately controlled type to diabetes mellitus

OBJECTIVES:

1. To assess the efficacy and safety of incretins based therapy in subjects with T2DM.
2. To assess the efficacy and safety of secretogogues based therapy in subjects with T2DM.

3. To compaere the safety and efficacy of incretins and secretogogues based therapy in patients with T2DM.

METHODOLOGY

STUDY DESIGN: The present study was conducted in the medicine department of Shri Mahant Indiresh Hospital. The subjects suffering with type 2 diabetes mellitus whose glycemic targets were not achieved (FBS>126mg/dl and HbAIC>6.5%), and who were prescribed with incretins or secretogogues were enrolled in the study based on the following inclusion and exclusion criteria.

INCLUSION CRITERIA:

Both male and female patients suffering with type2 diabetes melltius aged above 18 years and precribed with incretins and secretogugues.

Subjects with FBS>126mg/dl and HbAlC levels greater than 6.5% were included in the study.

EXCLUSION CRITERIA:

- Subjects with type 1 diabetes.
- Gestational diabetes.
- Subjects with other complications and on other anti diabetic drugs.
- Patient under critical conditions requiring critical care stay.

The enrolled subjects were treated under respective qualified medical consultant.

The subjects in the study were divided into two groups:

Group A: Patients receiving incretin based therapy i.e either DPP-4 inhibitors along with secretogogues.

Group B: patients receiving secretogogues based therapy.

ALL the subjects were evaluated for the following parameters at start of the treatment-

- Anthropometry
- Glycemic parameters- FBS, PPBS, HbAlC
- Test for pancreas
- Lipid parameters

All the subjects were followed for a period of 3 months on monthly basis.

The efficacy was evaluated on the basis of glycemic control. Glycemic parameters FBS, PPBS, HbAlC and test for pancreas were evaluated at the start of treatment and after 3 months.

SOURCE OF DATA:

- Prescription of the patients.
- Laboratory records of the patients.

ANTHROPOMETRIC ANALYSIS : weight in kg and height in meters were taken in light clothing and without shoes, body mass index (BMI) was calculated from these values using the formula-

BMI = weight(kg)/Height*Height (meters)

BIOCHEMICAL PARAMETERS:

Glycemic Parameters and their method by which they are performed: All the investigations were done at the centrel laboratory of Shri Mahant Indiresh Hospital(SGRRIM&HS).

1. **Blood glucose:** Fasting and post prandial blood glucose would be done by GOD-POD method, diatek kit, fully automated analyzer, XL-300 and RBS would be done by glucometer. The blood sample would be collected from the patient after 8 hour fasting for investigating fasting blood-sugar. For investigating PPBS, a 2 hour after meal blood sample would be collected.
2. **HbAlC:** This test would be done by immune turbidimetry, direct technique, future system kit, by using an appropriate calibrator.

Metabolically healty patient-<6% HbAlC
Good-Control-upto7% HbAlC
Poor control->8% HbAlC

In vitro determination of HbAlC in whole blood is utilised in long term monitoring

The HbAlC correlates with the mean gulcose concentration prevalling in the cource of patient recient history (approx 6-8 weeks), therefore provide much more reliable information for glycemia monitoring.

3. **Lipid parameters:** serum cholesterol (in mg /dl) and serum triglyceride (in mg /dl) were evaluated using bio-chemical analyzer.
4. **Statistical Analysis :** statistical analysis was performed using T test for analyzing glycemic and lipid parameters

OBSERVATION AND RESULTS

The present prospective study was conducted on 123 subjects with type 2 diabetes mellitus out of which 101 subjects completed their 12 week follow up.

Group 1 prescribed with DPP4 inhibitors along with secretogogues and group 2 prescribed with secretogogues. There are 42 subjects in group 1 and 59 subjects in group 2.

Group 1: Patients receiving DPP4 inhibitor therapy along with secretogogues.

Table 1: Distribution of subjects on the basis of age in DPP4 inhibitor therapy group.

Age group(yrs)	No of patient	%
>30	1	2.380
31-40	1	2.380
41-50	11	26.190
51-60	10	23.809
61-70	15	35.714
71-80	4	9.523

There were 42 subjects in group 1 receiving DPP4 inhibitors, subjects between 29 to 73 years of age with mean age of 56.44 years were enrolled . Maximus numbers of subjetcs 15(35.714%) were found in the age group of 61-70.

Table 2: Distribution of subjects according to gender.

Age group(yrs)	male	Female
>30	1	0
31-40	1	0
41-50	7	5
51-60	4	6
61-70	10	4
71-80	2	2
Total (%)	25(59.52)	17(40.47)

Out of 42 subjects enrolled in the study 25 (59.52%) were male and 17(40.47%) were female. Maximum numbers of female subjects were between 51-60 yrs.

Table 3. Distribution of the subject to co-morbid conditions along with type 2 diabetes mellitus.

Co-morbid conditions	No. of patients (%)
Dyslipidaemia	11(26.19)
Hypertension	18(42.85)
Hypothyroidism	5(11.90)
CAD	2(4.76)
Diabetic Foot	2(4.76)
Neuropathy	4(9.52)
Bronchial Asthma	1(2.38)
Seizure Disorder	1(2.38)

Table 4. Table showing baseline general characteristics'.

Baseline general characteristics.	Mean	SD
Age(yrs)	56.547	11.11
Weight(kg)	63.261	10.45
Height(cm)	164.214	6.01
BMI(kg/m²)	23.443	3.60
Duration of diabetes(yrs)	6.352	3.14

Mean BMI(Body Mass Index) of patients in this group at baseline was 23.443Kg/m2

Table 5. Mean and SD of biochemical parameters at baseline.

Baseline biochemical parameters	Mean	SD
FBAS(mg/dl)	203.952	79.03
PPBS(mg/dl)	285.595	111.62
HbAlC(%)	8.909	2.50
Sr. Amylase (U/L)	60.714	21.32
Sr. Lipase(U/L)	117.363	44.77
Sr. Cholesterol (mg/dl)	177.363	44.77
Sr. Triglyceride (mg/dl)	163.545	38.49

The mean and SD (standard deviation) of all the biochemical parameters at baseline i.e before the start of treatment were: FBS (203.952 ± 79.03), PPBS (285.595 ± 116.62), HbAlC (8.909±2.50), Sr. Amylase (60.714 ± 21.32),Sr. Lipase (117.690 ±84.26), Sr, cholestrol (117.363 ±44.77) and Sr. Triglyceride (163.545 ±38.49).

Table 6. Response to DPP4 inhibitor after12 weeks of treatment.

Biochemical Parameters	Baseline values mean + SD	After tratment Mean + SD	T value	P value
FBS (mg/dl)	203.95± 79.03	156.83 ± 50.17	6.237	0.000***
PPBS(mg/dl)	285.59±111.62	202.11±61.37	8.204	0.000***
HbAlC(%)	8.90±2.50	7.46± 2.03	9.093	0.000***
Sr. Amylase(U/L)	60.71± 21.32	66.76± 21.40	-3.602	0.001**
Sr. Lipase(U/L)	177.36± 44.77	114.30± 74.06	0.553	0.583
Sr. Cholesterol (mg/dl)	177.36± 44.77	169.09± 33.74	1.156	0.275
Sr. Triglyceride (mg/dl)	163.54± 38.49	153.90± 26.92	1.550	0.152

*p<0.05 significant, **p<0.01 very significant, ***p<0.001 extreme significant.

A significant change was observed in glycemic parameters after the treatment with DPP4 inhibitor therapy. Table 7 shows the mean value of biochemical parameters at baseline and after the treatment with DPP4 inibitors. After 12 week treatment, an extremely significant decrease was observed (p<0.001) in the FBS (203.95→156.83), PPBS (285.59→202.11), HbAlC (8.90→7.46).

Table 7. Change in biochemical parameters after 12 week of treatment.

Change in biochemical parameters	Average change (mean)	% change (Mean + SD)
Decrease in FBS	47.121	20.305± 14.97
Decrease in PPBS	83.476	26.06±13.59
Decrease in HbAlC	1.448	15.76±8.65
Decrease in Sr. cholesterol	8.273	2.39±17.14
Decrease in Sr. Triglyceride	9.645	3.62±16.78
Decrease in Sr. Amylase	-6.05	-12.38± 19.27
Decrease in Sr. Lipase	3.39	-11.19± 43.86

After 12 week of tretment, mean reduction in FBS, PPBS and HbA1C were 47.121 (20.305%), 83.476 (26.06%) and 1.448 (15.76%) respectively, Mean reduction in serum chlesterol was 8.273 (2.39%) and serum triglyceride was 9.645 (3.62%).

Table 8. Relationship between general characteristics and decrease in blood sugar levels using Karl Pearson correlation coefficent.

General characteritics	Decrease in FBS (%change) r value	Decrease in PPBS (%change) r value	Decrease in Hb1C (%change) r vaue
Age(yrs)	-0.37 (0.818)	-0.098 (0.537)	-0.203 (0.196)
BMI (kg/m)	-0.001 (0.997)	0.577 (0.577)	0.175 (0.175)

 # shows r values using Karl Pearson coeficient

Group2: Patients receiving secretogogues based therapy

Table 9: Distribution of subjects on the basis of age in the secretogogues based therapy group.

Age Group (yrs)	No. Of patient	%
>30	0	0
31-40	6	10.169
41-50	18	30.508
51-60	17	28.813
61-70	14	23.728
71-80	4	6.779

There were 59 subjects in group 2 receiving secretogogues based thrapy, subjects between 31 to 76 years with mean age 54.64 years were enrolled in the group Maximum number of subjects 18(30.50%) were found to be in the age group of 41-50.

Table 10: Distribution of subjects according to gender.

Age Group(yrs)	Male	Female
>30	0	0
31-40	2	4
41-50	7	11
51-60	10	7
61-70	4	10
71-80	3	1
Total	26	33

Out of 59 subjectas enrolled in the group 26 (44.06%) were male and 33 (55.93%) were female, Maximum numbers of subjects were females between the age group of 41-50. maximum numbers of amle subjects were between 51-60 yrs of age.

Table 11: Distribution of the subjects according to co-morbid conditions along with type 2 diabetes mellitus.

Co-morbid conditions	No. Of patients (%)
Dyslipidaemia	5 (8.47)
Hypertension	10 (16.94)
Hypothyroidism	6 (10.16)
Neuropathy	5 (8.47)
BPH	1 (1.69)
IHD	1 (1.69)

Table 12: Baseline general characteristics of the subjects along with mean and SD.

Baseline-general characteristics	Mean	SD
Age(yrs)	54.64	10.85
Weight(kg)	66.64	12.25
Height(cm)	161.92	5.94
BMI(kg/m)	25.34	3.94
Duration of diabetes (yrs)	6.448	3.61

Mean BMI(Body Mass Index) of patients in this group at baseline was 25.34 Kg/m2. The mean of general charactersistics at baseline were shown in table12.

Table 13: Mean and SD of biochemical parameters at baseline.

Baseline biochemical parameters	mean	SD
FBS(mg/dl)	172.80	76.92
PPBS(mg/dl)	238.37	93.78
HbA1C(%)	7.66	1.56
Sr. Amylase(U/L)	65.70	19.59
Sr. Lipase (U/L)	87.87	56.32
Sr. Cholesterol (mg/dl)	194.40	55.71
Sr. Triglyceride(mg/dl)	283.60	209.18

The mean and SD (standard deviation) of all the biochemical parameters at baseline i.e before the start of treatment were: FBS (172.80±76.92), PPBS(238.37±93.78), HbA1C (7.666±1.56), Sr. Amylase (65.70±19.59), Sr. Lipase (87.87±56.32), Sr. Cholesterol (194.40±55.71) and Sr. Triglyceride (283.60±209.18).

Table 14: Responce to secretogogues based therapy after 12 weeks treatment.

Biochemical parameters	Baseline values Mean ±SD	After treatment Mean±SD	t Value	P value
FBS(mg/dl)	172.80± 76.92	143.92± 46.17	4.183	0.000***
PPBS(mg/dl)	238.37± 93.78	192.55± 69.03	5.083	0.000***
HbA1C(%)	7.66±1.56	7.37±1.53	8.210	0.000***

Sr. Amylase (U/L)	65.70± 19.59	70.55± 18.40	-2.607	0.012**
Sr. Lipase (U/L)	87.87± 56.32	91.01± 50.92	-1.385	0.171
Sr. Cholesterol (mg/dl)	194.40± 55.71	181.20± 50.35	4.598	0.010**
Sr. Triglyceride (mg/dl)	283.60± 209.18	250.20± 159.35	4.598	0.010**

*p<0.05sinificant,**P<0.01verysignificant, **p<0.001 extreme significant.

A significant change was observed in glycemic parameters after the treatment with secretogogous based therapy. Table 22 shows the mean value of biochemical parameters at baseline and after the treatment with secretogogues. After 12 week treatment, an extremely significant decrease was observed (p<0.001) in the FBS (172.80→143.92), PPBS (238.37→192.55), HbA1C (7.66→7.37).

Table 15. Change in biochemical parameters after 12 weeks treatment

Change in biochemical parameters	Averange Charge (Mean)	% Charge (Mean±SD)
Decrease in FBS	28.88	1064± 28.81
Decrease in PPBS	45.82	15.61 ±23.25
Decrease in HbA1C	0.29	3.70± 3.43
Decrease in Cholesterol	13.20	661 ±1.76
Decrease in triglyceride	33.40	7.57 ±7.46
Decrease in Sr. Amylase	-4.85	-11.13 ±25.55
Decrease in Sr. Lipase	31.55	-9.17± 24.69

After 12 weeks of treatment, mean reduction in FBS, PPBS And HbA1C were28.88(10.64%), 45.82(15.61%) and 0.29(3.70%) respectively. Mean reduction in serum cholesterol was 13.20 (6.61%) and serum triglyceride was33.40(7.57%)

Table16. Relationship between general characteristics and decrease in blood sugar levels using Karl Pearson correlation coefficient.

General characteristics	Decrease in FBS (%Change) r value	Decrease in PPBS (%Change) r value	Decrease in HbA1C (%Change) r value
Age (Yrs)	-0.059#(0.657)	-0.122(0.356)	-0.180(0.172)
BMI (Kg/m2)	0.124(0.349)	0.235(0.073)	0.207(0.116)

shows r value using Karl Pearson coefficien

Table 17. Comparision of parameters between both the group (DDP4 Inhibitors and secretogogues)

Parameters	GroupI (mean + SD	GroupII (mean + SD	T value	P value
Age(years)	56.54 ±11.11	54.64 ±10.85	0.860	0,392
FBS(mg/dl)	20.30 ±14.97	10.64 ±28.81	1.988	0.050*
PPBS(mg/dl)	26.06 ±13.59	15.61 ±23.25	2.611	0.010**
HbA1C(%)	15.76 ±8.55	3.71± 3.43	9.695	0.000***
S. Cholesterol (mg/dl)	2.39± 17.14	6.61± 1.76	-0.539	0.598
S.Triglycerides (mg/dl)	3.65± 16.78	7.57± 7.46	-0.497	0.627
S. Amylase (U/L)	-12.38 ±19.27	-11.13 ±25.55	-0.267	0.790
S. Lipase (U/L)	-11.19± 43.86	-9.17 ±24.69	-0.296	0.768

*p 0.05significant **p 0.01 very significant ***p extreme significant

The glycemic parameters were found to be significant in both groups, but groupI receiving DDP4 inhibitors and secretogogues both showed a much better reponse in terms of glycemic parameters but other parameters were not significant.

DISCUSSION

The present study was conducted on 123 subjects with type 2 diabetes mellitus. The study was aimed to evaluate and comapre the safety and efficacy of incretins (DPP 4 inhibitors) and secretogogues (sulphonylureas) based therapy in subjects with uncontrolled type 2 diabetes mellitus. Out of 123 subjects 101 completed a 12 week of follow up.

In our study we observe that DPP 4 inhibitors has similar glycemic efficacy as with other hypoglycemic agents, while some studies has reported that DPP4 inhibitors have low glycemic efficacy as compared to other hypoglycemic agents and they do not support DPP4 inhibitors as adjunctive therapy to the on going treatment. A significant change was observed in glycemic parameters after the treatment with DPP 4 inhibitor therapy adjunctive to sulphonylureas. After 12 week treatment, an extremly significant decrese was observed (p<0.001) in the FBS from 203.95mg/dl to 156.83mg/dl. PPBS from 285.9mg/dl to 202.11mg/dl with p<0.001, HbA1C from 8.90% to 7.46% with p<0.001. in terms of lipid parameters no significant reduction was seen.

A significant change was observed in glycemic parameters after the treatment with secreatogogues base d therapy. After the 12 week treatment, an extremly significant decrease was observe (p<0.001) in the FBS from baseline 172.80mg/dl to 143.92mg/dl, PPBS from 238.37 mg/dl to 192.55mg/dl, HbAlC from 7.66% to 7.37%. in terms of lipid parameters, A significant improvement in serum cholesterol was observed after 12 week treatment.

An extremly significant reduction in the glycemic parameters (FBS, PPBS and HbAlC) was observed in both the groups . in the present study DPP 4 inhibitors therpy in combination with sulphonylureas showed a better glycemic responce as compare to sulphonylures monotherapy, similarly many studies suggest that gliptins can bbe combined with any antihyperglycemic drug except GLP-1 analogs. Many trials found that adding a DPP 4 inhibitor to metformim or sulphonylures shows a mean reduction in HbAIC of 0.6-0.8%.[9].

Another study suggest that, the HbAlC and FPG level were reduced at 3 months and at 12 months after treatment with sitagliptin at a dose of 25 to 100 mg/day[27].

In our study, Analysis between both the groups shows a significant improvement in glycemic parameters FBS (P=0.50), PPBS (p=0.01) and HbAlC (p=0.000), the changes were more significant in group 1 receiving DPP 4 inhibitors and sulphonylures than in group 2 receiving sulphonylureas alone, however there was no significant improvement in lipid parameters was seen in both the groups.

In the present study, there was no elevation in the pancreatic enzymes by the DPP4 inhibitors upon 12 week treatment. Presents study suggest that the use of DPP 4 inhibitors therapy is safe and effective, provided that they should not be used in subjects with acute pancreatitis.

Further studies are needed to evaluate the toxicity, effect of DPP 4 inhibitors on beta cells proliferation, insulin resistance and maintainance of beta cells function. Many studies reveal the effect of DPP4 inhibitors or immune system but to confirm these effects further studies are required. A abright future prospective for DPP 4 inhibitors is there, as they can play an important role and involves the potential use of pharmacological action of endogenous hormones to regulate glucosse levels. Dipetidyl peptidase-4 inhibitors are already considered as an important pharmacological class for the managemnet of T2DM, and will probably continue to increase their impact in the near future.

CONCLUSION

The present study revealed that incretin based therapy (i.e DPP4 inhibitors) may be the choice of treatment in Indian population with inadequately controlled type to diabetes mellitus. DPP4 inhibitors can be used in subjects with inadequarely controlled type to diabetes mellitus along with secretogogues based therapy (second generation sulphonylureas). DPP4 inhibitors similar efficacy as sulphonylureas but when used in combination provide a better glycemic control.

Higher proportion of patients achieved FBBS and PPBS target with DPP4 inhibitors group than with sulphonylureas group. The additive effect on glycemic improvement was more in DPP4 along with

sulphonylureas as compared to sulphonylureas alone..

Further studies are required to evaluate its effects on maintains of beta cell function, insulin resistananace and adverse effects on long terms use on pancreas and immune system.

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