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Original article:

A study of canagliflozin on post prandial blood sugar control

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ABSTRACT:

Introduction: Diabetes mellitus is now a leading cause of morbidity and mortality. SGLTR 2 inhibitors reduce proximal tubular glucose reabsorption and increases urinary glucose excretion. Canagliflozin is selected as the drug in this study for the treatment of control of PPG in TYPE 2 DM patients to see the effect without changing the base line medication.

Objectives: To observe the effect of Canagliflozin on postprandial blood glucose in Type2 DM.

Materials and Methods: Prior permission was obtained from Institutional Ethical Committee before study was undertaken in the Department of General Medicine of NRI Institute Of Medical Sciences, Sangivalasa, Visakhapatnam) on 100 patients admitted during January 2020 to December 2020.

Inclusion Criteria**:** The study will include Type 2 DM patient of >15 yr age having elevated FPG/ normal FPG with increasing PPG attended to this NRIIMS during study period.

Exclusion criteria (1) Pregnancy (2) Inflammatory bowel disease, IBS (3) Chronic Kidney Disease (4) Acute or chronic disease which may cause tissue hypoxia (4) Hepatic failure.

Results: Canagliflozin monotherapy is useful in the early stage Type2 DM with elevated post prandial plasma glucose. PPG results before and after therapy was of average 210 mg/dl and 130 mg/dl respectively after 24 wks. Patient on Biguanides when PPG is uncontrolled, adding Cangliflozin significantly reduced PPG in patients. Before and after therapy with Canagliflozin were on average 250 mg/dl and 146mg/dl respectively after 24 weeks.

Conclusion: Canagliflozin is very effective in controlling postprandial blood glucose either as monotherapy or with combination of other OHA or with Insulin.

INTRODUCTION:

Diabetes mellitus now a leading cause of morbidity and mortality.Type2 DM characterized by three Pathophysiological features 1) Impaired insulin secretion 2) Peripheral insulin resistance 3) Excessive Hepatic glucose production.[1] Type 2 DM patient are often hyper insulinemic but degree of hyperinsulinemia is inappropriately low for the glucose concentration. Clinically these patients demonstrate virtually absent 1st phase insulin and c- peptide response.[2,3,4] to i.v glucose, a reduced 2nd phase response and marked flattening of glucose insulin secretion dose response curve.[5] These patient also demonstrated abnormal temporal pattern of insulin secretion i.e. basal insulin secretion is greater and post prandial insulin secretion is attenuated.[2] Post prandial hyperglycemia (PPHG) is primarily due to decreased 1st phase insulin secretion. As insulin injection is not

always convenient by the people, oral anti diabetic drug is preferred. But there are insulin secretagogues which stimulate insulin and produce hypoglycemia.[1] Sodium glucose co transporter 2 inhibitors are devoid of this side effect. Sodium glucose co transporter2 inhibitors reduce proximal tubular glucose reabsorption and increases urinary glucose excretion. They significantly lower the HbA1c level in severe hyperglycemic Type 2 DM patients..It has been established that it is PPHG and not FPG which is the marker of cardiovascular disorder associated with diabetes with normal FPG.So controlling PPHG is imperative. Canagliflozin, a sodium glucose cotransporter (SGLT) 2 inhibitor, is also a low-potency SGLT1 inhibitor. This study tested the hypothesis that intestinal canagliflozin levels postdose are sufficiently high to transiently inhibit intestinal SGLT1, thereby delaying intestinal glucose absorption[5]**.** Canagliflozin is selected as the drug of choice in this study for the treatment of control of increasing PPG in TYPE 2 DM patients with rice as the staple diet to see the effect without changing the base line medication.

AIMS AND OBJECTIVES:

To observe the effect of Canagliflozin on postprandial blood glucose levels in Type2 DM.

MATERIALS AND METHODS:

Prior permission was obtained from Institutional Review Board / Institutional Ethical Committee before study was undertaken in the Department of Medicine of NRI Institute Of Medical Sciences, Sangivalasa, Visakhapatnam (Andhra Pradesh, INDIA) on 100 patients admitted during the year January 2020 to December 2020. Diagnosis is based on doing FPG, HbA1C, 2hr OGTT. Baseline medications should not be changed.

Only those cases having increased postprandial hyperglycemia were considered with Canagliflozin OD.BD doses.

Follow up of each case for 6 months.

Inclusion criteria

The study included Type 2 DM patient of >15 yr age having elevated FPG and normal FPG with increasing PPG attended to this NRIIMS during study period.

Exclusion Criteria

- Pregnancy
- Irritable bowel syndrome, inflammatory bowel disease
- Chronic Kidney Disease
- Acute or chronic disease which may cause tissue hypoxia such as:
  Hepatic insufficiency
  Acute alcohol intoxication, alcoholism

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RESULTS:

Table 1: Age and Sex Distribution.

Age(yrs)	Male	Female	Total
30 – 44	10	06	16
45 – 59	45	15	60
> 60	14	10	24
Total	69	31	100

Total 100 cases of Type 2 diabetes mellitus with various age group cases were enrolled in this study. Among the patents 69 cases were males (69%) and 31 cases were females (31%). Majority of the patients belong to 45 – 59 years (60%).

Table 2: Effect on plasma glucose levels 24 wks before and after Canagliflozin 100 mg administration without changing the base line treatment.

Sex and number of patients	2hr PPPG (mg/dl) before Canagliflozin therapy	2hr PPPG(mg/dl) after Canagliflozin therapy
Male (n = 69)	212	134.8
Female (n = 31)	209	128.9
Total (n = 100)	210	130.2

This study included total 100 cases of Type2 DM and was designed to evaluate the effects on 2hr PPG level. Before Canagliflozin therapy the mean PPPG was 210 mg/dl and after treatment (100mg, OD)it was decreased to 130 mg% at the end of 24weeks.The study showed that Canagliflozin significantly reduced the postprandial plasma glucose level at the end of 24 wks. ($p<0.0001$)

Table 3: Canagliflozin administration as an adjunct to Biguanide.

Sex and no. of patients	Plasma glucose level (mg/dl) during Biguanide therapy		Plasma glucose level(mg/dl) after Biguanide+Canagliflozin therapy	
	FPG	2hr PPPG	FPG	2hr PPPG
Male (n=69)	158.7	256.7	104.9	152.3
Female (n=31)	162.6	246.8	105.9	142.5

This study included total 100 cases of Type2 DM and was designed to evaluate the effects on 2hr PPG level. The average 2hr PPG in patients who are taking only metformin is 250 mg/dl. After starting therapy with Canagliflozin 100 mg the PPG values reduced to 146 mg/dl which is statistically significant.

DISCUSSION:

Post prandial plasma glucose contributes more to overall hyperglycemia in early stages of Type 2 DM. It is a direct and independent risk factor for cardiovascular complications. So controlling post prandial plasma glucose is imperative. Canagliflozin is selected as the drug of choice in this study because Canagliflozin effectively reduces PPG level without the disadvantages like additional burden on beta cell, hypoglycemia, weight gain and less side effects like abdominal discomfort, diarrhea and flatulence.[6,7]

In my study total 100 cases of type 2 DM are taken with various age group, majority of the people were between 45 – 59 yrs (60%). As per National Diabetes Statistics, the majority of diabetes population is in the age group 40-59 years (Table – 1). This study included total 100 cases of Type 2 DM was designed to evaluate the effects on 2hr PPG level. Before Canagliflozin therapy the mean PPPG 210mg/dl and after, it was decreased to 130mg/dl at the end of 24weeks. The study showed that Canagliflozin significantly reduced the postprandial plasma glucose at the end of 24wk. ($p<0.0001$) (Table – 2). In the present study, benefits of combination therapy of Biguanide + Canagliflozin was shown. Total 100 cases were taken with Biguanide alone having mean 2hrPPPG-256.7mg/dl in male and 246.8mg/dl in female. After adding Canagliflozin (dose 100mg, OD), 2hr PPG was reduced to 152.3mg/dl in male and 142.5mg/dlin female. Before and after therapy with Canagliflozin were on average 250 mg/dl and 146mg/dl respectively after 24 weeks (Table – 3).

So Canagliflozin significantly decreased postprandial plasma glucose level as an adjunct to Biguanide. The result suggested that the combined use of this sodium glucose cotransporter 2 inhibitor and Biguanides was effective in controlling plasma glucose in Type2 DM patients.

CONCLUSION:

Compared with placebo, canagliflozin treatment reduced postprandial plasma glucose and insulin excursions (incremental 0- to 2-h area under the curve [AUC_{0-2h}] reductions of 35% and 43%, respectively according to David et all. Canagliflozin significantly reduced postprandial blood glucose (mean difference − 40.2 mg/mL at 60 min) and increased postprandial total GLP-1 (mean difference 1.8 pg/mL at 60 min) during an MTT.

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