Effect of Pro-Kinetic Drugs on Post -Prandial Glycaemic Surge in Type 2 Diabetic Patients

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Abstract
Background: To study the effects of pro-kinetic agents on post-prandial glycaemia in type 2 diabetes mellitus.

Methods: In this comparative study one hundred and eighty patients with Type 2 diabetes mellitus and features of gastroparesis were randomly recruited. They were divided randomly into two groups of ninety each. Group I was given oral anti-diabetic agents and placebo. Group II was given oral anti-diabetic agents along with domperidone. Mean levels of glycaemic difference. Difference between Premeal and two hours postmeal and glycaemic levels were determined and compared in the two groups.

Results: Mean fasting blood sugar of Group I was 168.57 mg/dl and 2 hours postprandial was 296.73 mg/dl. In Group II mean fasting blood sugar was 201.24 mg/dl and mean 2 hours postprandial blood sugar was 296.42 mg/dl. Mean difference in fasting and 2 hours post prandial was 156.38 mg/dl and 114.15 mg/dl, respectively in Group I and II.

Conclusion: Mean difference between fasting and 2 hours postprandial blood sugar is significantly low in patients taking prokinetic drugs, as compared to the diabetics not taking pro-kinetic drugs.

Key words: Incretin;Glucagon like Peptide

Introduction
Gastric emptying is delayed in majority of patients with diabetes. This results in delayed delivery of macronutrients to intestine resulting in diminished incretin effect. As a result there is high post prandial glucose surge. Augmenting the gastric motility by the use of prokinetics optimises incretin secretion and decreases the post prandial glycaemic surge. Incretins are naturally occurring hormones released by the gut. Upon entry of macronutrients in small intestine, these augment insulin secretion from beta cells of pancreas. This helps in control of post prandial rise of glucose. This mechanism is altered in uncontrolled diabetic patients due to delayed gastric emptying.

Glycaemic response to meals is primarily controlled by delivery of carbohydrates into intestine and the subsequent release of insulin in response to absorbed glucose. These mechanisms are subject to regulation by gut hormones and neuro-transmitters. 1 Gastrointestinal tract is recognised as the largest endocrine organ of the body. The term incretins characteristically defines gastro intestinal hormones that act on pancreas to augment glucose dependant insulin secretion. 2 Incretins also inhibit gluconeogenesis by suppression of glucagon secretion and regulate gastrointestinal motility for controlled absorption of glucose from gut. 3 Incretins especially glucose dependant insulin trophic peptide (GIP) and glucagon like peptide (GIP-1) share the ability of controlling post prandial glucose excursion. 4 Upon entry of macronutrients in duodenum, incretins are released from the gut. 5 Gastric emptying time is significantly delayed in patients with diabetes. This may be due to hyperglycaemia or diabetic autonomic neuropathy. 6 In normal subjects as well as patients with diabetes the blood glucose response to oral carbohydrate as well as rate of gastric emptying are related. There is evidence that modulation of gastric emptying by dietary or pharmacological means can be used to optimise glycaemic control. 7 In patients with diabetic gastro paresis, delayed food entry to the intestine may delay incretin release and thus be a hindrance to post prandial glycaemic control. 8

Patients and Methods
This study was done in the diabetic clinic of Railway Hospital Rawalpindi. 180 patients with diabetes mellitus type 2 and clinical features of nausea, anorexia, bloating and early satiety were included in the study where as patients with pregnancy, old age, malignancy, known APD and patients on steroids and NSAIDS were excluded from the study. Patients were randomly divided into two groups of ninety each. One
group (group 1, control group) was given usual oral anti-diabetic medications with placebo. The second group (group 2, study group) was also given their usual oral anti-diabetic medicines along with Domperidone 10 mg, an oral prokinetic drug, in fasting state. Fasting blood sugar was estimated. One hour later both groups were given identical breakfast. Two hours after the breakfast, blood glucose levels were again measured in both groups. Difference between fasting and two hours post prandial blood sugars were compared between the two groups.

Results

Out of one eighty patients included in the study, ages ranged from 39 years to sixty years with mean age of 52.67 years. Mean age in group 1 was 52.13 years while in group 2 it was 53.15 years. Group 1 included 44 males and 46 females. Group 2 included 30 males and 60 females. Our analysis of data revealed that mean fasting blood sugar of group 1 was 168.57 mg/dl and mean 2-hour postprandial sugar 296.73 mg/dl. In group 2, mean fasting blood sugar was 201.24 mg/dl and mean 2 hour postprandial sugar was 296.42 mg/dl. Mean difference between two hour postprandial and fasting sugar in group 1 was 156.38 mg/dl. While in group 2 mean difference between two hour postprandial and fasting blood sugar was 114.15 mg/dl (p=0.03 in both groups)

Table 1: Comparison between diabetics with and without taking pro-kinetic drugs

<table>
<thead>
<tr>
<th></th>
<th>Group-I (not taking prokinetic drugs)</th>
<th>Group-II (taking prokinetic drugs)</th>
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</thead>
<tbody>
<tr>
<td>Total No of patients.</td>
<td>90(50%)</td>
<td>90(50%)</td>
</tr>
<tr>
<td>No of Male patients.</td>
<td>44(48.8%)</td>
<td>30(33.3%)</td>
</tr>
<tr>
<td>No of Female patients</td>
<td>46(51.1%)</td>
<td>60(66.6%)</td>
</tr>
<tr>
<td>Mean Age</td>
<td>52.13(SD 9.100)</td>
<td>53.15(SD 8.37)</td>
</tr>
<tr>
<td>Mean Fasting Glucose Level (mg/dl)</td>
<td>168.57(SD 12.082)</td>
<td>201.24(SD18.55)</td>
</tr>
<tr>
<td>Mean 2 Hours Post prandial Glucose Level (mg/dl)</td>
<td>296.73(SD9.38)</td>
<td>296.42(SD9.29)</td>
</tr>
<tr>
<td>Mean post prandial glycaemic Surge (mg/dl)</td>
<td>156.38(SD 10.04)</td>
<td>114.15(SD 8.01)</td>
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</tbody>
</table>

Discussion

Diabetes is a common clinical condition with substantial morbidity as well as mortality. The main goals of management are early diagnosis and optimal glycaemic control to prevent long term complications. Benefits of strict glycaemic control are well documented in UKPDS study. Glycosylated haemoglobin levels are dependent on both pre and post prandial level. Post- prandial levels of sugar play an active role in determining HbA1c levels. Post-prandial glucose excursions are affected by amount and nature of carbohydrate ingested, mechanical events occurring and hormones released by gut. Potential causes of post prandial hyperglycaemia include increased absorption of dietary sugar, increased carbohydrate digestion, decreased insulin secretion, increased glucagon or defects in glucose storage.

Gastric emptying is delayed in majority of patients with type 2 diabetes. “Incretin effect” describes the enhanced insulin response from orally ingested glucose compared with intra-venous glucose. Gastro intestinal hormones promoting the incretin effect are called incretins. It contributes to 60% of the postprandial insulin secretion. It is diminished in type 2 diabetes patients.

Glucagon like peptide(GLP-1) is an important incretin secreted by intestinal cells. Its secretion is dependent upon presence of nutrients in gut. Addition of pro-kinetics before meal facilitates macronutrient delivery to intestine optimising incretin secretion thus minimising post prandial glycaemic surge. In present study addition of prokinetic in the study group showed better post parandial glycaemic control as compared to control group. This suggests that addition of pro-kinetics before food can help in limiting post –prandial blood sugar surge. We compared results of our study with a study done by Stevens JE et al. He studied the role of Itopride a pro-kinetic in improving diabetic control and diabetic gastroparesis. In contrast to our observation he concluded that glycaemic control is not affected by be addition of pro-kinetic like Itopride. However analysis of Stevens JE study shows that all the patients enrolled were insulin requiring diabetics. Insulin is required in type2 diabetics when endogenous insulin secretion is diminished due to decrease in beta cell mass. This decreased beta cell mass might be responsible for impaired response to incretins even when they are adequately released by enhanced food delivery to intestine.
Conclusion
Augmenting the gastric motility by the use of prokinetics optimises incretin secretion and decreases the post prandial glycaemic surge.

References