

## Case study

### 55 YEAR OLD MALE WITH POST PRANDIAL HYPERGLYCEMIA

#### History

##### *H/o Present illness*

Mr. G. 55 year old retired gentleman presents to the physician for management of his diabetes.

##### *Past history*

Patient has been treated for Type 2 diabetes since the last 8 years. Also he has been under medication for hypertension since the last 8 years and dyslipidemia since the last 8 years

##### *Family history*

His father was a diabetic and hypertensive.

##### *Personal history*

The patient is a non smoker and does not consume alcohol.

#### Clinical examination

- Weight 80 kg,
- General examination normal, No pallor, cyanosis, clubbing or lymphadenopathy
- Pulse 80/min, regular, peripheral pulses well felt
- BP 130/90 mm of Hg.
- Systemic examination- normal
- Foot examination is normal
- Fundus examination Grade I non proliferative diabetic retinopathy

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## LABORATORY INVESTIGATIONS

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<b>Complete blood count</b> Hb WBC Differential count Platelets	12 g% 10, 300/mm <sup>3</sup> P <sub>62</sub> L <sub>26</sub> E <sub>4</sub> M <sub>8</sub> Adequate
<b>Blood glucose profile</b> Fasting blood glucose Postprandial blood glucose HbA <sub>1C</sub>	130 mg/dL 240 mg/dL 8.0%
<b>Lipid profile</b> Total cholesterol HDL-C LDL-C Triglycerides	200 mg/dL 39 mg/dL 103 mg/dL 150 mg/dL
<b>Renal function test</b> Blood urea nitrogen Creatinine	18 mg/dL 1.1 mg/dL
<b>Liver function test</b> SGPT	60 units
<b>Urine routine</b>	Sugar, ketones – negative; albumin - nil

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## OTHER INVESTIGATIONS

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- X-ray chest normal
- ECG normal
- 2D Echo normal

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## CURRENT MEDICATIONS

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His present medications include

- Glimepiride 2 mg daily twice daily
- Metformin sustained release preparations 1000 mg daily
- Telmisartan 40 mg daily
- Atorvastatin 10 mg at night
- Aspirin 75 mg at night

### Diagnosis;

This patient of type 2 DM with hypertension and dyslipidemia has raised post prandial blood glucose levels (240 mg%) inspite of treatment with metformin and glimepiride suggesting **post prandial hyperglycemia**.

### What is the importance of post prandial hyperglycemia?

- PPG is important to overall glycemic control and may be a better index of glucose regulation than FPG.
- Postprandial hyperglycemia is characterized by hyperglycemic spikes that induce endothelial dysfunction, inflammatory reactions and oxidative stress, which may lead to progression of atherosclerosis and occurrence of cardiovascular events.
- Postprandial hyperglycemia may predispose to progression of atherosclerosis and cardiovascular events.
- Postprandial hyperglycemia, but not fasting hyperglycemia, independently predicts the occurrence of cardiovascular events
- PPG levels be monitored as part of type 2 diabetes management, in addition to HbA<sub>1C</sub> and control and minimize the progression of microvascular and macrovascular abnormalities
- ACE guidelines recommend a treatment target for 2-h PPG levels of < 140 mg/dl (7.8 mmol/l),
- Importance of incorporating PPG measurements into the management of type 2 diabetes helps to maintain glycemic control and minimizes the progression of microvascular and macrovascular abnormalities

### Which are the OHAS which reduce PPG?

Traditional diabetic agents such as insulin and sulfonylureas predominantly lower fasting glucose and are less effective at reducing postprandial hyperglycemia. Although sulfonylureas target insulin secretion directly through the beta cell potassium channel, they may also have an impact on fasting and postprandial glycemia. However, the pharmacokinetics of the majority of these agents are not tailored toward acute insulin release, and therefore they do not correct abnormalities in early-phase insulin secretion. On the other hand, the pharmacokinetics and mechanisms of action of several agents are directed specifically at postprandial hyperglycemia. Such agents include the meglitinide class of drugs,  $\alpha$ -glucosidase inhibitors and thiazolidinediones. injectable glucagon-like peptide-1 (GLP-1) receptor agonists and oral dipeptidyl peptidase-4 (DPP-4) inhibitors

**What is the role of meglitinide analogues and thiazolidinediones in reducing PPG?**

The meglitinide analogues include repaglinide, nateglinide and mitiglinide, which are modern nonsulfonylurea secretagogues that restore the first-phase insulin response. A single dose of nateglinide has been shown to reduce postprandial endothelial dysfunction by lowering postload glycemia in patients with type 2 diabetes

The thiazolidinedione peroxisome proliferator-activated receptor- $\gamma$  (PPAR- $\gamma$ ) activating class of drugs, such as pioglitazone, are insulin-sensitizing agents and are not generally considered for their effects on insulin secretion. However, this class of compounds, when used in subjects with impaired glucose tolerance, may improve glucose-coupled insulin secretion and reduce the level of postprandial hyperglycemia

**What is the role of  $\alpha$ -glucosidase inhibitors in treating post prandial hyperglycemia?**

$\alpha$ -glucosidase inhibitors interfere with the breakdown of complex carbohydrates in the gut and, hence, with the absorption of dietary glucose. These agents must be taken with meals - carbohydrates must make up a minimum of 40% of the diet for these agents to be effective. Acarbose miglitol, voglibose are drugs in the class; available data support their use in the treatment of type 2 diabetes because they effectively lowers PPG and are not associated with weight gain.

**What is the role of glucagon-like peptide-1 (GLP-1) receptor agonists and DPPIV inhibitors in the management of post prandial hyperglycemia?**

GLP-1 receptor agonists, such as exenatide, stimulate nutrient-induced insulin secretion and reduce inappropriate glucagon secretion, whilst delaying gastric emptying and reducing appetite. These agents have a low risk of hypoglycaemia in combination with sustained weight loss.

Inhibition of dipeptidyl peptidase-4 (DPP-4) is a novel oral treatment for type 2 diabetes. DPP-4 inhibition increases insulin secretion and reduces glucagon secretion by preventing the inactivation of glucagon-like peptide-1 (GLP-1), thereby lowering glucose levels.

Dipeptidyl peptidase-4 inhibitors (sitagliptin, vildagliptin) are effective either as a single or combination therapy in lowering glycated hemoglobin, fasting and postprandial glucose levels, with a low incidence of hypoglycemia and no weight gain. The DPP-4 inhibitors, sitagliptin and vildagliptin, are generally weight neutral, and have less marked gastrointestinal adverse effects than the GLP-1 receptor agonists. Vildagliptin is generally well tolerated whether administered alone or in combination with glibenclamide or pioglitazone, and is not associated with hypoglycemia. Co-administration of vildagliptin with either glibenclamide or pioglitazone in patients with type 2 diabetes improves postprandial glycemic control without notable effects on drug pharmacokinetics

**Case Contd.**

Patient was given voglibose 0.4 mg with each meal. His PPG levels dropped to 154 mg/dL after treatment.