Relationship between postprandial Hyperglycemia and macroalbuminuria in type 2 diabetics

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Abstract:
Background: With the recent development of new methods to measure postprandial hyperglycemia and new treatment to modulate it, investigations have questioned whether postprandial hyperglycemia causes diabetic complications such as nephropathy.

Objectives
The aim of our study was to assess the influence of postprandial hyperglycemia on the incidence of nephropathy in patients with type 2 diabetics.

Patients and methods
The study was between 9/1/2008 to 14/11/2008. 100 patients attending diabetic clinic in Al-Dewania teaching hospital fulfilled in the criteria of the study. The patients investigated for macroalbuminuria. The patients divided into two groups according to the results of 2 successive measurements of post-challenge plasma glucose level (following 75 gm glucose solution) 2 weeks apart.

Results
Of total 100 patients with mild–moderate type 2 diabetes for last 5-7 years, about 68 patients (68%) had postprandial plasma glucose values >200 mg/dl, 32 (32%) patients of them had macroalbuminuria, whereas macroalbuminuria observed in 6 patients only (6% of total) in those with postprandial plasma glucose <200 (mg/dl total). Macroalbuminuria reported in 7 patients (of the total 100 had normal FPG). These findings suggest that patient with postprandial plasma glucose level >200 mg/dl had more albumin excretion rate which is the predictor of nephrology.
Introduction:

Diabetes mellitus is a chronic disease that affects approximately 200 million people in the world, more than 90% of whom have type 2 diabetes. Diabetes and the complication that result from it's ineffective management such as damage to kidneys, nerves and eyes, stroke, heart attack, and the need for amputation are now the fifth leading cause of death in the United States (2). The exact pathogenesis of type 2 diabetes mellitus is unknown, but the main factor is peripheral insulin resistance that results in hyperglycemia. Other factors include poorly regulated hepatic glucose production, impaired glucose tolerance, and declining beta cell function. After hyperglycemia occurs, the pre-existing pancreatic beta-cell dysfunction is worsened by glucotoxicity.

In healthy individuals, normal insulin secretion in response to intravenous glucose follows biphasic Pattern. A rapid sharp release of insulin into the portal circulation starts within minutes of glucose administration, lasts for about 10 min. and is followed by a slower and more prolonged phase of insulin release that begins at 10 min and lasts between 60-120 min. First phase of insulin secretion inhibits hepatic glucose production early in the absorptive state, whereas the second phase of secretion attenuates postprandial excursion by promoting glucose uptake by peripheral tissues. In individuals with type 2 diabetes, who have insulin resistance, the insulin secretary response can initially compensate for the insulin resistance; however, eventually, first-phase insulin secretion and second-phase secretion is impaired, causing postprandial hyperglycemia, one of the earliest markers of disease progression.

Convincing evidence has been reported that renal damage rarely occurs both in patients with 1 type and 2 diabetes when postprandial blood glucose levels <200mg/dl and glycated hemoglobin A1c is <7.5 to 8.0%). Growing awareness of the importance of PPG levels in the overall control of glycemia has led to the suggestion that PPG monitoring be integrated into routine diabetes care, particularly because patients diabetes may not be adequately controlled if monitoring is based on HbA1c and FPG data alone. Available data point toward the importance of incorporating PPG measurements into the managements of type 2 diabetes to help maintain glycemic control and minimize the progression of micro vascular and microvascular abnormalities. The new IDF (international diabetes federation) and AACE (American association of clinical endocrinologist) recombination for 2h PPG心境 -145mg, HbA1c < 6.5%& FBS = 80-110mg/dl (1). (2).

Patients and methods:

100 patients attending diabetes clinic in Al-dewaniha teaching hospital fulfilled the criteria of the study being (1) normotensive, (2) diagnosed to had mild-moderate types 2 diabetes (fasting plasma glucose are <200 mg/dl) for the last 6-7 years on regular treatment with diet control + 2.5-5mg glibenclamide daily, (3) the age: 40-55 years and (4) body weight (60-75Kg) i.e. exclude obese patients. All other possible causes of albuminuria had been excluded. The patients divided into two groups according to the results of 2 successive measurements of post-challenge plasma glucose (after 75 gm of glucose in liquid from ingestion) 2 weeks apart (those with PPG < 200mg/dl & those with PPG > 200mg/dl). Postprandial plasma glucose challenge is reliable predicator for postprandial hyperglycemia. Albumin detected by sensitive commercial reagent strips (detect albumin more than 150mg/l) plasma sugar measured by spectrophotometry.
Results:

FIGURE (1): distribution of patients according to presence or absence of PPH

FIGURE (2): distribution of patients with macroalbuminuria among total No. of patients, patients with PPH & those with no PPH
**Discussion**

Renal complication tends to occur after 5 years of duration of the disease, to reach a peak after 5 to 10 years, and thereafter rarely to occur. (5,17). Fig (1) revealed that 68% of patients with mild–moderate diabetes mellitus had PPH & this result should pay our attention to the extent of the problem in our patient. Avignon et al. found that post-lunch plasma glucose was more reliable in predicting poor glycemic control than pre-breakfast or pre-lunch plasma glucose. (3). Several other studies have also shown that post challenge and postprandial glucose values correlate better with HbA1c levels than do fasting/preprandial glucose values. (70). Furthermore, Soonthornpun et al. demonstrated that postprandial hyperglycemia, specifically the 2-h postprandial glucose level, is associated with high HbA1c levels. (20). For these reasons, clinicians should consider the use of PPG monitoring, in addition to FPG mentoring, in the management of type 2 diabetes (specially in the absence of measurement HbA1c levels in our country). Keeping in your mind that Solfanyurea inadequate treatment for postprandial hyperglycemia (22). Newer insulin secretagogues, such as repaglinide and nateglinide, and ultra short-acting insulin, such as insulin lispro and insulin aspart, had been used to reduce postprandial glucose level with great efficacy. (19) Fig (2) revealed high incidence of macroalbuminuria among those with PPG. Bastryr & colleagues confirmed that PPH.

In addition to being a marker for the onset of type 2 diabetes, PPG > 200 mg/dl appears to be associated with the development of renal complications of diabetes, independently of HbA1c and FPG levels. (4). Numerous epidemiological studies have shown elevated postprandial/post–challenge glucose to be independent and significant risk factor for diabetic nephropathy. (21). Similarly, after 11 years of follow-up in the Diabetes Intervention Study (DIS), newly diagnosed type 2 diabetic patients showed an association between mortality and PPG levels, independent of FPG levels. (15). In the retrospective DECODE analysis, more than 25,000 persons were studied for a mean period of 7.3 years.
Results demonstrated that PPG levels were associated with mortality, independent of FPG levels. (6) FPG levels were not significantly related to mortality after adjustment for PPG levels. (16). Similar to these findings, Jarret et al. found that the degree of risk conferred by the 2-h postprandial glucose concentration was nearly twice that conferred by HbA1c levels. (12). Further, recent studies by Stratton M et al. have demonstrated that even moderate postprandial hyperglycemia (148-199 mg/dl) is not only more indicative of atherosclerosis than is fasting glucose but, also may have direct adverse effect on the renal arteriolar endothelial cell and associated with an increase risk for nephropathy and retinopathy. (21). Indeed, in the mid-200 mg/dl range, the risk for nephropathy was increased by a factor of 10. (110. In addition, Golberg showed a relationship between PPG spikes and diabetic complication. (8). However, macroalbuminuria reported in 7 patients with normal FPS and Fig. (3), this findings is compatibles with many recent studies, the most important is Decode study. (6).

Although the American Diabetes Association (ADA) consensus panel did not specify a postprandial glucose target, it did recommended postprandial monitoring and therapy for type 2 diabetic patients with suspected postprandial hyperglycemia (2).

Recommendations:
Such evidence has led to recommendations that PPG levels should be monitored as part of type 2 diabetes management, in addition to HbA1C and FPG. Therapy to target elevated PPG level is needed to achieve an HbA1C below 7% and potentially reduce the risk for complications. Among the effective therapies available are alpha glucosidase inhibitors, such as acarbose, newer insulin secretagogue such as repaglinide and nateglinide; and ultra-short acting insulin such as insulin lispro and insulin aspart.

References: