Relationship between postprandial hyperglycaemia and Progression of Diabetic Nephropathy

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الخـــــلاصة: استهدفت الدراسة الوقوف على علاقة ارتفاع نسبة السكر في الدم بعد ساعتين من تناول 75 غم كلوكوز مع الاعتلال الكلوي السكري (ارتفاع نسبة الزلال في الادرار من علاماته المبكرة).كشفت الدراسة عن وجود علاقة وثيقة بين الاثنين بغض النظر عن نسبة السكر الصائم مما يثبت انه عامل مستقل ومن الضروري أخذه بنظر الاعتبار عند المعالجة

Summary:

BACKGROUND:

With the recent development of new methods to measure postprandial hyperglycemia and new treatments to modulate it, investigators have questioned whether postprandial hyperglycemia causes diabetic complications such as nephropathy.

OBJECTIVES:

the aim of our study was to assess the influence of postprandial hyperglycaemia on the incidence of nephropathy in patients with type 2 diabetes.)

Patients&METHODS:

112 patients attending diabetic clinic in Al-diwanyia teaching hospital fulfilled the criteria of the study. The patients investigated for macroalbuminuria. The patient divided into two groups according to the result of 2 successive measurements of post-challenge plasma glucose level (following 75 gm glucose solution)2 weeks apart .

RESULTS:

Of total 112 patients with mild-moderate type 2 diabetes for last 5-7 years, about84 patients(75%) had postprandial plasma glucose values>200 mg/dl, 69(82.1%) patients of them had macroalbuminuria,whereas macroalbuminuria observed in 6 patients only (25 % of total) in those with postprandial plasma glucose < 200 mg / dl total). Macroalbuminuria reported in 7 patients (of the total 112) had normal FPG.

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These findings suggest that patient with postprandial plasma glucose level >200 mg/dl had more albumin excretion rate which is the early predictor of nephropathy.

Abstract:

Measurement of glycosylated hemoglobin (HbA_{1C}) remains the gold standard for the assessment of glycemic control in patients with type 2 diabetes. Recent investigations have studied the correlation between HbA_{1C} levels and other aspects of glucose metabolism, specifically, postprandial glucose (PPG). The results suggest that PPG is also important to overall glycemic control and may be a better index of glucose regulation than no
effect on FPG. Thus, all aspects of glucose metabolism appear to be clinically relevant and should be monitored for effective diabetes management. This study defines the clinical significance of postprandial hyperglycaemia regarding the development of diabetic nephropathy.

Introduction:

Diabetes mellitus is a chronic disease that affects approximately 200million people in the world , more than 90% of whom have type 2 diabetes.(1) Diabetes and the complications that result from its ineffective management, such as damage to the 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.(10) 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. (10)

In healthy individuals, normal insulin secretion in response to intravenous glucose follows a biphasic pattern(18). 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 and 120 min.(18) First phase of insulin secretion inhibits hepatic glucose production early in the absorptive state, whereas the second phase of secretion attenuates postprandial excursions by promoting glucose uptake by peripheral tissues.(14) In individuals with type 2 diabetes, who have insulin resistance, the insulin secretory response can initially compensate for the insulin resistance; however, eventually, first-phase insulin secretion is lost, and second-

phase secretion is impaired, causing postprandial hyperglycemia, one of the earliest markers of disease progression.(10) Convincing evidence has been reported that renal damage rarely occurs both in patients with type 1 and 2 diabetes when postprandial blood glucose levels are <200 mg/dl and glycated hemoglobin A1c is <7.5 to 8.0%). (7) 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 HbA_{1C} and FPG data alone.(9) Available data point toward the importance of incorporating PPG measurements into the management of type 2 diabetes to help maintain glycemic control and minimize the progression of microvascular and macrovascular abnormalities.(4) the new IDF (international diabetes federation) and AACE (American association of clinical endocrinologist recommendation for2h PPG-145mg , HbA1c ≤ 6.5% & FBS=80-110mg\dl.(2)

Patients&Methods:

112 patients attending diabetic clinic in Al-diwanyia teaching hospital fulfilled the criteria of the study being (1)normotensive, (2)diagnosed to had mild-moderate type-2-diabetes(fasting plasma glucose are <200 mg/dl)for last 6-7 years on regular treatment with diet control + 2.5-5mg glibenclamide daily,(3)the age: 40-55 year 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 result of 2 successive measurements of post-challenge plasma glucose (after 75gm of glucose in liquid form ingestion) 2 weeks apart (those with PPG <200 mg / dl & those with PPG > 200 mg / dl).Postprandial plasma glucose challenge is reliable predictor for postprandial hyperglycaemia.Albumin detected by sensitive commercial reagent strips (detect albumin more then 150 mg / l). Plasma sugar measured by spectrophotometer.

Results:

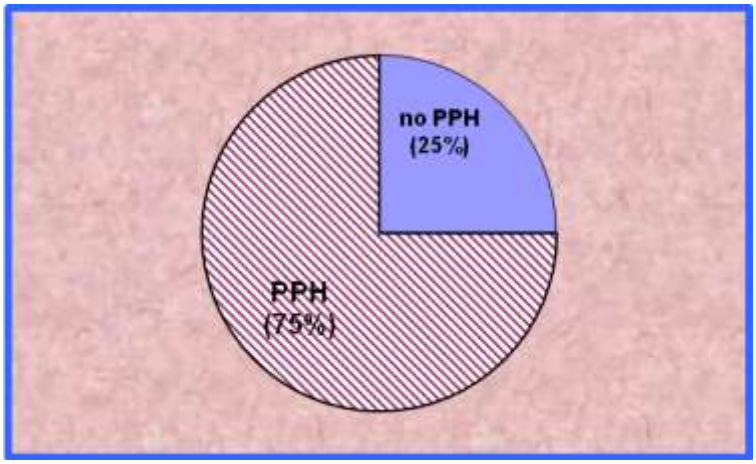
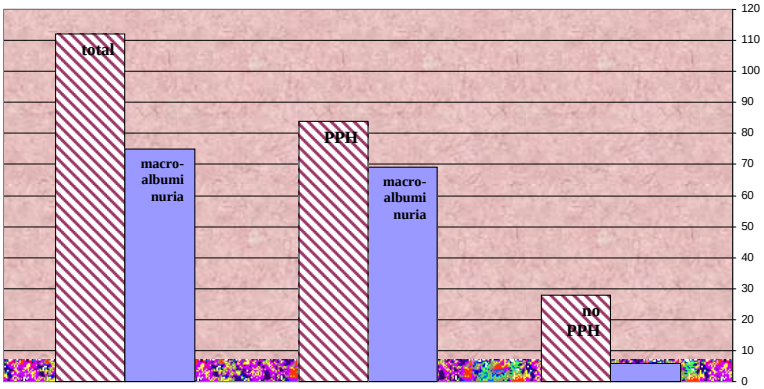


Figure (1): Distribution of patients according to presence &absence of PP



Figure(2): Distribution of patients with macroalbuminuria among total no.of patients,patients with PPH& those with non PPH

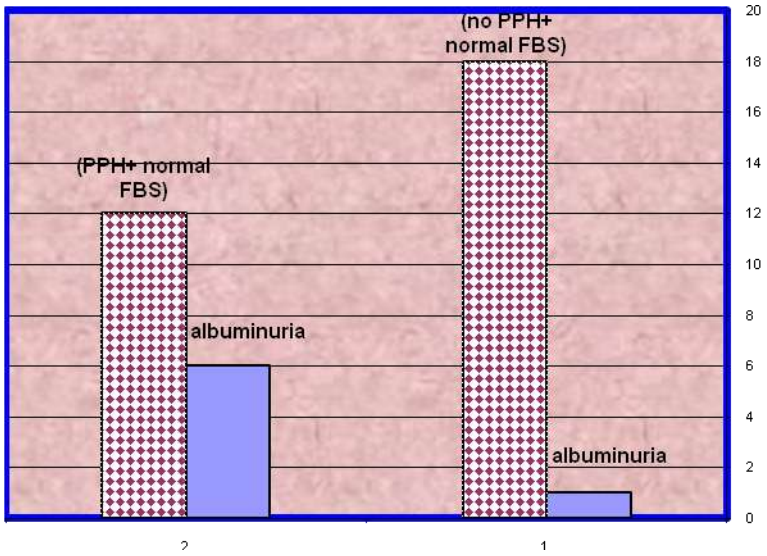


Figure (3): Distribution of patients with macroalbuminuria among those with normal FBS (with and without PPH)

Discussion:

Renal complications tend 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 75% of patients with mild –moderate diabetes mellitus had PPH & this result should pay our attention to the extent of yhe problem in our patients.Avignon et al. found that post-lunch plasma glucose and extended 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 postchallenge and postprandial glucose values correlate better with HbA1c levels than do fasting/preprandial glucose values.(7) 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 monitoring, in the management of type 2 diabetes (specially in the absence of measurement HbA1c levels in our country).Keeping in your mind that Solfanylurea inadequate treatment for postprndial

hyperglycaemia.(22) Newer insulin secretagogues, such as repaglinide and nateglinide; and ultra short-acting insulin, such as insulin lisp ro and insulin aspart had been used to reduce postprndial glucose level with great efficacy.(19) Fig.(2) revealed high incidence of macroalbuminuria among those with PPH.Bastryr & colleugs confirmed thatPPH

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 factors 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 level.(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 artherosclerosis than is fasting glucose, but also may have direct adverse effects on the renal arteriolar endothelial cells& associated with an increased risk for nephropathy and retinopathy.(21) Indeed, in the mid-200 mg/dl range, the risk for nephrophathy was increased by a factor of 10.(11) In addition, Goldberg showed a relationship between PPG spikes and diabetic complications.(8) However macroalbuminuria reported in 7 patients with normal FPS & fig.(3),this finding is compatable 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 recommend 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 levels 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 secretagogues, such as repaglinide and nateglinide; and ultra short-acting insulin, such as insulin lispro and insulin aspart .

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