

Postprandial Dysmetabolism (Postprandial Hyperglycemia and Hypertriglyceridemia) in Type 2 Diabetes Patients

Kuntarattanakool M¹, Isarakul N¹, Tangvarasittichai O¹ and Surapon Tangvarasittichai^{1*}

Chronic Diseases Research Unit, Department of Medical Technology, Faculty of Allied Health Sciences, Naresuan University, Phitsanulok 65000, Thailand

Article Info

***Corresponding author:**

Surapon Tangvarasittichai

Associate Professor
Department of Medical Technology
Faculty of Allied Health Sciences
Naresuan University
Phitsanulok, 65000
Thailand
Tel: +66-08-9638-8382
Fax: +66-0-5596-6300
E-mail: surapon14t@yahoo.com

Received: April 27, 2018

Accepted: June 11, 2018

Published: June 16, 2018

Citation: Kuntarattanakool M, Isarakul N, Tangvarasittichai O, Tangvarasittichai S. Postprandial Dysmetabolism (Postprandial Hyperglycemia and Hypertriglyceridemia) in Type 2 Diabetes Patients. *Madridge J Diabetes*. 2018; 2(1): 47-50. doi: 10.18689/mjd-1000109

Copyright: © 2018 The Author(s). This work is licensed under a Creative Commons Attribution 4.0 International License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Published by Madridge Publishers

Abstract

Postprandial dysmetabolism [postprandial hyperglycemia (PPG) and postprandial hypertriglyceridemia (PPTG)] was used as a cardiovascular disease (CVD) risk factor and as the biomarker for carbohydrates and lipids homeostasis assessment. Postprandial dysmetabolism is an underlying risk in type 2 diabetes mellitus (T2DM) patients even their have good control fasting glucose (FGlu) and triglyceride (FTG) levels. We tried to evaluate the postprandial dysmetabolism in T2DM patients. Twenty five T2DM patients, who reached the criteria volunteered to participate and answered the questionnaires in the present study. Anthropometric and blood pressure (BP) were measured. All patients were received their regular medication. Fasting blood samples were collected for plasma Glu, total cholesterol (TC) and TG analysis as in Fasting (F) condition. After that all patients received a conventional meal type as their lifestyle in everyday with a duration time about 10-15 min. Then, blood samples were drawn after 2 hour of this meal load as Postprandial condition. These patients were older, obese with good control on FGlu and FTG levels and demonstrated PPG with 41.83% Glu retention and PPTG with 17.30% TG retention after 2 hours of meal load. There is no significant change in FTC and PPTC levels. FGlu, FTC, FTG, PPG and PPTG were significantly correlated with PPG, PPTC, PPTG, % Glu retention and %TG retention. Conclusion, postprandial dysmetabolism is the good biomarker for CVD risk factor and the carbohydrates and lipids homeostasis assessment after meal load, especially in T2DM and obese patient even their apparently good Glu and TG control.

Keywords: Postprandial dysmetabolism; Postprandial hyperglycemia; Postprandial hypertriglyceridemia; Cardiovascular disease risk factor, Type 2 diabetes mellitus.

Introduction

It is well recognized that cardiovascular disease (CVD) is a major complication of patients with and type 1 and type 2 diabetes mellitus (T2DM) [1]. Individuals with diabetes have two- to four-fold increased risk of CVD morbidity and mortality [1]. The management of CVD risk remains an important goal of treatment in diabetes patients. Indeed, hyperglycemia, hypertension, obesity, hypertriglyceridemia, and hypercholesterolemia, coexisting conditions that often contribute to CVD in T2DM patients. These comorbidities do not explain all of the excess CVD risk in T2DM patients. Recent in the understanding of the role of insulin physiology implicate postprandial hyperglycemia (PPG) as the major driver of the increased CVD risk in T2DM patients and prediabetes obesity. Impaired glucose tolerance (IGT) condition was demonstrated as the first-phase of insulin response, while PPG was demonstrated as the early events in the T2DM progression.

Postprandial dysmetabolism was used as a new biomarker for carbohydrates and lipids homeostasis assessment. The conventional fasting state risk factors were evaluated for CVD risk, while postprandial dysmetabolism was a postprandial state distinguished by abnormally increased glucose and lipids levels in circulation, as the constitutes an independent risk factor for the onset of cardiovascular events [2]. Postprandial hyperglycemia may increase CVD risk by several mechanisms by which insulin may confer as the cardioprotective hormone, as antioxidant, antithrombotic, anti-inflammatory and vasodilatory effects, which are independent of its glucose-lowering activity. Therefore, controlling elevated PPG may a key step to reduce CVD risk in T2DM patients or prediabetes. Postprandial dysmetabolism in lipids is characterized by elevated triglycerides (TG) levels and its remnant lipoprotein particles (RLPs), as postprandial hypertriglyceridemia (PPTG) [2]. Insulin also plays a major role in the regulation of lipid homeostasis and balancing between lipolysis and lipogenesis, since it stimulates lipid synthesis and adipogenesis and inhibits lipolysis [3]. This present study tried to evaluate the postprandial dysmetabolism occurred in T2DM patients as CVD risk.

Materials and Methods

Subjects

A total of 25 T2DM patients (overt diabetes >10 years) were randomized from the general population in our district. These T2DM patients were diagnosed and received medications from any hospital in our district during Novemberto December 2017. All T2DM patients were given regular treatment with glycemic lowering, lipid lowering, and anti-hypertensive medication. Exclusion criteria wasun-control glucose and TG levels, heart failure, peripheral vascular disease, recent myocardial infarction, unstable angina, stroke, acute or chronic infection, cancer, hepatic disease, acute illness. All participants gave written informed consent. Our study protocol was approved by the Ethic committees of Naresuan University.

Physical and Biochemical Examination

All T2DM underwent anthropometry, blood pressure measurement and physical examination. Body mass index (BMI) was calculated andwaist circumference (WC) was measured at the midpoint between the rib cage and the top of lateral border of iliac crest at minimum respiration. BP was measured after the participants had been seated and rested for 5 minutes, as the mean value of at least two measurements for these participants on the same day with calibrated desktop sphygmomanometers. Venous blood samples were collected from all participants without stasis after 8-12 hour fast in a seated position as Fasting (F) condition.

Oral Glucose Tolerance Test (OGTT)

A 75-g of glucose was performed following after the overnight fasting blood drawing as in the conventional method. But in present study, all T2DM patients received a conventional meal type as their lifestyle in every day with aduration time about 10-15 min. Then, blood samples were drawn at 2 hour after meal load as postprandial condition.

Percentage Retention of Glucose and Triglycerides

The formula: [%Matter retention = (Concentration of matter at Postprandial condition - Concentration matter of at fasting condition)* 100/ Concentration matter of at Fasting condition] was used to estimate percentage retention of Glu and TG in plasma at the end of 2 hours. Blood specimens were processed and assayed in the clinical laboratory of Chronic Diseases Research Unit, Department of Medical Technology, Faculty of Allied Health Sciences, Naresuan University, Phitsanulok, Thailand. Plasma glucose (Glu), serum total cholesterol (TC) and triglycerides (TG) were measured by enzymatic method by using calibrators and control materials from Roche Diagnostics (Roche Diagnostic, Switzerland).

Classification of Glucose and Triglycerides Tolerance

Postprandial glucose tolerance was classified according to WHO criteria [4] as follows: (i). Normal glucose tolerance (NGT): Post load glucose <140 mg/dl (ii). Impaired glucose tolerance (IGT): Post load glucose 140–200 mg/dl (iii). Diabetes: postload glucose ≥200 mg/dl. According to the National Cholesterol Education Program [5], patients can be divided into 4 groups according to their TG levels: (i). normal TG (< 150 mg/dL), (ii). Borderline-high TG (≥ 150-199 mg/dL), (iii). high TG (≥ 200 - 499 mg/dL), and finally, (iv). very high TG (≥ 500 mg/dL).

Statistical Analysis

All data are presented as median and interquartile range for non-normally distributed data, tested by using Shapiro-Wilk test. All clinical characteristics of Fasting condition and postprandial condition were compared by using Wilcoxon Signed Ranks test and bivariate correlation between these clinical variables was assessed by using Spearman rank correlation test. All tests were two tailed, and *p*-values less than 0.05 were regarded as statistically significant. All analysis was performed by SPSS version 13.0 (SPSS, Chicago, IL, USA).

Results

These T2DM patients were older, had a longer duration of diabetes [15.4 (9.1-18.7)], obesity and abdominal obesity with good control of their blood pressure, glycemic and lipidemic status at Fasting condition. While demonstrated postprandial dysmetabolism, [(PPG: 12 were mild PPG and 13 severe PPG) and [(PPTG: 6 were normal PPTG, 10 wereborderline-high TG and 9 were high TG) as shown in Table 1.

Table 1. Clinical characteristics of patients with type 2 diabetes mellitus on fasting and postprandial condition

Variables	Fasting condition (n=25)	Postprandial condition (n=25)	p-value
Age (Years)	69.5(55.4-74.5)	-	-
BMI (kg/m ²)	25.4(23.6-27.5)	-	-
WC (cm)	92.5(88.4-96.8)	-	-
Syst BP (mmHg)	136.0(120.0-147.5)	-	-
Diast BP (mmHg)	78.0(64.8-87.3)	-	-
Glu (mg/dl)	145.99(130.14-163.50)	217.06 (173.22-283.79)	<0.001
TC (mg/dl)	161.88 (153.52-186.01)	168.72 (153.52-186.01)	0.421
TG (mg/dl)	138.01 (126.42-188.52)	168.97 (146.30-222.77)	<0.001
% Glu retention	-	41.83 (18.34-77.96)	-
%TG retention	-	17.30 (8.14-25.9)	-

The results demonstrated postprandial dysmetabolism with 41.83% (18.34%-77.96%) of Glu retention and 17.30% (8.14%-25.9%) of TG retention in circulation after 2 hours of meal load. There is no significant change in FTC and PPTC levels. Bivariate correlation, FGLu, FTC and FTG were significantly correlated with each other of PPG, PPTC and PPTG ($r=0.583$, $p=0.002$; $r=0.789$, $p<0.001$, and $r=0.711$, $p<0.001$) respectively, while PPG, PPTG were significantly correlated with %Glu retention and %TG retention ($r=0.610$, $p<0.001$; $r=0.549$, $p=0.004$) respectively, as shown in Table 2.

Table 2. Correlation of Glu, TC and TG levels on fasting and postprandial condition in type 2 diabetes patients.

Correlation between parameters		Correlation coefficient	
r		p-value	
Fasting Glu	Postprandial Glu	0.583	0.002
Fasting TC	Postprandial TC	0.789	<0.001
Fasting TG	Postprandial TG	0.711	<0.001
Postprandial Glu	%Glu Retention	0.610	<0.001
Postprandial TG	%TG Retention	0.549	0.004

These correlations may result from the linear insulin action or dysregulation in their physiological conditions, with the same insulin sensitivity in each phase of action.

Discussion

As expected, blood Glu levels were higher in T2DM patients at fasting state and remained higher at the postprandial state. Because of the plasma insulin response to the meal was more important in T2DM patients. Insulin action on Glu and TG homeostasis is to reduce the PPG and PPTG levels as follows: (i). Increased glucose uptake by peripheral tissues (skeletal muscles) is mediated via glucose transporters proteins, GLUT4, a major regulator of whole-body glucose homeostasis and stimulated by insulin [6]. (ii). promoted glycogen synthesis (iii) inhibited glucagon secretion, inhibited or reduced Glu and VLDL production by the liver [7]. Hence, the postprandial dysmetabolism is determined by carbohydrate and lipid absorption, insulin dysregulation and glucagon secretion, and their coordinated effects on Glu and TG metabolism in the liver and peripheral tissues.

Postprandial hypertriglyceridemia is more frequent in patients with T2DM and insulin resistance states. In the present study, many of these T2DM patients, despite normal FTG levels, had TG levels >200 mg/dl during the postprandial condition. This condition may indicate that most T2DM patients have plasma TG above the desired level for many hours after the meals. Moreover, the present study suggests that TG levels at fasting state may not always a good predictor of the normal TG metabolism in the postprandial state. In these T2DM patients, there are multiple abnormalities of lipoproteins of both endogenous and exogenous origin.

There are a large number of lipoprotein particles, as TG levels increased in these T2DM patients. This rising was used as a marker of the postprandial dysmetabolism state. Therefore, T2DM patients have PPG and PPTG even if they had good control for their FGLu and FTG normal levels.

Many research studies demonstrated that PPG and PPTG increase oxidative stress by elevated ROS production, as the major role of the diabetes complications, such as activated prothrombotic pathways [8], increases intercellular adhesion molecule-1 (ICAM-1), proinflammatory cytokines and transcription factors, such as nuclear factor kappa B (NF-κB), activator protein-1, early growth response factor-1 (Egr-1), hypoxia-inducible factor-α [9], increased carotid intima-media thickness [10], and endothelial dysfunction and atherosclerosis [11]. Thus, these T2DM patients with postprandial dysmetabolism (PPG and PPTG) are at CVD risk. Hence, it is important to identify postprandial dysmetabolism of T2DM or any insulin resistance state patients who apparently have good metabolic control, but may be at CVD risk. Plasma Glu and TG levels of PPG or post meal load test are more powerful predictor of CVD risk and progression of diabetic retinopathy than HbA1C or FPG levels [12, 13]. While PPTG was demonstrated more potent predictor of CVD risk than fasting TG [14].

Guidelines for management and treatment of PPG in T2DM recommend to use self-monitoring of blood glucose (SMBG) for glucose levels assessment, but may design the timing and frequency of SMBG for individualized with T2DM [15]. Fortreatment of postprandial dysmetabolism are dietary modification, exercise, weight loss and medication (insulin analogue, meglitinides (repaglinide and nateglinide), GLP1 receptor agonists (exenatide, exenatide LAR, liraglutide, lixisenatide), DPP4 inhibitors (sitagliptin, vildagliptin, saxagliptin, alogliptin, linagliptin), statins, ezetimibe, fibrates). Insulin degludec is developed as long-acting insulin analogue, insulin as part is fast acting insulin analogue which allows patients to adjust their insulin according to any changes [16, 17].

Conclusion

Postprandial dysmetabolism as PPG and PPTG is a non-fasting state demonstrated by elevated levels of plasma glucose and triglyceride after meal load. Many research and epidemiology studies demonstrated that postprandial dysmetabolism contributes to develop atherosclerosis and increased CVD risk morbidity and mortality. Postprandial dysmetabolism in T2DM patients contributes to cause macro- and micro vascular complications from the development of endothelial dysfunction and cardiovascular damage via oxidative stress and inflammation activation.

Acknowledgement

We sincerely thank Naresuan University and all co-workers of Clinical Laboratory of Department of Medical Technology, Faculty Allied Health Sciences for their technical assistance and supporting. We especially thank those who participated and donated blood samples for this study. Finally, we sincerely thank Asst. Prof. Dr. Ronald A. Markwardt, Burapha University, for his reading and correcting of the manuscript.

Conflict of Interest

The authors declare that they have no competing interests.

References

1. Duca L, Sippl R, Snell-Bergeon JK. Is the risk and nature of CVD the same in type 1 and type 2 diabetes? *Curr Diab Rep.* 2013; 13(3): 350-361. doi: 10.1007/s11892-013-0380-1
2. O'Keefe JH, Bell DS. Postprandial hyperglycemia/hyperlipidemia (postprandial dysmetabolism) is a cardiovascular risk factor. *Am J Cardiol.* 2007; 100(5): 899-904. doi: 10.1016/j.amjcard.2007.03.107
3. Saponaro C, Gaggini M, Carli F, Gastaldelli A. The subtle balance between lipolysis and lipogenesis: a critical point in metabolic homeostasis. *Nutrients.* 2015; 7(11): 9453-9474. doi: 10.3390/nu7115475
4. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabetic Medicine.* 1998; 15(7): 539-553. doi: 10.1002/(SICI)1096-9136(199807)15:7<539::AID-DIA668>3.0.CO;2-S
5. Executive Summary of the Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). *JAMA.* 2001; 285(19): 2486-2497. doi: 10.1001/jama.285.19.2486
6. Huang S, Czech MP. The GLUT4 glucose transporter. *Cell Metab.* 2007; 5(4): 237-252. doi: 10.1016/j.cmet.2007.03.006
7. Aronoff SL, Berkowitz K, Shreiner B, Want L. Glucose Metabolism and Regulation: Beyond Insulin and Glucagon. *Diabetes spectrum.* 2004; 17(3): 183-190. doi: 10.2337/diaspect.17.3.183
8. Ceriello A. Postprandial hyperglycemia and diabetes complications. Is it time to treat?. *Diabetes.* 2005; 54(1): 1-7. doi: 10.2337/diabetes.54.1.1
9. Dandona P, Chaudhuri A, Ghanim H, Mohanty P. Antiinflammatory effects of insulin and pro-inflammatory effects of glucose: Relevance to the management of acute myocardial infarction and other acute coronary syndromes. *Rev Cardiovasc Med.* 2006; 7(Suppl 2): S25-S34.
10. Esposito K, Giugliano D, Nappo F, Marfella R. Campanian Postprandial Hyperglycemia Study Group. Regression of carotid atherosclerosis by control of postprandial hyperglycemia in type 2 diabetes mellitus. *Circulation.* 2004; 110: 214-219. doi: 10.1161/01.CIR.0000134501.57864.66
11. Lacroix S, Rosiers CD, Tardif JC, Nigam A. The role of oxidative stress in postprandial endothelial dysfunction. *Nutr Res Rev.* 2012; 25(2): 288-301. doi: 10.1017/S0954422412000182
12. Wajchenberg BL. Postprandial glycemia and cardiovascular disease in diabetes mellitus. *Arq Bras Endocrinol Metab.* 2007; 51(2): 212-221. doi: 10.1590/S0004-27302007000200010
13. Shiraiwa T, Kaneto H, Miyatsuka T, et al. Postprandial hyperglycemia is a better predictor of the progression of diabetic retinopathy than HbA1c in Japanese type 2 diabetic patients. *Diabetes Care.* 2005; 28(11): 2806-2807. doi: 10.2337/diacare.28.11.2806
14. Berglund L, Brunzell JD, Goldberg AC, et al. Evaluation and treatment of hypertriglyceridemia: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2012; 97: 2969-2989. doi: 10.1210/jc.2011-3213
15. International Diabetes Federation Guideline Development Group. Guideline for management of postmeal glucose in diabetes. *Diabetes Res Clin Pract.* 2014; 103(2): 256-268. doi: 10.1016/j.diabres.2012.08.002
16. Mayer B, Davidson. Early insulin therapy for type 2 diabetic patients: More cost than benefit. *Diabetes Care.* 2005; 28(1): 222-224. doi: 10.2337/diacare.28.1.22
17. Sanjay Kalra. Insulin Degludec As part: The First Co-formulation of Insulin Analogues. *Diabetes Ther.* 2014; 5(1): 65-72. doi: 10.1007/s13300-014-0067-x