Role of lipase in glucose and lipid metabolisms

Oluwole O. Adedeji, FMC (Path), PhD, George K. Oyakhire, MSc, FRCOG, Dan M. Ene, MD, FRCP, Saeed A. Al-Ghamdi, CABS, FRCS.

ABSTRACT

Objective: To investigate the role of lipase in glucose and lipid metabolisms.

Methods: A prospective study involving 52 diabetics (28 males and 24 females, mean age 47.67 ± 15.63 years) and 118 normoglycemic controls (39 males and 79 females, mean age 38.91 ± 16.61 years) was conducted, between February 1st and August 31st, 2006, at King Abdullah Hospital, Bisha, Saudi Arabia. After 10-12 hours fasting, blood was taken from subjects and controls for the determination of glucose, total cholesterol, triglyceride, low-density lipoprotein (LDL)-cholesterol, high density lipoprotein (HDL)-cholesterol, and lipase. The results were analyzed by student's t-test and Pearson correlation coefficient.

Results: The levels of glucose, total cholesterol, triglyceride, LDL-cholesterol, and lipase were significantly more in the diabetics ($p<0.05$). However, HDL-cholesterol was less in the diabetics than the controls, although the difference was not significant ($p>0.05$). There were significant positive correlations between glucose, total cholesterol, triglyceride, and lipase; while, significant negative correlations were obtained between LDL-cholesterol, HDL-cholesterol, and lipase.

Conclusion: The higher concentrations of glucose, total cholesterol, triglyceride, and LDL-cholesterol, as well as the lower HDL-cholesterol in the diabetics were typical and not unexpected, as diabetes mellitus is associated with disturbance of lipid metabolism. The lipase activity was elevated at increased concentrations of glucose and lipids. Hence, it was concluded that the pancreatic lipase was possibly involved in the metabolisms of both glucose and lipids. Lipolysis has been suggested as the link between the 2 processes.

Saudi Med J 2007; Vol. 28 (6): 841-843

From the Department of Pathology and Laboratory Services, King Abdullah Hospital, Bisha, Kingdom of Saudi Arabia.

Received 14th October 2006. Accepted 11th February 2007.

Address correspondence and reprint request to: Dr. Oluwole O. Adedeji, Department of Pathology and Laboratory Services, PO Box 60, Bisha, Kingdom of Saudi Arabia. Tel. +966 (7) 6223333 Ext. 1149. E-mail: adedeji12us@yahoo.com

Lipases are glycoproteins with a molecular weight of 47,000 daltons. They catalyze the hydrolysis of triglycerides, diglycerides, and cholesteryl esters with subsequent formation of monoglycerides and fatty acids.[1,2] Lipases play an important role in the regulation of lipolysis in fat cells. They are sensitive to neurotransmitters and hormones including catecholamines and insulin, which stimulate or inhibit their activity.[2]

Clinically, the blood lipase levels are associated with pancreatic diseases. The lipase activity increases in acute pancreatitis. Furthermore, changes in lipase activity have also been linked to diabetes mellitus,[3] implying a role for lipase in the regulation of blood glucose level. This study is designed to provide further evidence of the association between pancreatic lipase activity, glucose, and lipid metabolisms in humans. The results could, also, be used to confirm the usefulness of lipase determination in the management of diabetes mellitus.

Methods. This is a prospective study involving 52 diabetic patients (28 males and 24 females, mean age 47.67 ± 15.63 and range 20-92 years) attending the Lipid Clinic and 118 normoglycemic individuals, serving as controls (39 males and 79 females, mean age 38.91 ± 16.61 and range 14-78 years). The study was conducted between February 1st and August 31st 2006, at the King Abdullah Hospital, Bisha, Saudi Arabia. Consent from the subjects and approval of the Hospital Ethical Committee was obtained. Blood was taken from the subjects into heparinized tubes, centrifuged at 5,000 rpm for 5 minutes and the plasma separated. Fasting plasma glucose, total cholesterol, triglyceride, high density lipoprotein (HDL)-cholesterol, and pancreatic lipase were determined using Cobas Integra Biochemistry Auto-analyzer with reagents supplied by Roche Company. Fasting plasma glucose (10-12 hours) ≥7.8 mmol/l was considered as hyperglycemia. The analysis of pancreatic lipase involved cleavage of a chromogenic substrate, 1, 2-O-dilauryl-

rac-glycero-3-glutaric acid-(6>methylresorufin) ester, emulsified with bile acids, releasing glutaric acid and methylresoruffin.[4]

The SPSS version 10.0 software package was used for statistical analysis of Student's t-test and Pearson correlation coefficient. A *p*-value for differences between means <0.05 was considered as significant. Also, Pearson correlation coefficient (r)=0.01 was considered as significant.

Results. The results show that the mean values of glucose, total cholesterol, triglyceride, low-density lipoprotein (LDL)-cholesterol, and lipase were significantly higher in the diabetics than the controls ($p<0.05$). However, the mean value of HDL-cholesterol was lower in the diabetics than the controls, although the difference was not significant ($p>0.05$). Furthermore, the results show significant positive correlations between glucose (+0.305), total cholesterol (+0.055), triglyceride (+0.200), and lipase. Whereas, significant negative correlations were obtained between LDL-cholesterol (-0.029), HDL-cholesterol (-0.070) and lipase (**Table 1**).

Discussion. Diabetic patients attending the lipid clinic provided an opportunity to assess the role of lipase in the metabolisms of glucose and lipid, as well as the usefulness of its determination in the management of diabetes mellitus. The pattern of change of the lipid profiles of the diabetics from the normal was typical and not unexpected as diabetes mellitus is associated with such disturbance of lipid metabolism. A survey in the population of United States of America showed that the mean total cholesterol and LDL-cholesterol levels were approximately 10% higher, HDL-cholesterol levels were 5-10% lower; while, triglyceride levels were significantly higher (180 versus 116 mg/dl) among diabetic individuals.[5] Thus, diabetes mellitus is usually characterized by a dyslipidemic profile showing elevations of plasma total cholesterol and triglyceride as well as reduced HDL-cholesterol. Generally, the results show that lipase was involved in glucose and lipid metabolisms. Thus, the lipase activity increased at elevated levels of glucose, cholesterol, and triglyceride. Furthermore, the results indicate that the levels of LDL-cholesterol and HDL-cholesterol decreased with increasing lipase activity. This is because the hydrolysis of cholesterol by lipase makes it unavailable for the formation of LDL-cholesterol and HDL-cholesterol. The lipids, cholesterol and triglyceride, are recognized as the natural substrates for lipase during lipolysis. A plausible explanation for the association between glucose and lipase could be that lipolysis might be involved in glucose metabolism. The suggested mechanism is that free fatty acids or other lipid intermediates generated during lipolysis serve as signaling molecules that are linked to the regulation of insulin secretion.[4,6] Thus, it was shown that in fasting humans, efficient glucose stimulated insulin secretion is absolutely dependent on elevated free fatty acids.[7] Also, it has been reported that the lipid derived signals probably participate in the transduction process implicated in the stimulation of insulin release, which is promoted by fuel stimuli.[3,8] The proposed lipid derived molecules such as c-kinase activator, diacylglycerol, long chain acyl CoA esters and phospholipids, act as coupling factors to fuel signaling.[9] The calculated reference ranges of plasma pancreatic lipase activity for the normoglycemic individuals was 28.18–32.18 U/L and for diabetic patients was 34.37–44.27 U/L. Therefore, a reasonable deduction is that pancreatic lipase level > 40 U/L (namely, control mean ± 2SD) may be associated with hyperglycemia. Hence, the level of pancreatic lipase activity could indicate the degree of glycemic control. Also, determination of lipase has an added advantage of aiding in the diagnosis of pancreatic disorders, which are the major causes of hyperglycemia.[10]

In conclusion, the results have shown that pancreatic lipase plays an important role in the metabolism of glucose and lipid. The suggested mechanism is the association between lipolysis and insulin secretion. Furthermore, pancreatic lipase determination could be useful in the management of diabetes mellitus.

Table 1 - Results of glucose, total cholesterol, triglyceride, low density lipoprotein-cholesterol, and lipase.

Analytes	Diabetics (n=52) mean ± SD	Controls (n=118) mean ± SD	*P* value	Correlation coefficient (r) with lipase
Glucose mmol/l	12.47 ± 3.32	5.64 ± 0.82	<0.05	+0.305
Total cholesterol mmol/l	5.21 ± 1.40	4.84 ± 1.12	<0.05	+0.055
Triclyceride mmol/l	2.13 ± 1.18	1.43 ± 0.70	<0.05	+0.200
LDL-cholesterol mmol/l	2.73 ± 1.12	2.67 ± 0.98	<0.05	-0.029
HDL-cholesterol mmol/l	1.40 ± 0.46	1.53 ± 0.45	<0.05	-0.070
Lipase U/I	39.32 ± 17.85	30.18 ± 1078	<0.05	-

LDL - low density lipoprotein. HDL - high density lipoprotein.

Acknowledgment. *We wish to acknowledge the following for their technical assistance, Messrs Asaad Ali Hag, Josse Aubrey, Policianos Apollo De Leon and Ms. Joan Anore.*

References

1. Yeaman SJ. Hormone-sensitive lipase: a multipurpose enzyme in lipid metabolism. ***Biochim Biophys Acta*** 1990; 1052: 128-132.
2. Holm C, Osterlund T, Laurel H, Cautreras JA. Molecular mechanisms regulating hormone sensitive lipase and lipolysis. ***Ann Rev Nutr*** 2000; 20: 365-393.
3. Mulder H, Holst LS, Svensson H, Degerman E, Ahrer E, Rorsman P, et al. Hormone sensitive lipase; the rate limiting enzyme in triglyceride hydrolysis is expressed and active in B-cells. ***Diabetes*** 1999; 48: 228-232.
4. Tietz NW. Clinical Guide to laboratory tests. 3rd ed. Philadelphia (PA): WB Saunders; 1995. p. 865-866.
5. Goldberg RB, Capuzzi D. Lipid disorders in type1 and type 2 diabetes. ***Clin Lab Med*** 2001; 21: 147-172.
6. Roduct R, Masiello P, Wong Chu P, Li H, Mitchell G, Prentki M. A role for hormone sensitive lipase in glucose stimulated insulin secretion. A study of Hormone sensitive lipase deficient mice. ***Diabetes*** 2001; 59: 1970-1875.
7. Dobbins RL, Chester MW, Daniels MB, McGarry JD, Stein DT. Circulating fatty acids are essential for efficient glucose-stimulated insulin secretion after prolonged fasting in humans. ***Diabetes*** 1988; 47: 1613-1618.
8. Prentki M. New insights into pancreatic B-cell metabolic signaling in insulin secretion. ***Eur J Endocrinol*** 1996; 134: 272-286.
9. Yaney GC, Korchak HM, Corkey BE. Long-chain acyl–CoA regulation of protein kinase-C and fatty acid potentiation of glucose stimulated insulin secretion in clonal B-cells. ***Endocrinology*** 2000; 141: 1989-1998.
10. Lerch MM, Zenker M, Turi S, Mayerle J. Developmental and metabolic disorders of the pancreas. ***Endocrinol Metab Clin North Am*** 2006; 35: 219-241.

Related topics

Shahbazian H, Reza A, Javad S, Heshmatollah S, Mahmood L, Ali A, Hosain HM. Beneficial effects of soy protein isoflavones on lipid and blood glucose concentrations in type 2 diabetic subjects. ***Saudi Med J*** 2007; 28: 652-654.

Aughsteen AA, Abu-Umair MS, Mahmoud SA. Biochemical analysis of serum pancreatic amylase and lipase enzymes in patients with type 1 and type 2 diabetes mellitus. ***Saudi Med J*** 2005; 26: 73-77.

Aughsteen AA, Mohammed FI. Insulin enhances amylase and lipase activity in the pancreas of streptozotocin-diabetic rats. An in vivo study. ***Saudi Med J*** 2002; 23: 838-844.