ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES Knowledge to Innovation

Vol 6, Issue 3, 2013

ISSN - 0974-2441

Research Article

EVALUATION OF APOLIPOPROTEIN-B LEVELS IN DYSGLYCEMIA

POONGUZHALI.D.V[1], VINODHINI.V.M[1*], EBENEZER WILLIAM.W[1], KUMAR.J.S[2]

[1]Department of Biochemistry, SRM Medical College Hospital and Research Center, SRM University, [2]Department of Medicine, SRM Medical College Hospital and Research Center, SRM University. Email: vinodhini239@gmail.com

Received: 2 April 2013, Revised and Accepted: 9 May 2013

ABSTRACT

Lifestyle modifications have resulted in an increased prevalence of dysglycemia in young individuals. Impaired Fasting Glucose (IFG) and Impaired Glucose Tolerance (IGT) represent intermediate stages of abnormal glucose regulation that exists between normal glucose homeostasis and diabetes. IFG is considered as a potential indicator of preventive importance for diabetes and cardiovascular diseases. The plasma concentration of apolipoprotein B (apo B) indicates the cumulative number of atherogenic particles. The study group included 50 patients with IFG and 50 euglycemic subjects in the age group of 20-35 years. Apo-B and lipid profile measurements were carried out. As compared to the euglycemic group, in the dysglycemic group the Body Mass Index (BMI) and apo-B levels were significantly elevated while there was no significant difference in Low Density Lipoprotein-Cholesterol (LDL-C) levels. The inclusion of apo-B in atherogenic risk assessment will be beneficial for early identification and intervention strategies.

Keywords: Dysglycemia, Impaired Fasting Glucose, apolipoprotein-B.

INTRODUCTION

Dysglycemia includes Impaired Fasting Glucose (IFG), Impaired Glucose Tolerance (IGT) and diabetes. Pre-diabetes includes IFG and IGT [1]. IFG and IGT represent intermediate stages of abnormal glucose regulation that exists between normal glucose homeostasis and diabetes [2]. IFG is defined as elevated Fasting Plasma Glucose (FPG) concentration ≥ 100 mg/dl and < 126 mg/dl [3]. Patients with IFG or IGT were approximately 5-10 times likely to develop diabetes within 1 year than people without IFG or IGT [4]. IFG has received increasing attention in recent years, because it is an intermediate stage in the development of diabetes and cardiovascular diseases (CVDs) [5, 6, and 7]. In a developing Country like India Obesity and Malnutrition are two ends of spectrum, obesity being an emerging issue which needs closed monitoring [8]. Diabetic dyslipidemia most commonly manifests as elevated triglycerides and low levels of HDL cholesterol, with a predominance of small dense LDL particles amid relatively normal LDL cholesterol levels [9]. Small dense LDL cholesterol is highly atherogenic due to its ability to penetrate the arterial wall and has low affinity for the LDL receptor [10].

Apolipoprotein B is the main structural protein of atherogenic lipoproteins VLDL, IDL and LDL [11]. Therefore the plasma concentration of apo B indicates the cumulative number of atherogenic particles. Modifications of lipoproteins by glycation and oxidation and variations in the size distributions of lipoprotein particles are not reflected in conventional lipid profiles [12]. Apo B levels are more stable than lipid levels particularly in individuals with hyperglycaemia and are not affected significantly by prandial status [13, 14]. Thus, the measurement of apo B provides additional information to that obtained by assessing LDL-C.

Inclusion of this parameter in the standard lipid profile, may aid in risk prediction. The relationship between IFG and markers of dyslipidemia vary in different populations. Numerous longitudinal studies indicate that both IFG and IGT are associated with a modest increase for CVD. Both IFG and IGT are independent risk factors for CVD in some studies but not in others [15-25]. Since IFG is the early stage of diabetes and cardiovascular diseases, identifying preventable risk factors associated with IFG at this early stage is very important in prevention and control of these diseases [26]. Hence we have analysed the levels of apolipoprotein B, along with lipid profile in young individuals with impaired fasting glucose.

MATERIALS AND METHODS

The study was conducted at SRM Medical College Hospital and Research Centre, SRM Nagar, Potheri. Biochemical characteristics of fifty subjects with Impaired Fasting Glucose (IFG) and fifty healthy euglycemic subjects were compared. The study was approved by the Institutional Ethical Committee. An informed consent was taken from all the participants. Individuals with history of ischemic heart disease, clinical evidence of acute infection, renal and hepatic disease, hypo and hyperthyroidism, recent surgery/major trauma and those using lipid lowering and hypoglycemic drugs were excluded from the study.

5 ml of venous blood was collected from the subjects after an overnight 12 hour fast. Serum total cholesterol (TC), triglycerides (TGL), HDL-C and plasma glucose were measured using standard enzyme kits in auto analyser on the same day of sample collection. LDL-C was calculated by Friedewald's formula. The serum was stored at -20°C and apo-B was analysed by immunoturbidimetric method using fully automated Beckmann Coulter analyser.

STATISTICAL ANALYSIS

All data were expressed as the mean and standard deviation. SPSS 20.0 software was used for statistical analysis. The statistical significance of biochemical parameters for subjects with impaired fasting glucose and healthy euglycemic subjects were analyzed by using unpaired students 't' test and $p<0.05$ was accepted as statistically significant.

RESULTS

Table I shows the laboratory characteristics of the participants. In patients with IFG, the serum levels of apo B [82.65±11.96 vs. 67.9±7.96 mg/dl, $p<0.01$] was significantly elevated when compared with the euglycemic group. BMI [25.90±3.04 vs. 23.12±1.2 kg/m^2, $p<0.01$] was significantly increased in the dysglycemic group when compared with the euglycemic group. The mean levels of TGL and TC were significantly higher in dysglycemic patients. There were no significant differences in LDL-C and HDL-C levels between the two groups.

Table 1: Comparison of Mean ± S.D of measured parameters between the euglycemic and dysglycemic groups and the statistical significance of the differences.

Parameters	Euglycemic Group (n=50) Mean ±S.D	Dysglycemic Group (n=50) Mean ±S.D	p Value
Fasting Plasma Glucose (mg/dl)	90.8±5.54	106.9±4.27	p<0.01
Body Mass Index (kg/m^2)	23.12±1.2	25.90±3.04	p<0.01
Apolipoprotein-B (mg/dl)	67.9±7.96	82.65±11.96	p<0.01
Total Cholesterol (mg/dl)	154.06±21.1	171.5±34.09	p<0.05
Triglycerides (mg/dl)	95.1±23.97	113.8±5.94	p<0.01
High Density Lipoprotein-C (mg/dl)	39.4±5.9	38.2±6.1	NS
Low Density Lipoprotein-C (mg/dl)	100.6±23.5	106.98±29.12	NS

The values are considered statistically significant if the p value is less than or equal to 0.05 (p≤0.05). NS = Not Significant

DISCUSSION

Type 2 diabetes is usually considered to be a disease of the middle-aged and elderly. IFG is considered to be a pre diabetic state [1]. Patients with diabetes or IFG have a substantially higher risk of cardiovascular events [27]. Lifestyle modifications have resulted in an increased prevalence of dysglycemia in young individuals. Hence the study group consisted of participants in the age group of 20-35 years. Impaired fasting glucose is considered to be predictive of an increased CAD risk [28]. A graded relationship between plasma glucose and cardiovascular risk is observed in non-diabetic individuals with high glucose levels that are below the diabetic cut-offs [29, 30].

Hyperglycemia due to insulin resistance is characterised by dyslipidemia and inflammation, The role of hormones like leptin, adiponectin and ghrelin have been reviewed in the progression of type-2 diabetes mellitus [31]. According to the consensus statement, the optimum cut-offs for BMI of Asian Indians is Normal BMI: 18.0-22.9 kg/m^2, Overweight: 23.0-24.9 kg/m^2, Obesity: >25 kg/m^2. The mean BMI of individuals with IFG was more than 25 kg/m^2. BMI was significantly increased in patients with IFG when compared with the euglycemic group. Obesity could result in higher insulin concentration, secretion and resistance. Yun Qian et al in a case control study of IFG in a Chinese population has demonstrated that the BMI is significantly related to FPG, TG, TC, HDL-C, Systolic blood pressure and Diastolic blood pressure. [26]

Drexel et al have reported on the prevalence of angiographic CAD in patients with IFG. The significantly increased levels of total cholesterol and triglycerides in the dysglycemic group of our study support this concept. Measurement of LDL cholesterol is relatively insensitive to the accumulation of small dense LDL particles which are believed to be highly atherogenic [32]. As there is one apo B per LDL particle, apo B detects the presence of these atherogenic particles. Apo B_{48} concentrations comprise less than1% of total apo B concentrations in the fasting or post prandial state [33]. In this study the dysglycemic group has significantly elevated apo B levels when compared to euglycemic individuals while there is no difference in LDL-C levels.

Martin et al have found that plasma apo B but not LDL cholesterol levels were associated with coronary artery calcification (CAC) in type 2diabetes [34]. Apo B is a measure of LDL particle number (LDL-P). Cross-sectional studies of healthy individuals showed that LDL-P was associated with CAC in post-menopausal women [35] and carotid intima-media thickness [36]. The meta-analysis by Sniderman et al has indicated apo B is a more accurate marker of cardiovascular risk than LDL cholesterol [37]. Thus the increased concentration of apo B in IFG group indicates the presence of increased levels of atherogenic particles. Once triglyceride levels exceed 100 mg/dl, the atherogenic small, dense LDL predominate [38].On the contrary, apolipoprotein-B levels were not associated with the presence of significant stenosis in a group of 750 patients who underwent coronary angiography [39].

Measurement of apolipoprotein levels has methodological advantages over measurement of LDL-C. Apo B can be measured directly, accurately, precisely, does not require fasting samples, is internationally standardized, may be conducted on frozen samples and can be easily automated [40,41,42]. Moreover even in patients receiving lipid-modifying therapy, determination of subsequent cardiovascular risk is likely to be more accurate if it is based on assessment of apo B level rather than LDL-C [41].

CONCLUSION

The results of the study indicate that IFG is characterised by the presence of cardiometabolic risk factors. The measurement of plasma levels of apolipoprotein-B provides additional information to that obtained by conventional lipid profile. Therefore the inclusion of this parameter for atherogenic risk assessment will be beneficial for early identification and intervention strategies.

REFERENCES

1. American Diabetes Association: Diagnosis and classification of diabetes mellitus. Diabetes Care 31 (Suppl. 1) 2008; S55-S60,.
2. David M Nathan MD, Mayer B. Davidson MD, Ralph A. Defronzo MD, Robert J. Heine MD, Robert R. Henry MD, Richard Pratley MD, Bernard Zinman MD. Impaired fasting glucose and Impaired glucose tolerance. Diabetes care 2007;vol 30, no 3 .
3. Genuth S, Alberti KG, Bennett P, Buse J, Defronzo R, Hahn R, Kitzmiller J, Knowler WC, Lebovitz H, Lenmark A, Nathan D, Palmer J, Rizza R, Saudek C, Shaw J, Steffes M, Stern M, Tuomilehto J, Zimmet P: Expert Committee on the Diagnosis and Classification of Diabetes Mellitus: follow-up report on the diagnosis of diabetes mellitus. Diabetes Care 2003; 26: 3160-3167.
4. Hertzel C. Gerstein, Pasqualina Santaguida, Parminder Raina, Katherine M. Morrison, Cynthia Balion, Dereck Hunt, Hossein Yazdi, Lynda Booker. Annual incidence and relative risk of diabetes in people with various categories of Dysglycemia: A systematic overview of meta-analysis of prospective studies. Diabetes Research and Clinical Practice 2007; 78 305-312.
5. Nichols GA, Hillier TA, Brown JB: Progression from newly acquired impaired fasting glucose to type 2 diabetes. Diabetes care 2007; 30(2):228-233.
6. De Vegt F, Dekker JM, Jager A, Hienkens E, Kostense PJ, Stewhouwer CD, Nijpel G, Bouter LM, Heine RJ: Relation of impaired fasting and postload glucose with incident type 2 diabetes in a Dutch population: the Hoorn Study. JAMA 2001; 285:2109-2113.
7. Levitzky YS, Pencina MJ D'Agostina RB, Meigs JB, Murabito JM, Vasan RS, Fox CS: Impact of impaired fasting glucose on cardiovascular disease: the Framingham Heart Study. J Am Coll Cardiol 2008; 51(3):264-270.
8. Ambili remesh, Obesity: Pathophysiology and Management-A Pharmacological Perspective. AJPCR 2013; 6(1):11-13.
9. Anne L.Peters, MD. Clinical Relevance of Non-HDL Cholesterol in patients with Diabetes. Clinical Diabetes 2008; 26;3-7.
10. Koba S, Yokoya Y, Hirano T, Ito Y, Ban Y, Tsunoda F : Small LDL-C is superior to LDL-C for determing severe coronary atherosclerosis. J Atheroscler Thromb 2008; 15(5):250-60.
11. Marcovina S, Packard CJ. Measurement and meaning of apolipoprotein A1 and apolipoprotein B plasma levels. J Intern Med 2006; 259:437-446.
12. Lyons TJ, Jenkins AJ. Glycation, oxidation, and lipoxidation in the development of the complications of diabetes: a carbonyl stress hypothesis. Diabetes Rev. 1997; 5:365-391.

13. Lyons TJ, Jenkins AJ, Zheng D, et al. Diabetic retinopathy and serum lipoprotein subclasses in the DCCT/EDIC cohort. Invest Ophthalmol Vis Sci 2004; 45:910-918.
14. Davidson MH. Apolipoprotein measurements: is more widespread use clinically indicated? Clin Cardiol 2009; 32:482-486.
15. Countinho M, Gerstein HC, Wang Y, Yusuf S: The relationship between glucose and incident cardiovascular events: a metaregression analysis of published data from 20 studies of 95, 783 individuals followed for 12.4 years. Diabetes Care 1999; 22:233-240.
16. Levitan EB, Song Y, Ford ES, Liu S: Is non-diabetic hyperglycaemia a risk factor for cardiovascular disease? A Meta-analysis of prospective studies. Arch Intern Med 2004; 164:2147-2155,.
17. DECODE Study Group, on behalf of the European Diabetes Epidemiology Group: Glucose tolerance and cardiovascular mortality: comparison of fasting and 2-hour diagnostic criteria. Arch Intern Med 2001; 161: 397-405.
18. DECODE Study Group, on behalf of the European Diabetes Epidemiology Group: Is the current definition for diabetes relevant to mortality risk from all causes and cardiovascular and non-cardiovascular diseases? Diabetes Care 2003; 26:688-696.
19. Barzilay JI, Spiekerman CF, Wahl PW, Kuller LH, Cushman M, Furgerg CD, Dobs A, Polak JF, Savage PJ: Cardiovascular disease in older adults with glucose disorders: comparison of American Diabetes Association criteria for diabetes mellitus with WHO criteria. Lancet 1999; 354:622-625.
20. Balkau B, Forhan A, Eschawege E: Two hour plasma glucose is not unequivocally predictive for early death in men with impaired fasting glucose: more results from Paris Prospective Study. Diabetologia 2002; 45:1224-1230.
21. Balkau B, Hu G, Qiao Q, Tuomilehto J, Borsh-Johnsen K, Pyorala K, DECODE Study Group, European Diabetes Epidemiology Group: Prediction of the risk of cardiovascular mortality using a score that includes glucose as a risk factor: the DECODE Study. Diabetologia 2004; 47:2118-2128.
22. Stern MP, Fatehi P, Williams K, Haffner SM: Predicting future cardiovascular disease : do we need the oral glucose tolerance test? Diabetes Care 2002; 25:1851-1856.
23. Gabir MM, Hanson RL, Dabetea D, Imperatore G, Roumain J, Bennett PH, Knowler WWC : Plasma glucose and prediction of microvascular disease and mortality : evaluation of 1997 American Diabetes Association and 1999 WHO criteria for diagnosis of diabetes. Diabetes Care 2002; 23:1113-1118.
24. Meighs JB, Nathan DM, D'Agostino RB Sr, William PW: Fasting and post-challenge glycemia and cardiovascular disease risk: the Framingham Offspring Study. Diabetes Care 2002; 25: 1845-1850.
25. Tominaga M, Equchi H, Manaka H, Igarashi K, Kato T, Sekikawa A : Impaired glucose tolerance is a risk factor for cardiovascular disease, but not impaired fasting glucose: the Funagata Diabetes Study. Diabetes Care 1999; 22:920-924.
26. Yun Qian, Yudi Lin, Tiemei Zhang, Jianling Bai, Feng Chen, Yi Chang, Senlin Luo, Hongbing Shen. The characteristics of impaired fasting glucose associated with obesity and dyslipidaemia in a Chinese population. BMC Public Health 2010; 10:139.
27. Anthony Keech, David Colquhoun, James Best, Adrienne Kirby, R.John Simes, David Hunt, Wendy Hague, Elaine Beller, Manjula Arulchelvam, Jennifer Baker, Andrew Tonken. Secondary prevention of cardiovascular events with long term pravastatin in patients with diabetes or impaired fasting glucose. Diabetes Care October 2003; volume 26, no 10,.
28. Julie St-Pierre, Isabelle Lemieux, Marie-Claude Vohl, Patrice Perron, Gerald Tremblay, Jean-Pierre Despres, Daniel Gaudet. Contribution of abdominal obesity and hypertriglyceridemia to impaired fasting glucose and coronary artery disease. The American journal of cardiology 2002; vol. 90 july 1,.
29. Countinho M, Gerstein HC, Wang Y, Yusuf S: The relationship between glucose and cardiovascular events: a metaregression analysis of published data from 20 studies of 95,783 individuals followed for 12.4 years. Diabetes Care 1999; 22:223-240.
30. Bjornholt JV, Erikssen G, Aaser E, Sandvik L, Nitter-Hauge S, Jervell J, Erikssen J, Thaulow E: Fasting blood glucose: an underestimated risk factor for cardiovascular death: results from a 22-year follow up study of healthy non-diabetic men. Diabetes Care 1999; 22: 45-49.
31. Kothandam hariprasath1, paturi umamaheswari1, samuel david wicket2. Hormone based therapy in type 2 diabetes mellitus, AJPCR 2013; vol. 6 (1); 1-5.
32. Heinz Drexel MD, Stefan Aczel MD, Thomas Marte MD, Werner Benzer MD, Peter Langer, Willi Moll MD, Christopher H. Saely MD. Is atherosclerosis in diabetes and impaired fasting glucose driven by elevated or by decreased HDL cholesterol HDL Cholesterol? Diabetes Care, 2005; volume 28, number 1, LDL cholesterol.
33. Mudd JO, Borlaug BA, Johnston PV, Kral BG, Rouf R, Blumenthal RS, K witrovic PO Jr. Beyond low-density lipoprotein cholesterol : defining the role of low-density heterogenecity in coronary atery disease. J Am Coll Cardiol 2007; 50:1735-1741.
34. Elovson J, Chatterton JE, Bell GT, Schumaker VN, Reuben MA, Puppione DL, Reeve JR, Jr, Young NL. Plasma very low density lipoproteins contain a single molecule of apolipoprotein B. J Lipid Res. 1988;29: 1461-1473.
35. Campos H, Khoo C, Sacks FM. Diurnal and acute patterns of post prandial apolipoprotein B-48 in VLDL, IDL and LDL from normolipidemic humans. Atherosclerosis .2005;181:345-351.
36. Seth S. Martin, Atif N. Qasim, Nehal N. Mehta, Megan Wolfe, Karen Terembula, Stanley Schwartz, Nayyar Iqbal, Mark Schutta, Roshanak Bagheri, Muredach P. Reilly. Apolipoprotein B but not LDL cholesterol is associated with coronary artery calcification in type 2 diabetic whites. Diabetes, august 2009; vol 58,.
37. Mora S, Szklo M, Otvos JD, Greenland P, Psaty BM, Goff DC Jr, O'Leary DH, Saad MF, Tsai MY, Sharrett AR. LDL particle subclasses, LDL particle size, and carotid atherosclerosis in the Multi-Ethnic Study of Atheroclerosis (MESA). Atherosclerosis 2007; 192:211-217.
38. Allan D. Sniderman, MD; Ken Williams, John H. Contois, Howard. M, Monroe, Matthew J. McQueen, MBChB, Jacquiline de Graaf, Curt D.Furberg. A meta-analysis of low-density lipoprotein cholesterol, non-high-density lipoprotein cholesterol and apolipoprotein B as Markers of cardiovascular risk. Circ Cardiovasc Qual Outcomes , May 2011.
39. Austin MA, King M-C, Vranizan KM, Krauss RM: Atherogenic lipoprotein phenotype: a proposed genetic marker for coronary heart disease risk. Circulation 1990; 82:495–506.
40. Walldius G, Jungner I, Holme I, Aastveit A, Kolar W, Steiner E. High apolipoprotein B, low apolipoprotein A-I, and improvement in the prediction of fatal myocardial infarction (AMORIS study): a prospective study. Lancet 2001; 358 : 2026–33.
41. Bhatnager D, Durrington PN. Measurement and clinical significance of apolipoproteins A-I and B. In: Rifai N, Warnick GR, Dominiczak MH, eds. Handbook of Lipoprotein Testing, 2nd edn. Washington, DC: AACC Press, 2000; 287–310.
42. Durrington PN. Can measurement of apolipoprotein B replace the lipid profile in the follow-up of patients with lipoprotein disorders? Clin Chem 2002; 48: 401–2.