ORIGINAL ARTICLE

SERUM LEPTIN LEVELS IN PATIENTS WITH CORONARY ARTERY DISEASE

Shama Akram, Zamir Ahmed, Iram Fayyaz, Sadia Mehmood, Mansoor Ghani, Anbreen Mazhar Choudhary, Imran Shah

Department of Biochemistry, University of Health Sciences, Lahore, Pakistan

Background: Cardiovascular diseases (CVD) are the leading cause of morbidity, mortality and disability worldwide. Leptin, a 16kDa product of ob gene, is an endocrine hormone produced by white adipose tissue. It is primarily involved in the regulation of food intake and energy expenditure. Hyperleptinemia is one of the novel risk factors contributing in many ways to CVD. **Objective:** The objective of the study was to find the level of leptin in patients with coronary artery disease (CAD) and compare it with healthy people in our population. **Methods:** Our study was an analytical and cross-sectional study. Our study included 60 patients with a history of CAD and 60 healthy controls (aged 40–60 years, both sexes). Leptin levels were measured by ELISA. **Results:** Mean serum leptin level in patients was 11.48±11.25 ηg/ml, while control group had a mean leptin level of 8.22±8.01 ηg/ml (p=0.071). **Conclusion:** Leptin levels were higher in patients but the difference was non-significant. More studies are needed with larger sample size in our population.

Keywords: Coronary Artery Disease (CAD), Leptin

INTRODUCTION

Coronary Artery Disease is the epidemic of our time and set to remain the single most important disease in the world in terms of mortality, morbidity, disability and economic loss until 2020 year.[1,2] Despite many conventional risk factors, 50% of the CAD still remains unexplained. This led to the discovery of novel risk factors, which might cause CAD.[3] Leptin is one such risk factor discovered by positional cloning of the ob gene.[4] Ob gene is located on chromosome 7q31.3.[5–7]

Leptin, is a 167-amino acid protein with a molecular mass of 16 kDa. Its name is derived from the Greek word '*leptos*' which means 'thin'. Leptin, an important signal in regulation of adipose tissue mass and body weight, operates by inhibiting or stimulating food intake and energy expenditure through release of several neurotransmitters, by acting on the receptor site in the hypothalamus.[7,8] Leptin may be structurally similar to proteins of the long-chain helical cytokine family, including IL-2, IL-12 and growth hormone.[9] Leptin is involved in the regulation of reproduction, immune function, blood pressure, renal function, bone formation, angiogenesis and vascular disorders.[10]

The biologic activities of leptin on target tissues are carried out through selective binding to a specific leptin receptor.[11] Leptin receptor exists in at least 6 isoforms, Ob-Ra through Ob-Rf. All leptin receptors share the common extracellular (except Ob-Re) and transmembrane domains but differ in their intracellular domains.[12] Among these isoforms, only the long isoform (Ob-Rb) is fully functional.[13] The structure of the leptin receptor is similar to that of the helical gp130 cytokine receptor (class-I). Leptin receptors perform signal transduction through JAK-STAT pathway.[14,15]

Elevated plasma leptin level in obese individuals reflects increased amount of adipose tissue and desensitisation of leptin signal referred to as leptin resistance.[16] Gene expression of leptin undergoes significant seasonal fluctuations associated with food availability, body reserves, and day length.[17] Serum leptin levels follow a circadian rhythm, with a peak during the night.[18] Compared with males, females have higher leptin levels because of their different body fat distribution or the inducing effects of hormones.[19]

Leptin through various mechanisms has been linked to cardiovascular outcomes and it may be used as a maker for the diagnosis of CHD.[20,21]

The objective of this study was to see the level of leptin in patients with coronary artery disease (CAD) and compare it with healthy people in our population.

MATERIAL AND METHODS

This is a cross-sectional study conducted in University of Health Sciences, Lahore. Sixty patients within 40–60 years of age (both sexes), with angiographically proven CAD and 60 age and sex matched controls with no history of angina pectoris or myocardial infarction were included in the study. Patients with diabetes mellitus, renal and liver diseases were excluded from the study. Fasting venous blood samples of patients and controls were taken. Leptin levels were measured by using biosource leptin EASIA kit (Catalouge Number KAP2281, Bio-Source Europe S.A.) based on sandwich ELISA. The data was analysed using SPSS-16.

RESULTS

Serum leptin levels in patients ranged from 0.36 to 41.52 ηg/ml. The mean serum leptin level in patients was 11.48±11.25 ηg/ml. In controls, the leptin levels

ranged from 0.22 to 30.87 ηg/ml with a mean value of 8.22±8.01 ηg/ml. No statistically significant differences were observed in the leptin levels of patients and controls (p=0.071).

DISCUSSION

Leptin levels were higher in patients as compared to controls but the difference was non-significant. In a study by Galluccio *et al*[22] leptin level in patients was 9.6±5.8 while in controls it was 6.0±3.8 ηg/ml. These values are comparable to our results. Dasheng *et al*[23] also verified hyperleptinemia in CHD patients. Abdella *et al*[24] like our study could not find a significant difference in leptin levels of patients and controls. This may be due to the potential confounding effect of treatment with aspirin and statins. In a study by Wallace *et al*[25] leptin levels were 16% higher in cases than in controls and higher leptin concentrations were associated with higher risk of a future coronary events. Leptin levels were higher in patients with MI compared to controls in studies by Taneli *et al*[26], Tamer *et al*[27] and Soderberg *et al*[28]. Schulze *et al*[29] observed that patients with congestive heart failure exhibit elevated plasma leptin levels.

CONCLUSION

It is concluded that patients with a history of myocardial infarction or angina pectoris have higher leptin levels compared to healthy controls but the differences were not significant. More detailed studies with larger number of patients are needed to be done in our population.

ACKNOWLEDGEMENTS

A gratitude to Dr. Abdul Ghaffar Khan, Dr. Asim Mumtaz and Dr. Shahjahan for their support in research work. We are thankful to Mr. Waqas Sami for his assistance in statistical evaluation and my colleagues for their support.

REFERENCES

1. Hajilooi M, Sanati A, Ahmadieh A, Ghofraniha A, Massoud A. Circulating ICAM-1, VCAM-1, E-Selectin, P-Selectin, and TNFRII in patients with coronary artery disease. Immunol Invest 2004;33(3):263–75.
2. Hatmi ZN, Tahvildari S, Motlag AG, Kashani AS. Prevalence of coronary artery disease risk factors in Iran: a population based survey. BMC Cardiovasc Disord 2007;7:32.
3. Haidari M, Javaidi E, Sanati A, Hajilooi M, Ghanbili J. Evaluation of C-reactive protein, a sensitive marker of inflammation, as a risk factor for stable coronary artery disease. Clin Biochem 2001;34(4):309–15.
4. Zhang Y, Proenca R, Maffei M. Positional cloning of the mouse obese gene and its human homologue. Nature 1994;372:425–32.
5. Friedman JM, Leibel RL, Siegel DS, Walsh J, Bahary N. Molecular mapping of the mouse ob mutation. Genomics 1991;11:1054–62.
6. Geffroy S, DeVos P, Staels B, Duban B, Auwerx J, de Martinville B. Localization of the human OB gene (OBS) to chromosome 7q32 by fluorescence in situ hybridization. Genomics 1995;28:603–4.
7. Moran O, Philip M. Leptin: Obesity, diabetes and other peripheral effects —a review. Pediatr Diabetes 2003;4(2):101–9.
8. Meier U, Gressner AM. Chemical Aspects of Leptin, Ghrelin, Adiponectin, and Resistin. Clin Chem 2004;50:1511–25.
9. Zhang F, Basinski MB, Beals JM, Briggs SL, Churgay LM, Clawson DK *et al*. Crystal structure of the obese protein leptin-E100. Nature 1997;387(6629):206–9.
10. Koh KK, Park SM, Quon MJ. Leptin and Cardiovascular Disease: Response to Therapeutic Interventions. Circulation 2008;117:3238–49.
11. Paracchini V, Pedotti P, Taioli E. Genetics of Leptin and Obesity: A HuGE Review. Am J Epidemiol 2005;162(2):101–14.
12. Ren J. Leptin and hyperleptinemia –from friend to foe for cardiovascular function. J Endocrinol 2004;181(1):1–10.
13. Sweeney G. Leptin signaling. Cellular Signalling 2002;14:655–63.
14. Giandomenico G, Dellas C, Czekay R-P, Koschnick S, Loskutoff DJ. The leptin receptor system of human platelets. J Thromb Haemost 2005;3:1042–9.
15. Yang R, Barouch LA. Leptin Signaling and Obesity: Cardiovascular Consequences. Circ Res 2007;101(6):545–59.
16. Beltowski J. Leptin and Atherosclerosis. Atherosclerosis 2006;189(1):47–60.
17. Bernabucci U, Basirico L, Lacetera N, Morera P, Ronchi B, Accorsi PA *et al.* Photoperiod Affects Gene Expression of Leptin and Leptin Receptors in Adipose Tissue from Lactating Dairy Cows. J Dairy Sci 2006;89:4678–86.
18. Melanson KJ, Mclnnis KJ, Rippe JM, Blackburn G, Wilson PF. Obesity and cardiovascular disease risk: research update. Cardiol Rev 2001;9(4):202–7.
19. Hafeezullah, Aslam M. Leptin: fights against obesity! Pak J Physiol 2006;2(1):54–60. [Review]
20. Sierra-Johnson J, Romero-Corral A, Lopez-Jimenez F, Gami AS, Sert Kuniyoshi FH, Wolk R *et al*. Relation of increased leptin concentrations to history of myocardial infarction and stroke in the United States population. Am J Cardiol 2007;100(2):234–9.
21. Al-Daghri NM, Al-Attas OS, Al-Rubeaan K, Mohieldin M, Al-Katari M, Jones AF *et al*. Serum leptin and its relation to anthropometric measures of obesity in pre-diabetic Saudis. Cardiovasc Diabetol 2007; 6:18.
22. Galluccio E, Piatti P, Citterio L, Lucotti PCG, Setola E, Cassina L, *et al*. Hyperinsulinemia and impaired leptin:adiponectin ratio associate with endothelial nitric oxide synthase (nos3) polymorphisms in subjects with in-stent restenosis. Am J Physiol Endocrinol Metab 2008;294:E978–86.
23. Xia D, Song Y, Li C, Zhang F, Wei M. The change of serum leptin and its relationship with platelet membrane glycoprotein Ib in patients with coronary heart disease. Frontiers Med China 2007;1(4):352–5.
24. Abdella NA, Mojiminiyi OA, Moussa MA, Zaki M, Al Mohammedi H, Al Ozairi ES, *et al*. Plasma leptin concentration in patients with Type 2 diabetes: relationship to cardiovascular disease risk factors and insulin resistance. Diabet Med 2004;22(3):278–85.
25. Wallace AM, McMahon AD, Packard AJ, Kelly A, Shepherd J, Gaw A, *et al*. Plasma leptin and the risk of cardiovascular disease in the West of Scotland Coronary Prevention Study (WOSCOPS). Circulation 2001;104:3052–56.
26. Taneli F, Yegane S, Ulman C, Tikiz H, Bilge AR, Ari Z, *et al*. Increased serum leptin concentrations in patients with chronic stable angina pectoris and ST-elevated myocardial infarction. Angiology 2006;57:267–72.
27. Tamer L, Ercan B, Unlu A, Sucu N, Pekdemir H, Eskandari G, *et al*. The relationship between leptin and lipids in atherosclerosis. Indian Heart J 2002;54:692–6.
28. Soderberg S, Ahren B, Jansson JH, Johnson O, Hallmans G, Asplund K *et al*. Leptin is associated with increased risk of myocardial infarction, J Intern Med 1999;246:409–18.
29. Schulze PC, Kratzsch J, Linke A, Schoene N, Adams V, Gielen S *et al*. Elevated serum levels of leptin and soluble leptin receptor in patients with advanced chronic heart failure. Eur J Heart Fail 2003;5(1):33–40.

Address for Correspondence:

Shama Akram, Department of Biochemistry, University of Health Sciences, Lahore. **Cell:** +92-322-4667315.
Email: shamaakram@yahoo.com