Diagnostic Value of Lipoprotein (a) in Cardiovascular Disease due to Atherogenic Diet in Rats

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ABSTRACT

This research was conducted to evaluate cardiovascular disease caused by atherogenic diets, based on immunological assay by measuring the concentration of lipoprotein (a) [Lp (a)]. Eighty male Sprague Dawley rats, 150-200 grams of body weight and three months of age were used in this research. The rats were randomly allotted into four groups, 20 of each. Group I as control was fed normal diet, group II was fed diet containing high cholesterol, group III was fed diet containing high fat and group IV was fed diet containing high cholesterol and high fat (atherogenic). After 2, 4, 8, 16 weeks on experimental diet, 20 rats were selected randomly (5 rats of each group), and blood sample were withdrawn for Lp (a) analysis. All animal were then killed and the heart were taken for histopathological analysis. The statistical analysis for Lp (a), data showed that there were significant differences (p<0.05) among of all the treatments, high fat diet had the greatest influence on Lp (a) concentration. Treatment period and interaction between treatment period and diet did not influence Lp (a) concentration.

It can be concluded that Lp (a) concentration could be influence by high fat diet, but not by period of treatment. Lp (a) concentration seems connected with the incidence of atherosclerosis in rats. For this reason, evaluation of Lp (a) concentration should be considered as a routine procedure in general health evaluation.

INTRODUCTION

Cardiovascular disease are still major public health problems and the first cause of death in modern countries, especially in United States and other Western countries. In Indonesia, based on Health Department survey in 1986, cardiovascular disease has become the third cause of death after acute pneumonia and diarrhea. However, in 1992, cardiovascular disease has become the first cause of death (Anonim, 1993).

Atherosclerosis is a complex disease, because to single factor is an absolute cause of cardiovascular disease. The risk factor include: cigarette smoking, hypertension, obesity, psychosocial factor, physiological inactivity and diabetes mellitus (Kaplan, 1979). In fact, atherosclerosis is a slowly progressive disease of the large arteries that begins early in life, but rarely produces symptoms until middle age. Often the disease goes undetected until the time of the first heart attack which usually fatal. Based on those facts, a routine procedure in general health evaluation became important to prevent progressivity of the atherosclerosis.

In 1965, Berg described a new antigenic component, Lp (a), among human plasma lipoproteins. Initially it was thought that the antigen was present in about one-third of individuals. With the advent of more sensitive assay, it is apparent that the serum of virtually all huminiti contain this antigen, but in highly variate amount (Kane and Havel, 1990). Detailed studies of the structures of Lp (a) lipoproteins were initially hampered by the tendency of these lipoproteins to become denatured under conditions which do not appear to affect the structure of LDL. From initial immunochromical studies of the Lp (a) lipoproteins it was known that they contain material cross-reactive with apo B as well as Lp (a) specific antigen. Further studies then established that there were two principal proteins, one it corresponding to the apo B of LDL, and the other is unrelated, heavily glycosylated protein responsible for the Lp (a) reactivity (Fahlin et al. 1972). In recent years, Lp (a) become interesting object for investigator. They believed that Lp (a) concentration have strong correlation with early atherosclerosis (Dahlen et al. 1993). The amount of Lp (a) in plasma varies from less than 1 mg/
di to greater than 100 mg/dl, with a two-fold increase in coronary artery disease (Armstrong, 1986).

The present study was conducted to evaluate atherosclerosis, cause by atherogenic diet, based on immunological assay by measuring the concentration of LP (a), using rats as animal models.

MATERIALS AND METHODS

Eighty male Sprague Dawley rats, 150-200 grams of body weight and three months of age were used in this research. The rats were randomly allocated into four groups, 20 of each. Group I as control was fed normal diet, group II was fed diet containing high cholesterol, group III was fed diet containing high fat and group IV was fed containing high cholesterol and high fat (atherogenic). After 2, 4, 8, 16 weeks on experimental diets, 20 rats were selected randomly (5 rats of each group), and blood sample were withdrawn for LP (a) analysis. All animal were then killed and the heart taken out for histopathological analysis.

Analytical methods

Lipoprotein (a) concentration was assayed by using a commercial h-lipoprotein (a) ELISA kit produced by Biovendor Mannheim ELISA and measured at 450 nm using ELISA reader.

Data of the experiments were analyzed statistically using Multifactorial Randomized design. The difference was considered to be significant if p<0.05.

RESULTS AND DISCUSSION

The effects of various diets and treatment periods on rats plasma LP (a) concentration are presented on Figure 1. Statistical analysis showed that there were significant differences (p<0.05) among all of the treatments, high fat diet had the greatest influence on LP (a) concentration.

Although, it has been generally accepted that LP (a) is mainly under genetic control and therefore hardly sensitive to dietary change, a few studies show that specific dietary fatty acids do affect the LP (a) concentration. Incidence of atheroma from group III (high fat diet) is a specific marker for atherosclerosis. Studies of atherosclerotic lesions with modern techniques of cell and molecular biology has revealed that each lesion contains significant elements of three cellular phenomena. These are smooth-muscle proliferation; formation by the proliferated cells of large amounts of connective tissue; and the presence of collagen fibers. This is consistent with the findings of the present study.
tissue matrix including collagen, elastic fibres, and proteoglycans; and accumulation of intracellular and extracellular lipid. The lesions of atherosclerosis occur principally within the innermost layer of the artery wall, the intima. They include fatty streaks, and the fibrous plaque. Secondary changes have been noted in the media of the artery underlying the lesion, principally in association with the more advanced lesions of atherosclerosis (Ross, 1993).

Incidence of cardiomiophathy which showed low level of Lp(a) concentration in this research it might be caused by multiple form of apoprotein (a), with variation in molecular weight among the apo (a) proteins. The apo (a) molecule contains a variable amount of kringle 4 repeats, accounting for the considerable apo (a) size heterogeneity, with isoform varying between 400 and 700 kDa (Leuf et al., 1994). Utermann et al. (1983) first described the existence of six apo (a) isoform. They classified the isoform according to their electrophoretic mobility relative to apo B-100 as I (faster than apo B-100), B (similar to apo B-100); S1, S2, S3 and S4 (all slower than apo B-100). Phenotype B, S1, S2 showed an association with high level of Lp (a) concentration, and S3, S4 phenotype showed an association with moderate level of Lp (a) concentration.

CONCLUSION

Based on the present study result, it can be concluded that 1 (1) Lp (a) concentration could be influenced by high fat diet, have been noted in the treatment. (2) Lp (a) concentration seems connected with the incidence of atheroerosclerosis in rats. For this reason, evaluation of the Lp (a) concentration should be considered as an accurate technique in general health evaluation.

ACKNOWLEDGEMENT

We wish to thank Mr. Yuly and Mr. Dalijo for their technical assistance. This work was supported by the Directorate General of Higher Education, Ministry of Education and Culture.

REFERENCES


Indonesian Food and Nutrition Progreesa, 1998 Vol 5, no 4