Lipoprotein (a) levels in hemodialysis patients with chronic renal failure

Yavuz BAYKAL, H.LEVENT, Bayram KOÇ, Refik MAS, Murat ŞALK, Kenan SAĞLAM, Tahir ÜNAL, Fikri KOCABALKAN

Dept. of Internal Medicine, Gülhane Military Medical School, Ankara, TURKEY

Lipoprotein (Lp) (a) has recently been recognized to be an independent risk factor for coronary heart disease. Lp (a) may inhibit fibrinolysis, and is deposited in atherosclerotic lesions. Patients undergoing hemodialysis have an increased risk of atherosclerotic cardiovascular complications. In order to examine whether Lp (a) may contribute to atherogenesis in hemodialysis patients, we compared Lp (a) levels in the sera of hemodialysis patients with chronic renal failure and healthy controls. Lp (a) levels were measured in 40 hemodialysis patients and in 40 healthy controls. Hemodialysis patients had significantly higher Lp (a) levels (21.2±1.3 mg/dl) compared with healthy control group (11.2±0.9 mg/dl). Lp (a) did not correlate with the levels of cholesterol, triglyceride, HDL cholesterol, and LDL cholesterol. In conclusion, the mean serum level of Lp (a) was higher in the hemodialysis patients than the healthy controls. Although Lp (a) may contribute to atherosclerosis in hemodialysis patients, further studies are needed to define the metabolic regulation of Lp (a) and its role in atherosclerotic disease. [Turk J Med Res 1996; 14(2):78-80]

Key Words: Chronic renal failure, Atherosclerosis, Lipoprotein

The risk of atherosclerotic cardiovascular complications increase in hemodialysis patients with chronic renal disease and these complications are the leading cause of death in those people (1).

Many studies on the incidence of atherosclerotic disease in patient with chronic renal insufficiency disclosed the case to be related with various factors (2). High sera levels of potentially atherogenic lipid fractions contribute largely to the increase of cardiovascular diseases in hemodialysis patients (3). Increase in the levels of HDL are common forms of abnormalities in lipoprotein fraction in hemodialysis patients (4,5).

Several studies report LP (a) to be an independent risk factor for coronary heart disease recently (2,6). Some of them report increased concentrations of Lp (a) in patients with chronic renal insufficiency and nephrotic syndrome (7,8).

We performed our study to determine concentrations of Lp (a) which is suggested to be an important and independent risk factor in the pathogenesis of atherosclerosis in patients with chronic renal disease on hemodialysis. We also measured the levels of total cholesterol, triglyceride, LDL-cholesterol, HDL-cholesterol and looked for any probable relation between Lp (a) and them.

Received: Nov. 25, 1995 **Accepted:** March 15, 1996

Correspondence: Yavuz BAYKAL
Dept. of Internal Medicine,
Giilhane Military Medical Academy,
Ankara, TURKEY

MATERIALS AND METHODS

The study involved 40 patients (20 male, 20 female) in the nephrology department of GATA and Türkiye Yüksek İhtisas Hospital. Their ages ranged from 16 to 79 years (45.2±2.5). They had been an hemodialysis for 17.9±1.7 months and were dialyzed on every second days. The control group was formed of healthy people all of when admitted to GATA check-up clinic. They were all guaranteed not to have any disease that could effect lipids by physical examination, history and laboratory. They were also 40 persons (20 male, 20 female) and ages ranged from 22 to 66 years (41.02±2.9).

Fasting blood samples were obtained just before the hemodialysis in the patient group. The levels of serum Lp (a), total cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol, creatinine and albumin were measured.

Total cholesterol (by the enzymatic method of cholesterol oxydase peroxydase), HDL cholesterol (Polyetilen Glikol 20000 centrifugation/by the enzymatic method of peroxydase, glyceral 3-phosphate-oxydase), triglyceride (by the enzimatic method of peroxydase, glyceral 3-phosphate-oxydase), albumin (by the method of brom cresol purple), creatinine (by the method of alcoholic picrote) were analysed in Technicon RA 1200 otoanalyser. LDL was estimated by the formula LDL-cholesterol=Total cholesterol-(HDL-cholesterol+Triglyceride/5) (9). The results were given in mg/dl.

Lp (a) was measured by the method of enzyme immunoassay (ELISA) (Lp (a) stripwell ELISA IMUBIND American Diagnostica Inc.) in the sera which was obtained from the venous blood samples of the patients and kept at -22°C. The results were given in mg/dl. The intraassay and interassay exchange coefficient of the method is 2.3%-2.7% in average.

The significance of variances between two mean values test (Student's t test) was performed. Statistical significance was assumed when p<0.005. Correlation analysis was performed to assess the relation between Lp (a) and cholesterol, HDL-cholesterol, LDL-cholesterol, creatinine, albumine, age, the duration of the hemodialysis (10).

RESULTS

80 persons involved in the study in two groups. Both group normal of 40 people (20 male, 20 female). In the patient group, the mean age was 45.2+2.5 years. The mean age of controls was 41.02±2.9 statistically significant variation in mean ages between two groups was not found. The mean function of the hemodialysis in patient group was 17.9+1.7 months.

In the assessment of the results, groups were compared with each other (Table 1).

The levels of serum Lp (a) in hemodialysis patients (21.2±0.9 mg/dl) was significantly higher than controls (11.2±0.9 mg/dl) (p<0.01).

The mean cholesterol levels didn't show any significant variance between patients and controls (p>0.05). Triglyceride level was higher in hemodialysis patients (192.5±7.3) than controls (115.3±5.6). On the other hand, HDL-cholesterol level of hemodialysis patients was lower (25.3±0.7) than that of controls (40.1 ±0.7) (p<0.01).

Patient and control group didn't have variance statistically in mean LDL-cholesterol levels (p>0.05). The level of serum albumin was found to be lower in hemodialysis patients (3.8±0.08) than controls (4.6±0.06) (p<0.01). The level of creatinine was higher in hemodialysis group (13.3±0.3) than control group (0.8±0.02) on the other hand (p<0.01).

The serum level of Lp (a) correlated with neither the duration of the hemodialysis (r=0.18) nor the ages (r=0.06). Serum albumin level did not correlate with the serum level of Lp (a) (r=0.01). No significant correlation between the serum creatinine level and the Lp (a) was found either (r=0.19).

Table 1. The results of patients and controls

	Patient	Control	P
Lp (a)	21.2±1.3	11.210.9	p<0.01
T.Cholesterol	182±7.1	192.514.7	p>0.05
Trigliseride	192.5±7.3	115.315.6	p<0.01
HDL-Cholesterol	25.3±0.7	40.110.7	p<0.01
LDL-Cholesterol	129.1 ±6.4	12914	p>0.05
Creatinine	10.3±0.3	0.810.02	p<0 01
Albumin	3.8±0.08	4.610.06	pO.01

The results are given as meanistandart deviation in mg/dl

DISCUSSION

High level of Lp (a) strongly correlates with atherosclerosis, the risk of which increases two-fold when the level of Lp (a) is higher than 30 mg/dl. In the case of the levels of both Lp (a) and LDL cholesterol to be high together, the relative risk of atherosclerosis increases five-fold compared with healthy subjects. The high level of triglyceride and the low level of HDL-cholesterol can also contribute to the pathogenesis of atherosclerosis (11,12).

In hemodialysis patients, the potential role of Lp (a) as a risk factor in atherosclerosis was first defined by Parra et at, who measured Lp (a) level in patients in hemodialysis three-fold higher than controls, suggested the kidney might have a role in the regulation of Lp (a) metabolism (13).

Nakahama et al measured higher Lp (a) levels in 40 hemodialysis patients than controls (14). They also reported that Lp (a) did not correlate with age, duration of hemodialysis, total cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol.

Barbagallo et al studied the serum levels of Lp (a) in 93 patients with chronic renal insufficiency before and after hemodialysis (15). The level of Lp (a) did not vary before and after hemodialysis and in both case, level was higher than controls. They also reported that the hemodialysis didn't have any effect on the metabolism of Lp (a).

Karadi et al measured higher serum levels of Lp (a) in 37 patient with heavy hematuria of various etiologies than healthy controls (16). Lp (a) did not correlate with proteinuria and creatinine, on the other hand. They concluded that the kidney may have a role in the regulation of Lp (a) metabolism and depending on the type of renal impairment, serum level of Lp (a) may vary.

Our results correlate with all these reports. We measured higher serum levels of Lp (a) in 40 patients with chronic renal disease on hemodialysis than that of healthy controls. Lp (a) didn't correlate with age, the duration of hemodialysis, the level of albumin, the level of creatinine respectively in our study either.

Assessment of the relation between the kidney and Lp (a) is not easy for because there have not been enough many reports on the subject in the literature yet. It is not clear which mechanisms change the levels of Lp (a) in chronic renal diseases yet. Lp (a) catabolism may have deteriorated in renal insufficiency. Alternatively, the uremic plasm may be suggested to include some factor which may deteriorate the metabolism of Lp (a), Lp (a) is synthesized in liver and serum level correlates with the synthesis (17). The synthesis may be induced in patient with chronic renal insufficiency by some unknown mechanisms and/or some factor in the uremic plasm.

It was also suggested that proteinurea may increase Lp (a) level (18). Thomas et al reported higher levels of

Lp (a) in 76 patients with proteinurea than that of healthy controls (19). However, Lp (a) did not correlate with age, creatinine clearence, cholesterol levels, triglyceride levels, HDL cholesterol, LDL cholesterol, Apo-A-1, apo B-100, albumin levels, creatinine levels, in their study either. Appel et al reported that the synthesis of lipoproteins containing apo-B-100 is increased in the liver of patients with nephrotic syndrom (20).

In an invivo study performed in patients with familial hypercholesterolemiae who had high levels of Lp (a) concentrations, LDL receptors were suggested to have a role in the catabolism of Lp (a). Whenever LDL-cholesterol concentrations increase, Lp (a) catabolism decreases. The theory might explain Lp (a) increases in the renal transplant patients with high concentrations of LDL-cholesterol (15,18).

Lp (a) has been considered to be a hederitary risk factor in atherosclerosis and it was suggested that the levels of Lp (a) to be assessed as an independent factor besides cholesterol and after lipoproteins. We did not any significant correlation between Lp (a) concentrations and cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol. The results suggested the mechanisms responsible for the increase of Lp (a) and the other lipids in chronic renal failure are different.

In conclusion, we found the Lp (a) levels to be high in patients with chronic renal failure on hemodialysis. The high level of Lp (a) can have a role as an independent risk factor in the pathogenesis of atherosclerosis in those people and increase the mortality rates that stem from cardiovascular complications. Further studies are required to define the metabolic regulation of Lp (a) and its role in atherosclerotic disease.

Kronik böbrek yetmeziği olan hemodiyaliz hastalarında lipoprotein (a) düzeyi

Son zamanlarda lipoprotein (Lp) (a)'nın koroner kalb hastalığı için bağımsız bir risk faktörü olduğu farkedilmiştir. Hemodiyalize giren hastalarda aterosklerotik kardiyovasküler komplikasyonlar artmıştır. Lp (a)'nın hemodiyaliz hastalarındaki aterogeneze katkısının olup olmadığını belirlemek için, kronik böbrek yetmezlikli hemodiyaliz hastalarında bulunan Lp (a) düzeylerini sağlıklı kontrol grubundaki Lp (a) düzeyleriyle karşılaştırdık. Lp (a) düzeyi 40 hemodiyaliz ve 40 sağlıklı bireyde ölçüldü. Hemodiyaliz hastaları sağlıklı kontrollerle karşılaştırıldığında, hemodiyaliz hastalarının Lp (a) düzeylerinin belirgin olarak yüksek olduğu görüldü (hemodiyaliz hastalarının Lp (a) düzeyi: 21.2±1.3 mg/dL, kontrol düzeyinin Lp (a) düzeyleri: 11.2+0.9 mg/dL). Lp (a) kolesterol, trigliserid, HDL kolesterol ve LDL kolesterol seviyeleriyle korelasyon göstermiyordu. Sonuç olarak, serum Lp (a) düzeyi hemodiyaliz alan hastalarda kontrollere göre yüksek bulunmuştur. Lp (a) hemodiyaliz hastalarında ateroskleroza katkıda bulunuyor olsa da, Lp (a)'nın metabolik regülasyonunu ve aterosklerotik hastalıkta rolünü tam belirlemek için ileri çalışmalara ihtiyaç vardır.
[Türk J Med Res 1996; 14(2):78-80]

REFERENCES

. 1. Docci D, Manzoni G, Bilancioni. R, et al. Serum Lp (a) and coronary artery disease in uremic patients on chronic hemodialysis. Int J Artif Organs 1994 (abstract); 17(1):41-5.

2. Rhoads GG, Dahlen G, Berg K, et al. Lp (a) lipoproteins as a risk factor for miocardial infarction. JAMA 1986; 25:2540-4.

3. Cheung AK, Wu LL, Kablitz C, et al. Atherogenic lipids and lipoproteins in hemodialysis patients. Am J Kidneys-Dis 1993; 22(2):271-6.

4. Goldberg IJ. Lipoprotein methabolism in normal and uremic patients. Am J Kidney Dis 1993; 21(1):87-90.

5. Olbricht CJ. Pathophysiology and therapy of lipid metabolism disorders in kidney diseases. Klin Wochenschr 1991; 69(11):455-62.

6. Dahalen GH, Guyton JR, Attar M. Association of lipoprotein Lp (a), plasma lipids and other lipoproteins with coronary artery disease documented by angiography. Circulation 1986; 74:758-65.

7. Barbagallo CM, Averna MR, Scafidi V, et al. Increased lipoprotein (a) levels in subjects with chronic renal failure on hemodialysis. Nephron 1992; 62:471-2.

8. Wanner C, Bohler J, Eckardt HG, et al. Effects of simvastatin on lipoprotein (a) and lipoprotein composition in patients with nephrotic syndrome. Clin Nephrol 1994; 41 (3):138-43.

9. Fridewald WT, Levy RI, Frederlcson DS. Estimation of the concentration of low-density lipoprotein cholesterol In plasma without use of the reperative ultracentrifuge. Clin Chem 1972; 18:499-502.

lO. Sümbüloğlu K, Sümbüloğlu V. Bioistatistik. Yenilenmiş 4.baskı. Ankara: Özdemir Yayıncılık, 1993.

11. Armstrong VW, Cremer P, Elberle E. The association between serum Lp (a) concentration and angiographically assesed coronary atherosclerosis. Dependence on serum LDL levels. Atherosclerosis 1986; 62:249-57.

12. Knight BL. Lp (a) catabolism in hypercholesterolemic individuals. Chem Phys Lipids 1994 (abstract); 67-68:233-9.

13. Parra HJ, Mezdour H, Cachera C, et al. Lp (a) lipoprotein in patients with chronic renal failure treated by hemodialysis. Clin Chem 1987; 33:721.

14. Nakahama H, Nakanishi T, Uyama O, et al. Plasma Lp (a) levels in patients undergoing maintenance hemodialysis. Ren Fail 1993 (abstract); 15(2): 189-93.

15. Barbagallo CM, Averna MR, Sparachio V, et al. Lp (a) levels in end-stage renal failure and renal transplantation. Nephron 1993; 64:560-4.

16. Karadi I, Romics L, Palos G, et al. Lp (a) lipoprotein concentration in serum of patients with heavy proteinuria of different origin. Clin Chem 1989; 35(1):2121-3.

17. Krempler F, Kostner GM, Bolzano K. Turnover of Lp (a) in man. J Clin Invest 1980; 65:1483-90.

18. Heiman P, Josephson MA, Feliner SK, et al. Elevated Lp (a) levels in renal transplantation and hemodialysis patients. Am J Nephrol 1991; 11:470-4.

19. Thomas ME, Freestone A, Varghese Z, et al. Lipoprotein (a) in patients with proteinuria. Nephrol Dial Transplant 1992; 7(7):597-601.

20. Appel G, Blum C. The hyperlipidemia of the nephrotic syndrome. N Engl J Med 1985; 312:1544-8.