Analysis of Serum Lipids and Lipoprotein Electrophoresis Fractions in Hypertensive Patients

Chong-Ho Kim[†]

Department of Clinical Laboratory Science, Wonkwang Health Science University, Jeonbuk 570-750, Korea

We analyzed the concentration of serum total cholesterol (TC), high density lipoprotein cholesterol (HDLC), low density lipoprotein cholesterol (LDLC), triglyceride (TG) and the serum lipoprotein electrophoresis fractions in hypertensive patients (hypertension group, n=182). The average concentration of lipids and lipoprotein fractions in the hypertension group was compared to that of the normal group. The average concentrations of serum TC, LDLC and TG in the hypertension group were significantly higher than those of the normal group (3.3%, 11% and 70%, respectively) ($P<0.05$). But HDLC was nonsignificantly lower (2%) ($P<0.05$). In the hypertension group, the percentages of patients who had an abnormally high level of total cholesterol, HDLC, LDLC and TG were 12.1%, 8.2%, 24.2% and 44.5%, respectively. The average of β-lipoprotein (27.5%) and pre β-lipoprotein (12.6%) were significantly higher, whereas α-lipoprotein (15.2%) was significantly lower in the hypertension group than in the normal group ($P<0.05$). The percentages of patients who had an abnormally high level of very low density lipoprotein (pre β-LP), LDLC (β-LP) and chylomicron were 31.3%, 17.0% and 12.6%, respectively. This study suggests that an increasing of total cholesterol, LDLC and TG, pre β-LP, β-LP and chylomicron are associated with a risk factor for hypertension.

Key Words: Hypertension, Cholesterol, Triglyceride, Lipoprotein electrophoresis

INTRODUCTION

Hypertension is an important public health challenge because of the associated morbidity and mortality and is one of the most common chronic diseases afflicting humans. Hypertension is considered to be present when a person's blood pressure is consistently at least 140/90 mmHg (systolic pressure/diastolic pressure) or above. A blood pressure of 120/80 mmHg or lower is considered to be normal blood pressure (Cornoni et al., 1989). Hypotension is generally considered as blood pressure less than 90/60 mmHg. Persistent hypertension is the most common risk factors for cardiovascular diseases such as heart failure, strokes, heart attacks and arterial aneurysm, and is a leading

cause of chronic renal failure (Gotto et al., 2005). Even moderate elevation of arterial blood pressure leads to shortened life expectancy. At severely high pressures, defined as mean arterial pressures 50% or more above average, a person can expect to live no more than a few years unless appropriately treated (Groop and Orho, 2001). Dyslipidemia and hypertension have been well established and partially overlapping risk factors for cardiovascular disease (Austin et al., 1998; Ginsberg, 2002). Moreover, hypertension and dyslipidemia are manifestations of the metabolic syndrome which is a consequence of the interaction of genes and the environmental change (Laaksonen et al., 2004). The pathogenesis of hypertension and the metabolic syndrome is only partly understood, but endothelial dysfunction likely plays a role in both (Oparil et al., 2003; Kim et al., 2006). In the health study, physicians reported that total cholesterol (TC), low density lipoprotein cholesterol (LDLC) and high density lipoprotein cholesterol (HDLC) predicted onset of hypertension in men without self-reported hypertension (Halperin et al., 2006). These findings agree with some of the pro-

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spective studies on dyslipidemia and incident hypertension (Haffner et al., 1996; Sesso et al., 2005). Determination of the circulating levels of plasma lipoproteins is important in the diagnosis of primary and secondary disorders of lipid transport and in risk assessment for atherosclerosis and coronary artery disease (Naito et al., 1973). In the fasting state, three main lipoprotein classes of α-lipoprotein (α-LP), pre β-lipoprotein (pre β-LP) and β-lipoprotein (β-LP) have been identified. Each of lipoprotein classes differs in size and density, and in lipid and apolipoprotein composition. It is well established that there is a positive correlation between risk of premature coronary heart disease and total plasma cholesterol and LDLC (Pyrorala et al., 1994). We hypothesized that hypertension should be intercorrelated with the abnormal content of total cholesterol, LDLC, HDLC, triglyceride (TG) and lipoproteins in plasma. Therefore, we measured serum lipids and fractions of lipoprotein electrophoresis in hypertensive patients.

MATERIALS AND METHODS

Preparation of blood sample

To evaluate the concentration of serum lipids and lipoprotein electrophoresis fractions in hypertension patients, we obtained fasting blood samples from the hypertension outpatients (n=182, 115 men and 67 women) with blood pressure above 140 mmHg/90 mmHg (systolic pressure/ diastolic pressure) and normal outpatients (n=190, 125 men and 65 women) with blood pressure below 120 mmHg/80 mmHg who visited a hospital for the first time. Mean ages for the hypertension patients group (hypertension group) and normal outpatients group (normal group) were 45±7.5 years and 40±10 years, respectively. Hypertension was diagnosed according to the seventh report of the joint national committee on prevention, detection, evaluation and treatment of high blood pressure (Chobanian et al., 2003).

Analysis of lipids

We isolated sera from bloods and analyzed the concentration of lipids in sera. TC, HDLC and TG were measured by enzymatic method with a Hitachi 7600 automatic chemical analyzer (Hitachi High Technologies Co., Tokyo,

Table 1. Lipid profiles in the normal and the hypertension group

Variable	Group		P-value
	Normal	Hypertension	
Total cholesterol (mg/dL)	180.0±25.0	186.0±39.0	0.046
HDLC (mg/dL)	50.0±7.5	49.0±12.0	0.092
LDLC (mg/dL)	100.0±15.0	111.0±12.0	0.000
Triglyceride (mg/dL)	100.0±25.0	170.0±112.0	0.000

Data represent the mean ± SD.
Abbreviation: HDLC, high density lipoprotein cholesterol; LDLC, low density lipoprotein cholesterol.

Japan), and LDLC was calculated by means of the formula of Friedewald and colleagues (Friedewald et al., 1972). Other reagents that we used are Sigma reagents (Sigam Chemical Company, Saint Louise, MO, USA).

Lipoprotein electrophoresis

Several serum samples were applied simultaneously to a strip of cellulose acetate membrane wetted with tris-barbital buffer solution (pH 8.7). The cellulose acetate membrane with samples was run on the electrophoresis chamber for 25 minutes at 180 voltage. We bought cellulose acetate membrane, tris-barbital buffer and other reagents from Helena company (East Princeton, NY, USA). The lipoprotein fractions were stained in oil red O solution and were analyzed the concentration of each lipoprotein fraction with image analyzer (Viler Lourmat, Cedex, France).

Statistical analysis

The concentrations of lipids and lipoprotein fractions in sera of the hypertension group were compared to reference group. All data were expressed mean ± standard deviation (SD). Data were analyzed by One-Sample t-test using the SPSS statistical software package, version 8.0 (SPSS Inc., Chicago, IL, USA). A P value less than 0.05 was considered to be statistically significant.

RESULTS

Concentration of lipids

We determined the concentration of serum TC, HDLC, LDLC and TG in the hypertension group (Table 1) and

Table 2. Lipoprotein electrophoresis fractions (%) in the normal and the hypertension group

Variable	Group		P-value
	Normal	Hypertension	
α-lipoprotein	23±4.0	19.5±13.0	0.000
pre β-lipoprotein	12±4.0	15.3±11.0	0.000
β-lipoprotein	65±8.0	73.2±19.0	0.000
Chylomicron	0.5±0.25	2.0±3.0	0.000

Data represent the mean ± SD.
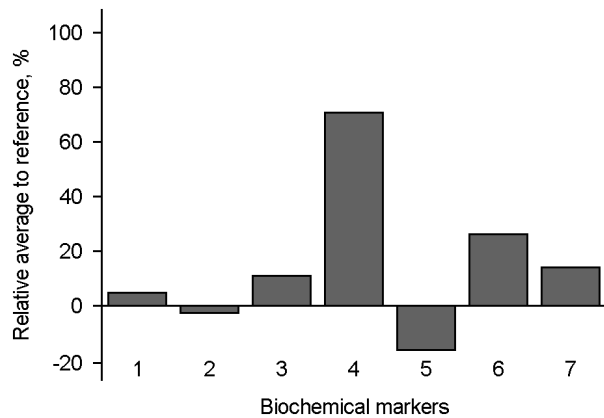
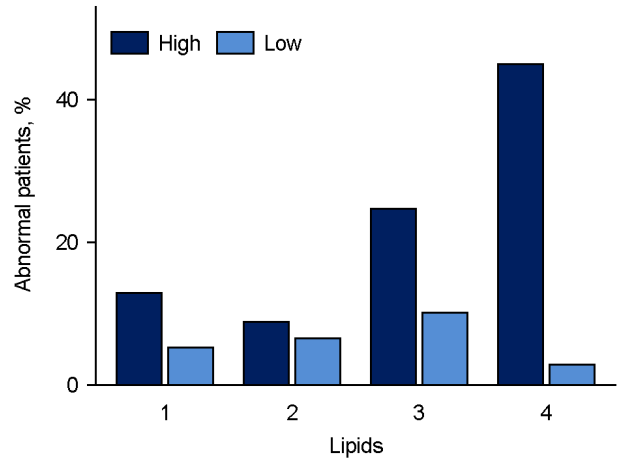**Fig. 1.** The relative average concentration of total cholesterol (1), HDL cholesterol (2), LDL cholesterol (3), triglyceride (4), α-lipoprotein (5), pre β-lipoprotein (6) and β-lipoprotein (7) in sera of hypertensive patients to the average of the normal group.

Fig. 2. The rate of patients who had an abnormal high or low level of total cholesterol (1), HDL cholesterol (2), LDL cholesterol (3) and triglyceride (4) in sera of hypertensive patients.

Fig. 3. The rate of patients who had an abnormal high or low level α-lipoprotein (1), pre β-lipoprotein (2) and β-lipoprotein (3) and chylomicron (4) in sera of hypertensive patients.
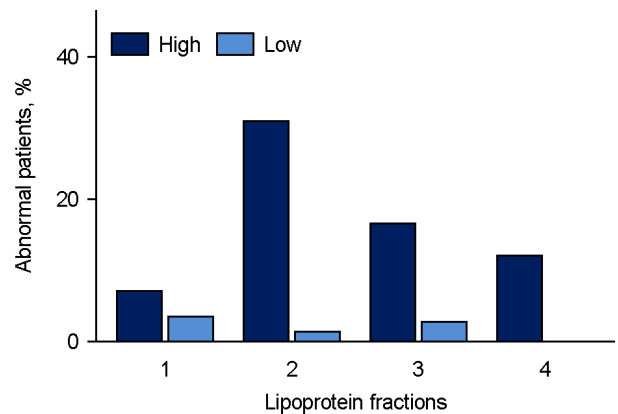
compared the each average concentration with that of average in the normal group (Fig. 1). In comparison with the average of reference, the average concentration of serum TC, LDLC and TG in the hypertension group was significantly increased by 3.3% ($P<0.05$), 11% ($P<0.05$) and 70% ($P<0.05$), respectively. HDLC was decreased by 2%, but not significant ($P>0.05$). The percentage of hypertensive patients who had an abnormal level of TC, HDLC, LDLC and TG was shown in Fig. 2. In the hypertension group, the percentage of patients who had an abnormally high level of TC, HDLC, LDLC and TG was 12.1%, 8.2%, 24.2% and 44.5%, respectively. The percentage of patients who had an abnormally low level of TC, HDLC, LDLC and TG was 9%, 12%, 17% and 5%, respectively.

Analysis of lipoprotein electrophoresis fractions

We carried out electrophoresis of serum lipoprotein in hypertensive patient and analyzed the relative average concentration of fractions to total lipoprotein (Table 2). In comparison of the average of serum lipoprotein fractions in patients with that of the average of reference (Fig. 1), the average of β-lipoprotein and pre β-lipoprotein in the hypertension group was significantly increased by 27.5% ($P<0.05$) and 12.6% ($P<0.05$), and α-lipoprotein was significantly decreased by 15.2% ($P<0.05$). Fig. 3 shows the percentage of hypertensive patients who had an abnormal level of α-lipoprotein, pre β-lipoprotein, β-lipoprotein and chylomicron. In the hypertension group, the percentages of patients who had an abnormally high level of α-LP, pre β-LP, β-LP and chylomicron were 6.6%, 31.3%, 17.0% and 12.6%, respectively. The patients who had an abnor-

mally low level of α-LP, pre β-LP, β-LP and chylomicron were 3.8%, 1.1%, 2.7% and 0%, respectively.

DISCUSSION

According to National Cholesterol Education Program guidelines (Scott et al., 2001), the risk stratification of lipid levels appeared to be clinically relevant for identifying patients at greatest risk for the development of hypertension. Subsequent stratification by JNC 7criteria (Chobanian et al., 2003) for those adults who are healthy or prehypertensive suggests that even adults with low baseline blood pressure levels but elevated lipid levels may be at risk for hypertension, as the absolute risks of hypertension remains relatively high. Previous studies have provided evidence of an association between plasma lipid levels and the risk of hypertension. In a study of men and women in incident cases of hypertension, baseline triglyceride and TC levels significantly increased with increasing levels of blood pressure (Skarfors et al., 1991; Hunt et al., 1991). Other studies reported that subjects with higher baseline triglyceride and lower HDL cholesterol levels had a significantly greater risk of developing hypertension (Haffner et al., 1996), whereas higher total cholesterol and LDL cholesterol levels were associated with nonsignificantly increased risk (Haffner et al., 1992).

The present data show that total cholesterol, LDL cholesterol and TG were significantly increased in hypertensive patients, but HDL cholesterol was nonsignificantly decreased. These data are similar to some previous reports which demonstrated the levels of total cholesterol and TG in hypertensive patients were significantly increased (Skarfors et al., 1991 Haffner et al., 1996). However, a nonsignificant decrease of HDL cholesterol and a significant increase of LDL cholesterol in our data are not identical to previous reports (Hunt et al., 1991; Haffner et al., 1992; Sesso et al., 2005). Our data suggest that increased total cholesterol, LDL cholesterol and TG are associated with a risk factor for hypertension. Abnormal concentrations of lipoproteins are well-described risk factors for cardiovascular disease and hyperlipidemia (Naito et al., 1973), but are not demonstrated well with hypertension. A number of previous studies

in hypertensive patients have indicated that α-LP is a complex lipoprotein macromolecule that contains apolipoprotein (a), which shares homology with plasminogen (McLean et al., 1987). It acts as a competitive inhibitor of tissue type plasminogen activator and there by helps in modulating the fibrinolytic system consistent with an atherogenic role (Hajjar et al., 1989; Falco et al., 1998). Lp (a) levels are known to exhibit significant inter individual variation and are strictly under genetic control. Elevated serum Lp (a) levels are associated with an increased risk of cardiovascular disease and renal failure in hypertensive patients (Dahlen and Stenlund, 1997). There are very limited case-control studies determining association between Lp (a) excess and essential hypertension. One of reports suggested that hypertension and dyslipidaemia are often associated with a higher plasma concentration of Lp (a). However, the higher plasma concentration of Lp (a) could be an independent risk factor for atherosclerosis, and could contribute towards increasing the incidence of cardiovascular disease in person with essential hypertension (Labeur et al., 1992). In this study, our data show that pre β-LP, β-LP and chylomicron are increased significantly in hypertensive patients, but α-LP is significantly decreased. These results suggest that an increasing of pre β-LP, β-LP and chylomicron and decreasing of α-LP are associated with a risk factor for hypertension. The percentage of patients who had an abnormal higher level of total cholesterol, LDL cholesterol, TG, pre β-LP, β-LP and chylomicron are 12.1%, 24.25, 44.5, 31.3%, 17.0% and 12.6%, respectively. The increase of concentration of TG has been dependant absolutely on increase of pre β-LP and chylomicron (Wilson et al., 1981; Wilson et al., 1985; Tremblay et al., 2004). In conclusion, these results suggest that an abnormally higher level of total cholesterol, LDL cholesterol, TG, pre β-LP, β-LP and chylomicron in blood might be a risk factor for hypertension among adults.

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