Serum lipid, homocysteine, and platelet derived growth factor in patients with hypertension

Patcharaporn Aree
Faculty of Nursing, Christian University of Thailand, Nakhon Pathom, Thailand
Tanyarat Jomgeow
Faculty of Associated Medical Sciences, Chiang Mai University, Chiang Mai, Thailand
Krid Thongbunjob
Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand, and
Chiraporn Tachaudomdach
Faculty of Nursing, Chiang Mai University, Chiang Mai, Thailand

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Abstract

Purpose – The purpose of this paper is to study serum lipids, lipoproteins, homocysteine (Hcy) and platelet-derived growth factor (PDGF), and to evaluate the relationship between serum lipids, lipoproteins, Hcy and PDGF in patients with hypertension.

Design/methodology/approach – In total, 85 patients with hypertension (34 males, 51 females) were recruited from October to December 2015 at Saraphi Hospital, Chiang Mai Province using purposive sampling. PDGF mRNA levels of the patients were analyzed using the RT-PCR method. Hcy was analyzed by high-performance liquid chromatography. An enzymatic-colorimetric method was used to measure serum cholesterol, high-density lipoprotein cholesterol and triglyceride. A low-density lipoprotein cholesterol (LDL-C) level was calculated using Friedewald's formula. Descriptive statistics and the Pearson product moment were also used in the analysis.

Findings – Among the patients with hypertension, hypercholesterolemia, high levels of LDL-C, hypertriglyceridemia and hyperhomocysteinemia were found in 54.1, 70.7, 25.9 and 44.7 percent, respectively. In addition, PDGF was significantly correlated with Hcy ($r = 0.705$; $p < 0.005$). There was no association between serum lipids or lipoproteins and Hcy or PDGF in patients with hypertension.

Practical implications – The results of this study provide direction on how serum lipids, lipoproteins, Hcy and PDGF can be used as a guide to improving dietary management as a means of reducing cardiovascular disease, and stroke in patients with hypertension.

Originality/value – This manuscript is not currently under consideration, in press or published elsewhere. This manuscript is truthful original work without fabrication, fraud or plagiarism. The authors have made important scientific contributions to this study. The authors are familiar with the primary data, and have read the entire manuscript and take responsibility for it content. No benefits were received by the authors or any member of the authors' family or the research team, from any commercial source, directly or indirectly related to this work. Moreover, no one affiliated with has any financial interest related to the subject matter of this manuscript.

Keywords Serum lipid, Homocysteine, Platelet-derived growth factor, Hypertension

Paper type Research paper

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Introduction

Hypertension or raised blood pressure is a major risk factor not only for coronary heart disease but also for ischemic and hemorrhagic stroke[1]. Stroke is a leading cause of death and disability in adults worldwide and the overall global burden of stroke is great and increasing[2]. Hypertension is a common health problem in Thailand with records from 2008, indicating that approximately 34.2 percent of the adult population had hypertension[3]. About 87 percent of strokes are ischemic, and the rest are hemorrhagic[4]. An ischemic stroke (IS) is defined as a loss of brain function due to a disturbance in the blood supply to the brain. This is caused by either blockage of a blood vessel via thrombosis or an arterial embolism, or by cerebral hypoperfusion[4]. Reducing blood pressure by 10 mmHg systolic or 5 mmHg diastolic reduces the risk of both ischemic and hemorrhagic strokes by about 40 percent[5]. Risk factors for IS include diabetes, high cholesterol levels, high levels of homocysteine (Hcy), platelet-derived growth factor (PDGF), tobacco and atrial fibrillation[6–8]. Increased serum cholesterol levels can lead to atherosclerosis, but the relationship of serum cholesterol to the risk for stroke remains controversial[9]. PDGF is a dimeric glycoprotein that can be composed of either two A subunits (PDGF-AA), two B subunits (PDGF-BB), or one unit of each (PDGF-AB)[10]. PDGF is likely to be angiogenic and neuroprotective in strokes because PDGF-BB mRNA and its receptor are expressed on microvessel endothelial cells[11]. Hcy, a non-protein α-amino acid, is an intermediate sulfur-containing amino acid in the metabolism of methionine. Hcy is an independent risk factor for atherosclerosis, cardiovascular disease, hypercoagulability[12, 13], IS[14, 15] and target organ damage[16]. One study reported that 58.3 percent of IS patients had hyperhomocysteinemia (HHcy)[17]. Several studies have found a relationship between an elevated Hcy level and the risk of coronary, cerebrovascular and peripheral vascular diseases[18–20] as well as the occurrence of blood clots, heart attacks and strokes[21]. These findings suggest that the possible biological mechanisms serum lipid, lipoprotein, Hcy and PDGF as exacerbated risk factors for cerebrovascular disease in patients with hypertension should be explored. A serum lipid profile includes four basic parameters: total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and triglycerides (TG)[22]. An understanding of the relationship among these parameters in patients with hypertension is necessary in order to determine appropriate treatment. The aim of this study was to investigate the relationships between serum lipids, lipoproteins, Hcy and PDGF in patients with hypertension. The findings could provide a better understanding of the prevention and control of IS in patients with hypertension. That understanding could be used as a guideline for determining the possible biological mechanisms of these parameters as exacerbated risk factors for cerebrovascular diseases. The results of this study might provide evidence of the rate of hyperlipidemia and HHcy, and the relationships of serum lipids, PDGF and Hcy in patients with hypertension. The treatment may be needed to consider the greater beneficial effect of reducing cardiovascular disease. Understanding those relationships could help identify biological mechanisms which cause these parameters to be significant risk factors for cerebrovascular disease and thus help reduce the incidence of cardiovascular disease.

Materials

Study design and research settings

This correlational descriptive study was conducted at Saraphi Hospital, Chiang Mai Province.

Participants

In 2015, there were 1,049 cases of patients with hypertension registered at Saraphi hospital. Consecutive sampling was used to recruit 85 participants from October to December 2015. The number of samples was estimated by defining an α of 0.05, a power of 0.8 and a

correlational coefficient of 0.3[23]. The inclusion criteria were male or female, aged over 19 years, and possibly co-morbid with diabetes mellitus (DM) and/or hyperlipidemia which could be controlled (reduced to a tolerable level). They were excluded if they had heart disease, kidney disease, liver disease, respiratory disease and cancer; could not speak and write Thai; and could not cooperate in this study.

Outcome measures

Venous blood samples (15–20 ml) were taken after a 12–14 h fast under strictly standardized conditions. Blood was collected into sodium using a Vacutainer (Becton-Dickinson, Plymouth, UK) system. Blood was centrifuged (2,000 g for 30 min at 4°C), and the plasma was stored in aliquots at −80°C until use. The PDGF mRNA level was analyzed by the RT-PCR method (Invitrogen). Hcy was analyzed by using the chemiluminescence method (Architect, Abbott). Hcy was analyzed by high-performance liquid chromatography[24]. Serum samples were analyzed for lipid levels, i.e., TC, TG, LDL-C and HDL-C. An enzymatic-colorimetric method (Architect, Abbott) was used to measure serum cholesterol, HDL-C and TG. The LDL-C level was calculated using Friedewald's formula[25].

Statistical analysis

Descriptive statistics were used to identify demographic characteristics, serum lipids and lipoproteins, Hcy and PDGF. The inferential statistics and the Pearson product moment correlation coefficient were used to investigate the relationships between serum lipids and lipoproteins, PDGF and Hcy.

Ethical considerations

This research was approved by the Research Ethics Review Committee of the Faculty of Nursing, Chiang Mai University, Chiang Mai, Thailand (FULL-035-2558).

Results

A Kolmogorov-Smirnov test showed that the sample data were normally distributed ($p > 0.05$), and the Pearson product moment correlation coefficient was used.

Characteristics of the participants

In total, 85 patients with hypertension (34 males, 51 females) with a mean age of 63.33 years were studied. All subjects were Buddhists: 65.9 percent were married; 69.4 percent had completed primary school; 36.5 percent were employed; and 38.9 percent had a monthly income of THB 1,001–5,000. They were co-morbid with either hyperlipidemia (35.3 percent), DM (8.2 percent) or both (2.4 percent). All patients received antihypertensive drugs during the study. In total, 30 patients with hyperlipidemia also received lipid-lowering drugs, and 7 patients with DM received oral hypoglycemic agents. Two patients who were co-morbid with hyperlipidemia and DM received both lipid-lowering drugs and oral hypoglycemic agents (Table I). In patients with hypertension, hypercholesterolemia, high level of LDL-C, hypertriglyceridemia and HHcy were found 54.1 (31.8%+18.8%+3.5%), 70.6 (23.5%+47.1%), 25.9 and 44.7 percent, respectively (Table II).

The relationships between serum lipids and lipoproteins, PDGF and Hcy

PDGF in the patients with hypertension was found to be significantly correlated with Hcy ($r = 0.705$; $p < 0.01$) (Table III). No association was found between either serum lipids or lipoproteins and Hcy or PDGF in patients with hypertension (Table III).

Variables	Male ($n = 34$)	Female ($n = 51$)	Total ($n = 85$)	%
Age(years) (mean = 63.33, SD = 10.61, min. = 28, max. = 85)				
28–30	1	0	1	1.2
31–40	1	0	1	1.2
41–50	2	4	6	7.1
51–60	9	15	24	28.2
61–70	10	18	28	32.9
71–80	9	13	22	25.9
80–85	2	1	3	3.5
Marital status				
Single	3	5	8	9.4
Married	27	29	56	65.9
Widowed	3	13	16	18.8
Separated	1	4	5	5.9
Religion				
Buddhist	34	51	85	100.0
Education				
Primary school	20	39	59	69.4
Secondary school	9	6	15	17.7
Diploma	3	1	4	4.7
Bachelor's degree	2	2	4	4.7
Higher than bachelor's degree	0	3	3	3.5
Occupation				
Employee	13	18	31	36.5
Small owner business	6	0	6	7.0
No work	5	7	12	14.1
Agriculture	4	8	12	14.1
Housewife	3	16	19	22.4
Customer	2	2	4	4.7
Officer	1	0	1	1.2
Monthly income (Baht) (mean = 4,611.76, SD = 5,402.43, min. = 0, max. = 25,000)				
< 1,000	7	22	29	34.1
1,001–5,000	14	19	33	38.9
5,001–10,000	6	9	15	17.6
10,001–15,000	3	0	3	3.5
1,5001–20,000	2	1	3	3.5
20,001–25,000	2	0	2	2.4
Diseases				
Hypertension	16	30	46	54.1
Hypertension and hyperlipidemia	13	17	30	35.3
Hypertension and diabetes mellitus	4	3	7	8.2
Hypertension, hyperlipidemia, and diabetes mellitus	1	1	2	2.4

Table I.
Characteristics of the participants according to sex

Discussion

The rate of hyperlipidemia in patients with hypertension was very high, even though 37.7 percent of the patients received cholesterol-lowering drugs. The study also found that 44.7 percent of the patients had HHcy at a rate similar to that in chronic kidney disease patients[16]. The Serum Hcy level was significantly correlated with PDGF, but serum lipids and lipoprotein levels were not correlated with either Hcy or PDGF (Table III). The Serum Hcy level was statistically significantly correlated with PDGF which was explained by the fact that it is an indication that the patients with hypertension were also at high risk for atherosclerosis.

Variables	Male		Female		Total	
	n	%	*n*	%	*n*	%
Total cholesterol (TC)						
Normal level (< 200 mg/dL)	17	20.0	22	25.9	39	45.9
Mild level (200–239 mg/dL)	10	11.8	17	20.0	27	31.8
Moderate level (240–300)	5	5.9	11	12.9	16	18.8
High level (> 300 mg/dL)	2	2.4	1	1.2	3	3.5
Low-density lipoprotein cholesterol (LDL-C)						
Normal level (< 100 mg/dL)	12	14.1	13	15.3	25	29.4
Mild level (100–129 mg/dL)	11	12.9	9	10.6	20	23.5
Severe level (> 130 mg/dL)	11	13.0	29	34.1	40	47.1
High-density lipoprotein cholesterol (HDL-C)						
Normal level (> 35 mg/dL)	30	35.3	51	60.0	81	95.3
High level (> 150 mg/dL)	4	4.7	0	0	4	4.7
Triglyceride (TG)						
Normal level (< 150 mg/dL)	24	28.2	39	45.9	63	74.1
High level (> 150 mg/dL)	10	11.8	12	14.1	22	25.9
Homocysteine (Hcy)						
Normal (5–15 mole/L)	14	16.5	33	38.8	47	55.3
High (> 15 mole/L)	20	23.5	18	21.2	38	44.7

Note: $n = 85$

Table II.
Serum lipid, lipoprotein and homocysteine in patients with hypertension

	TC	LDL-C	TG	HDL-C	Hcy	PDGF
TC						
Pearson correlation	1	0.919**	0.215*	0.472**	−0.119	−0.005
Sig. (2-tailed)		0.001	0.049	0.001	0.278	0.967
n	85	85	85	85	85	85
LDL-C						
Pearson correlation	0.919**	1	−0.005	0.241*	−0.132	−0.016
Sig. (2-tailed)	0.001		0.965	0.026	0.228	0.883
n	85	85	85	85	85	85
TG						
Pearson correlation	0.215*	−0.005	1	−0.261*	0.149	0.111
Sig. (2-tailed)	0.049	0.965		0.016	0.174	0.310
n	85	85	85	85	85	85
HDL-C						
Pearson correlation	0.472**	0.241*	−0.261*	1	−0.156	−0.073
Sig. (2-tailed)	0.001	0.026	0.016		0.153	0.508
n	85	85	85	85	85	85
Hcy						
Pearson correlation	−0.119	−0.132	0.149	−0.156	1	0.705**
Sig. (2-tailed)	0.278	0.228	0.174	0.153		0.001
n	85	85	85	85	85	85
PDGF						
Pearson correlation	−0.005	−0.016	0.111	−0.073	0.705**	1
Sig. (2-tailed)	0.967	0.883	0.310	0.508	0.001	
n	85	85	85	85	85	85

Notes: $n = 85$. *,**Significant at 0.05 and 0.01 levels (two-tailed)

Table III.
Pearson product moment correlations among serum lipid, lipoprotein, Hcy and PDGF in patients with hypertension

Nitric oxide (NO) plays a central atheroprotective role through the regulation of vascular tone, inhibition of platelet aggregation, suppression of vascular smooth muscle cell proliferation, and blockage of leukocyte adhesion and transmigration[26]. In addition, the damaging effects of Hcy through the inhibition of endothelial NO synthase drive the development of inflammation, oxidative stress and apoptosis of endothelial cells, and can eventually lead to atherosclerosis, plaque progression and the occurrence of atherosclerotic complications by disrupting normal blood clotting mechanisms[27–29]. Thus, the results of this study suggest that patients with hypertension, who are co-morbid with hypercholesterolemia and/or HHcy which can cause additional damage, were at higher risk of atherosclerosis and stroke than patients having either condition alone. This indicates that special attention should be paid to patients with hypertension in addition to hyperlipidemia and/or HHcy and that they should be provided with cholesterol and Hcy lowering therapy. The benefits of cholesterol-lowering therapy are supported by strong evidence provided by a large number of studies[30]. Other therapies, including supplementation with folic acid, vitamin B_6 and vitamin B_{12} to reduce Hcy, have also been found to be beneficial[31]. Other factors, including smoking, lack of physical activity and obesity[31], may also elevate plasma cholesterol levels, Hcy and blood pressure, indicating that quitting smoking, increasing physical activity and reducing weight are also suitable therapies.

Future studies should investigate whether the degree to which patients with hypertension plus hypercholesterolemia and/or HHcy could benefit from the provision of cholesterol and Hcy lowering therapy in conjunction with antihypertensive therapy. It is recommended that nurses and health personnel should identify the PDGF and Hcy parameters, which may help reduce the incidence of cerebrovascular disease and cardiovascular disease. This study provides evidence of the high rate of hypercholesterolemia and HHcy in patients with hypertension. Hcy is correlated significantly with PDGF, but no association was observed between either plasma Hcy concentration or PDGF and levels of either plasma lipids or lipoproteins. The results of this study support the hypothesis that plasma Hcy concentration, as well as lipid and lipoprotein concentrations are independent parameters.

Further studies are needed to determine whether combined treatment consisting of dietary modification to control lipids and Hcy plus antihypertensive drugs either with or without cholesterol-lowering drugs has a greater beneficial effect when compared with antihypertensive drugs alone or when compared with antihypertensive drugs plus cholesterol-lowering drugs in reducing cardiovascular disease.

In conclusion, hyperlipidemia and hyperhomocysteinemia are commonly found in patients with hypertension. In addition, PDGF was significantly correlated with Hcy. So the prevention and control of serum lipid levels, PDGF and Hcy can decrease the number of coronary heart disease cases and ischemic and hemorrhagic stroke.

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Corresponding author
Patcharaporn Aree can be contacted at: areepatcharaporn@gmail.com