

Relationship between Hyperhomocysteinemia and Atherosclerosis in Chronic Hemodialysis Patients

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Background: Hyperhomocysteinemia is an independent risk factor of coronary artery heart disease (CAHD) and atherosclerosis in a normal population. However, it is still controversial in end-stage kidney disease patients who underwent long-term dialysis. Carotid intima-media thickness (IMT) is the standard non-invasive measurement of atherosclerosis. The aims of the present study were to determine the homocysteine (Hcy) level, and to evaluate its role as a risk factor of atherosclerosis in hemodialysis (HD) patients.

Material and Method: Clinical data and blood chemistries were assayed in 62 HD patients. Atherosclerosis was defined by clinical presentations of CAHD, cerebrovascular or peripheral vascular diseases, or carotid plaque by ultrasound. IMT was also measured by ultrasound.

Results: Plasma Hcy level in HD patients was significantly higher in HD patients than normal controls (28.3 vs 9.7 \pm 2.9 μ mol/L, $p < 0.001$). Older age ($p < 0.001$), male sex ($p = 0.05$), longer duration of HD ($p = 0.05$), and higher plasma Hcy level ($p = 0.01$) correlated with atherosclerosis by univariate analysis, but plasma Hcy did not show significant correlation by multivariable analysis. There was also correlation between IMT and atherosclerosis in HD patients ($p < 0.001$) but no correlation was observed between plasma Hcy level and IMT.

Conclusion: Hyperhomocysteinemia is not an independent factor in the genesis of atherosclerosis in HD patients. Advanced age plays a major role of hyperhomocysteinemia and IMT is a useful marker of atherosclerosis in these patients.

Keywords: Homocysteine, Atherosclerosis, HD patients, Carotid intima-media thickness

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It is widely accepted now that hyperhomocysteinemia is an independent risk factor of atherosclerosis, that causes coronary artery heart disease, cerebrovascular disease, and peripheral vascular disease⁽¹⁻³⁾. Decreasing blood homocysteine level can decrease the incidence of atherosclerosis^(4,5).

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Hemodialysis patients have 5-10 times higher risk of cardiovascular mortality⁽⁶⁻⁸⁾, and 2-4 times higher blood homocysteine level than a normal population^(9,10). Bostom reported that 83% of hemodialysis patients had hyperhomocysteinemia (fasting level $> 13.9 \mu$ mol/L)⁽¹¹⁾. The mechanisms of hyperhomocysteinemia in such patients are decreasing in renal clearance from abnormal renal homocysteine metabolism⁽¹²⁾, and/or deficiency of vitamins that play a role in homocysteine metabolism, i.e. folate, B₂, B₆, and B₁₂^(8,11). Several

previous studies found that higher blood homocysteine level correlated with a higher incidence of atherosclerosis in hemodialysis patients^(11,13-15). However, some studies did not find such a correlation^(8,16). Thus, the correlation between higher blood homocysteine level and higher incidence of atherosclerosis in hemodialysis patients is still inconclusive.

Intima-media thickness (IMT) measurement of carotid artery by ultrasound is the standard non-invasive method to detect atherosclerosis⁽¹⁷⁾. This method is safe, available, inexpensive, can detect the early stage of atherosclerosis, and can be used to monitor progression or regression of atherosclerosis⁽¹⁸⁾. Previous studies about carotid ultrasound measurement in hemodialysis patients showed that IMT had a correlation with atherosclerosis and blood homocysteine level^(7,19,20), as in a normal population^(21,22). However, one study in hemodialysis patients did not show such a correlation⁽²³⁾.

The objectives of the present study were to determine plasma homocysteine level and associated vitamin level, i.e. folate, B₂, B₆, and B₁₂ in Thai hemodialysis patients, and to evaluate their roles of them and other factors as risk factors of atherosclerosis in such patients.

Material and Method

Study design

Cross-sectional, analytic study.

Patients

Sixty-two end stage renal disease patients, 29 men and 33 women, aged 25-77 years, who underwent chronic hemodialysis at least twice a week at Siriraj Hospital, Bangkok, Thailand, were included in the present study. One hundred and eight healthy volunteers, 55 men and 53 women, aged 20-77 years, were also included as the normal control group.

The patients who had histories of chronic alcohol consumption, chronic smoking, malnutrition (serum albumin level < 3 g/dl), had received a blood transfusion within 3 months, medications (methotrexate, trimethoprim, phenytoin, carbamazepine, theophylline), underlying diseases (malignancy, chronic obstructive pulmonary disease (COPD), chronic infectious disease, connective tissue disease), were excluded from the present study.

Tools and measurement

Laboratory techniques

At least 12 hours fasting blood was collected

from the patients. The specimens were frozen in ice and were spun for 20 minutes with 2,000 g speed, 4 C temperature, within 30 minutes after collection. The plasma was separated and kept at -70 C temperature. Then, it was examined for homocysteine (by fluorescence polarization immunoassay method, ABBOT Laboratories – The IMx[®] Homocysteine), vitamin B6 (by erythrocytes glutamate oxaloacetate transaminase activity and activity after stimulation with pyridoxal-5-phosphate (p-5-p), described by Hoffman CA Roche), vitamin B12 (by electrochemiluminescence immunoassay “ECLIA”, Boehringer Mannheim - Elecsys[®] vitamin B₁₂ Immunoassay), and folate (by electrochemiluminescence immunoassay “ECLIA”, Boehringer Mannheim - Elecsys[®] folate Immunoassay).

Carotid ultrasound measurement

Only one experienced radiologist made all the ultrasound measurements. Ultrasonography was performed with a Toshiba, Power vision 6000 equipped with a linear probe 7.5 MHz. The patients were examined in the supine position. Their necks were supported and slightly extended. Images were obtained and carotid plaque was searched bilaterally of the proximal common carotid artery (CCA) to distal CCA, including bifurcation, internal carotid artery (ICA) and external carotid artery (ECA). Patients with plaque on, either the CCA, bulb, bifurcation, ICA or ECA were defined as having carotid atherosclerosis. Each patient was measured Intima-media thickness (IMT) at the far wall of both CCA, in longitudinal view, 2 points of each side (1 and 2 cm. away from the origin of the bulb), 4 points totally. Then the present calculated for mean IMT and maximum IMT.

Definitions

Hypertensive patients: The patients who received antihypertensive medications regularly and/or had a mean of the last 3-time pre-hemodialysis blood pressures more than 140/90 mmHg.

Atherosclerotic patients: The patients who had clinical presentations of coronary artery heart disease (CAHD); cerebrovascular disease (CVD); or peripheral vascular disease (PVD), and/or had past histories of such diseases, and/or had carotid plaques from carotid ultrasound measurement.

Method

Baseline data of hemodialysis patients were collected by history taking, physical examination, and

chart review. These data were sex, age, dry weight, blood pressure, underlying diseases i.e. hypertension; diabetes mellitus; atherosclerosis, duration since the initiation of hemodialysis, hemodialysis adequacy (Kt/V), and dosages of vitamin supplements (folate, B₂, B₆, and B₁₂). Twelve-hour fasting blood from the patients were collected for measurements of complete blood count, BUN, creatinine, fasting blood sugar, albumin, cholesterol, triglyceride, HDL, LDL, homocysteine, folate, vitamin B₂, B₆, and B₁₂. Carotid artery ultrasound for plaque detection and intima-media thickness (IMT) measurement were performed by an experienced radiologist.

Statistical analysis

Statistical analysis was performed using SPSS for Windows v10.0. The data were shown as mean \pm SD. Some data with abnormal distribution (plasma folate, vitamin B₂, vitamin B₁₂, triglyceride, and HDL) were adjusted by log_e (ln) before further statistical analysis. The data were compared for the difference between groups by student t-test, Chi-square, and analysis of covariance at $p < 0.05$, and were detected for the correlation by Pearson correlation coefficient at $p < 0.05$.

Results

Plasma homocysteine level in hemodialysis patients

Mean age of the hemodialysis patient and control group was 55.89 ± 12.84 and 37.04 ± 10.34 years, respectively. The patient group were 29 men (41.9%) and 33 women (58.1%), and the normal control group was 55 men (50.9%) and 53 women (49.1%).

Fasting plasma homocysteine level of the hemodialysis patients and normal control group were 28.27 ± 8.32 and 9.66 ± 2.89 $\mu\text{mol/l}$, respectively. After adjusting values for age and sex, there were still statistically significant differences between both groups ($p < 0.001$) (Table 1).

Factors affecting plasma homocysteine level in hemodialysis patients

The authors found that older age had a statistically significant correlation with a higher plasma

homocysteine level ($r = 0.34$, $p = 0.006$). As sex, duration since the initiation of hemodialysis, hemodialysis adequacy (Kt/V), and plasma vitamin levels that play a role in homocysteine metabolism (folate, B₂, B₆, and B₁₂) had no statistically significant correlation with plasma homocysteine level.

Factors affecting atherosclerosis in hemodialysis patients

Among 55 hemodialysis patients, atherosclerosis was detected in 41 patients (74.5%). Mean age of the patients with atherosclerosis was significantly higher than the ones without atherosclerosis (60.56 ± 9.60 and 42.43 ± 12.23 years, respectively) ($p < 0.001$). Proportion of male patients was significantly higher in the atherosclerosis group than the non-atherosclerosis group (24 men (58.5%), 17 women (41.5%) ($n = 41$) and 4 men (28.6%), 10 women (71.4%) ($n = 14$), respectively) ($p = 0.05$). Mean duration since the initiation of hemodialysis in the atherosclerosis group was also significantly longer than the non-atherosclerosis group (67.89 ± 49.27 and 39.58 ± 32.44 months, respectively) ($p = 0.05$).

However, the well-known conventional risk factors affecting atherosclerosis, such as hypertension; diabetes mellitus and dyslipidemia, had no statistically significant difference between both groups in the present study (Table 2).

Plasma homocysteine level, a non-conventional risk factors affecting atherosclerosis, was significantly higher in the atherosclerosis group, compared to the non-atherosclerosis group (28.66 ± 8.12 and 24.01 ± 4.79 $\mu\text{mol/l}$, respectively) ($p = 0.01$). As there was no significant difference in dosages of vitamin supplements and plasma vitamin levels that play role in homocysteine metabolism (folate, B₂, B₆, and B₁₂) between both groups (Table 3). Plasma phosphate level and calcium x phosphate product also showed no significant difference between both groups.

By univariate analysis, the authors found that older age, male sex, longer duration since the initiation of hemodialysis, and higher plasma homocysteine level

Table 1. Age, sex, and fasting plasma homocysteine level of the hemodialysis patient and normal control group

	Hemodialysis (n = 62)	Control (n = 108)
Age (year)	55.98 ± 12.84	37.04 ± 10.34
Sex (male/female) (% male)	29/33 (46.8%)	55/53 (50.9%)
Plasma homocysteine level ($\mu\text{mol/L}$)	$28.27 \pm 8.32^*$	9.66 ± 2.89

* $p = 0.001$ by analysis of covariance, adjusted for age, sex

Table 2. Clinical and laboratory data of the hemodialysis patients with and without atherosclerosis

	All (n = 55)	Atherosclerosis (n = 41)	Non-atherosclerosis (n = 14)	p-value
Age (year)	55.98 ± 12.84	60.56 ± 9.60	42.43 ± 12.23	< 0.001
Sex (% male)	50.9%	58.5%	40.0%	0.05
Duration since the initiation of HD (month)	59.16 ± 46.38	67.89 ± 49.27	39.58 ± 32.44	0.05
Weekly Kt/V	4.28 ± 1.25	4.17 ± 0.91	4.50 ± 1.74	NS
Systolic BP (mmHg)	149.55 ± 20.59	149.85 ± 22.30	149.05 ± 18.60	NS
Diastolic BP (mmHg)	81.09 ± 9.76	79.40 ± 10.20	85.50 ± 8.98	NS
DM (% disease)	41.0%	34.1%	14.3%	NS
Total cholesterol (mg/dl)	181.85 ± 39.80	178.19 ± 43.01	186.86 ± 32.59	NS
LDL-cholesterol (mg/dl)	112.55 ± 31.72	110.73 ± 33.72	114.30 ± 17.36	NS
Triglyceride (mg/dl)	115.87 ± 59.17	121.37 ± 65.77	108.50 ± 40.24	NS ^a
HDL-cholesterol (mg/dl)	46.13 ± 14.05	43.49 ± 14.20	50.86 ± 13.72	NS ^a
Fasting blood sugar (mg/dl)	111.37 ± 48.28	112.41 ± 48.10	109.93 ± 57.05	NS
Uric acid (mg/dl)	9.02 ± 1.65	9.13 ± 1.67	8.94 ± 1.83	NS
Albumin (g/dl)	4.10 ± 0.35	4.10 ± 0.38	4.14 ± 0.30	NS
Globulin (g/dl)	3.19 ± 0.71	3.21 ± 0.70	3.21 ± 0.79	NS
Phosphate (mg/dl)	6.11 ± 1.99	5.98 ± 1.93	6.35 ± 2.18	NS
Calcium x Phosphate product (mg ² /dl ²)	58.17 ± 19.55	58.22 ± 19.43	57.24 ± 20.53	NS
Alkaline phosphatase (U/l)	110.62 ± 66.26	110.00 ± 70.61	108.46 ± 47.84	NS
Potassium (mmol/l)	5.09 ± 0.81	5.10 ± 0.84	4.86 ± 0.74	NS
HCO ₃ ⁻ (mmol/l)	20.48 ± 3.03	20.46 ± 2.72	20.14 ± 3.44	NS
Hemoglobin (g/dl)	8.45 ± 1.53	8.48 ± 1.38	8.72 ± 1.42	NS
MCV (fl)	88.44 ± 8.42	89.07 ± 8.77	87.50 ± 6.82	NS
White blood cell (/μl)	5893 ± 1813	5988 ± 1933	5411 ± 1305	NS

^a adjusted data to normal distribution by log_e (ln) before further statistical analysis

Table 3. Plasma homocysteine, folate and vitamin B level of the hemodialysis patients with and without atherosclerosis

	Normal value	All (n = 55)	Atherosclerosis (n = 41)	Non-atherosclerosis (n = 14)	p-value
Homocysteine (μmol/l)	5-12	28.28 ± 8.32	28.66 ± 8.12	24.01 ± 4.79	0.01
Folate (ng/ml)	4.2-19.9	273.66 ± 258	330.03 ± 276	182.74 ± 179	0.065 ^a
Vitamin B ₂ (activation coefficient)	1.29-1.80	1.13 ± 0.17	1.11 ± 0.17	1.15 ± 0.14	NS ^a
Vitamin B ₆ (activation coefficient)	1.5-2.0	1.62 ± 0.33	1.64 ± 0.33	1.58 ± 0.35	NS
Vitamin B ₁₂ (pg/ml)	243-894	1243.3 ± 2093	1356.7 ± 2533	1018.5 ± 410	NS ^a

^a adjusted data to normal distribution by log_e (ln) before further statistical analysis

correlated with atherosclerosis. Since plasma homocysteine level, however, was not an independent factor, the authors found that plasma homocysteine level did not significantly correlate with atherosclerosis by analysis of covariance.

Correlation between carotid intima-media thickness (IMT) and atherosclerosis in hemodialysis patients

Mean IMT of the atherosclerosis group was significantly higher than the non-atherosclerosis group (0.69 ± 0.23 mm and 0.50 ± 0.08 mm, respectively)

Table 4. Carotid intima-media thickness (IMT) of the hemodialysis patients with and without atherosclerosis

	All (n = 55)	Atherosclerosis (n = 41)	Non-atherosclerosis (n = 14)	p-value
Maximum IMT (mm)	0.88 ± 0.38	0.96 ± 0.40	0.63 ± 0.11	<0.001
Mean IMT (mm)	0.64 ± 0.22	0.69 ± 0.23	0.50 ± 0.08	<0.001

($p < 0.001$). Maximum IMT of the atherosclerosis group was also significantly higher than the one (0.96 ± 0.40 mm and 0.63 ± 0.11 mm, respectively) ($p < 0.001$) (Table 4).

The factor that significantly correlated with a higher mean IMT was older age ($r = 0.38$, $p = 0.005$). As sex, duration since the initiation of hemodialysis, hypertension, diabetes mellitus, dyslipidemia, plasma phosphate level, and calcium x phosphate product did not correlate with mean IMT.

Correlation between plasma homocysteine level and IMT in hemodialysis patients

Pearson correlation coefficient was used to detect correlation between plasma homocysteine level and IMT. Neither mean IMT ($r = 0.15$, $p = 0.27$) nor maximum IMT ($r = 0.12$, $p = 0.37$) correlated with the plasma homocysteine level in the hemodialysis patients.

Discussion

In the present study, the authors found that fasting plasma homocysteine level in hemodialysis patients was 28.27 ± 8.32 $\mu\text{mol/l}$ (range 10.29-44.34 $\mu\text{mol/l}$). After adjusting values for age and sex, it was still significantly higher than in the normal control group (27.19 $\mu\text{mol/l}$ (25.59 - 28.80, 95% CI) and 10.29 $\mu\text{mol/l}$ (9.15-11.42, 95% CI), respectively, at age 44.0 years and male:female ratio 49%, $p < 0.001$). Plasma homocysteine level of these patients was approximately 3-times higher than the normal population, which corresponded with previous Western and Asian studies^(9,10). In addition, plasma homocysteine level was also higher in hemodialysis patients than the normal control group in every sex and age ranges (shown in Fig. 1).

The factor affecting hyperhomocysteinemia in hemodialysis patients from the present study was older age. Sex, duration since the initiation of hemo-

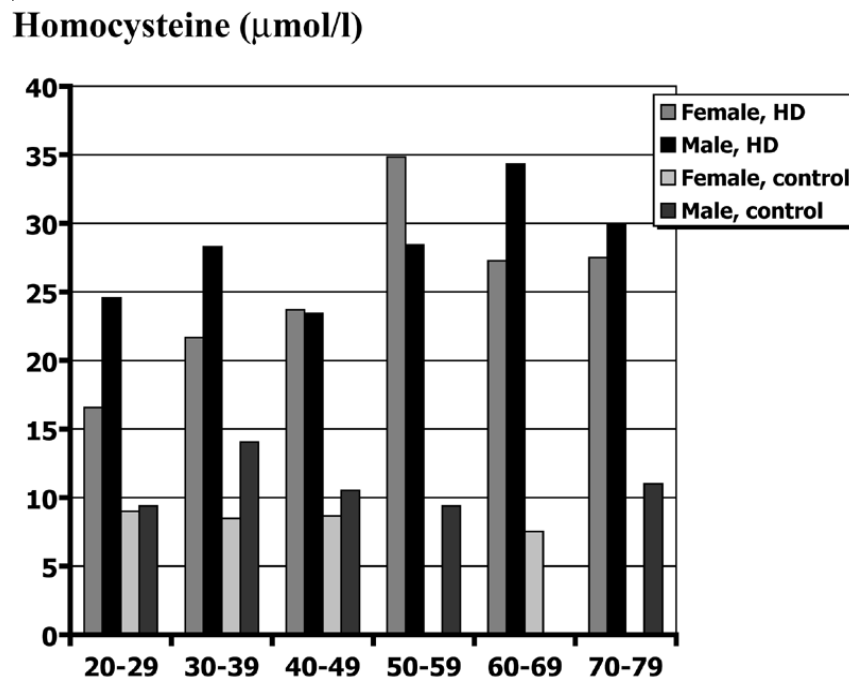


Fig. 1 Plasma homocysteine level of the hemodialysis patient and normal control group, divided by age and sex

dialysis and hemodialysis adequacy (Kt/V) had no significant correlation with a plasma homocysteine level. In addition, plasma vitamin levels, that play a role in homocysteine metabolism (folate, B₂, B₆, and B₁₂), had also no correlation with the plasma homocysteine level. These were probably caused by rather high baseline plasma folate level in most of the present hemodialysis patients, that made such correlation less clearly than in the ones with lower baseline level. Although Manns et al found an invert correlation between plasma homocysteine level and erythrocytic folate level, they also did not find a correlation between plasma homocysteine level and plasma vitamin B₁₂ level like the present study⁽¹⁴⁾.

A daily dosage of folate, vitamin B₂, B₆, and B₁₂ supplements of hemodialysis patients were 5.65 ± 2.53 , 2.91 ± 3.69 , 9.30 ± 63.45 , and 0.02 ± 0.07 mg, respectively. With these trivial dosages, plasma vitamin B₂ and B₆ level in these patients were nearly normal and plasma vitamin B₁₂ and folate level were rather high. (Table 3). Despite a plentiful level of such plasma vitamins, plasma homocysteine level was still high. These showed that vitamin deficiency may not play a major role in hyperhomocysteinemia in hemodialysis patients. Decreased renal clearance from abnormal renal homocysteine metabolism⁽¹²⁾ probably plays more important role. However, previous studies showed that a higher dosage of vitamin supplements (supraphysiologic dosage) could reduce more plasma homocysteine level, although it did not reach normal level^(24,25). Thus, the high plasma homocysteine level in the presented patients probably caused by vitamin supplements may not reach an optimal dosage. Therefore, increased vitamin dosage may be beneficial in these patients.

From previous studies, atherosclerosis was defined as clinical presentations of coronary artery heart disease (CAHD); cerebrovascular disease (CVD); or peripheral vascular disease (PVD), and/or past histories of such diseases. They were diagnosed by history taking, physical examination, chart review, and investigations, such as angiography, thallium scan, exercise stress test, doppler ultrasound, electron beam computed tomography (EBCT)^(14,26,27). Some investigations are invasive, expensive and unavailable in most hospitals, so they are not practical to use widely. Intima-media thickness (IMT) measurement of carotid artery by ultrasound is one of the standard non-invasive methods to detect atherosclerosis⁽¹⁷⁾. This method is safe, available, inexpensive, can detect the early stage of atherosclerosis, and can be used to monitor progression or regression of atherosclerosis⁽¹⁸⁾. Therefore, this method

was chosen to detect atherosclerosis in the present study.

Factors associated with atherosclerosis in hemodialysis patients in the present study were older age, male sex, and longer duration since the initiation of hemodialysis. The well-known conventional risk factors affecting atherosclerosis, such as hypertension; diabetes mellitus and dyslipidemia, however, had no correlation with atherosclerosis. These findings corresponded with previous studies^(7,14,20,26). It shows that there are some, other than conventional, risk factors that play an important role in atherosclerosis in these patients.

By univariate analysis, the authors found that plasma homocysteine level, a non-conventional risk factors, correlated with atherosclerosis in hemodialysis patients. Since plasma homocysteine level, however, depends on other factors. By analysis of covariance, the authors found that it did not correlate with atherosclerosis. Therefore, hyperhomocysteinemia was not an independent risk factor in hemodialysis patients.

Some previous studies showed that a high plasma phosphate level and high calcium x phosphate product influenced vascular calcification formation and enhanced risks of cardiovascular mortality in hemodialysis patients⁽²⁸⁾. However, both factors had no correlation with atherosclerosis in the present study.

The present study showed that IMT of the patients with atherosclerosis was higher than the those without atherosclerosis. These findings corresponded with previous studies in a normal population^(21,22) and hemodialysis patients^(7,19,20). Therefore, IMT measurement could be used to detect and monitor atherosclerosis in hemodialysis patients as well as in a normal population.

IMT of hemodialysis patients was higher than normal population. Kennedy found that adjusted mean IMT in these patients and a normal population were 0.72 and 0.58 mm, respectively ($p < 0.001$)⁽⁷⁾. These findings corresponded with more prevalence of atherosclerosis in these patients than a normal population. In the present study, IMT that provided maximum sensitivity and specificity to diagnose atherosclerosis was 0.56 mm. (73% sensitivity, 93% specificity), compared to a previous study of 1781 normal subjects in Taiwan (1131 men, 650 women, mean age 49 years), IMT that provided maximum sensitivity and specificity in that study was 0.68 mm. (70% sensitivity, 70% specificity) and IMT of 0.55 mm. (near the value of the present study) had 95% sensitivity but only 20% specificity⁽²¹⁾.

The authors found that older age correlated with higher mean IMT in hemodialysis patients. As sex, duration since the initiation of hemodialysis, hypertension, diabetes mellitus, dyslipidemia, plasma phosphate level, calcium x phosphate product did not correlate. Plasma homocysteine level also did not correlate with mean IMT. The authors' further prospective controlled study, that prescribed oral combined vitamin supplements (folate, B₆, and B₁₂) to these hemodialysis patients, expect to decrease plasma homocysteine level and consequently decrease progression of IMT, may show correlation between plasma homocysteine level and IMT more clearly.

Conclusion

Plasma homocysteine level of hemodialysis patients is approximately 3-times higher than a normal population. Advanced age plays a major role of hyperhomocysteinemia in the hemodialysis patients. Factors associated with atherosclerosis in these patients are older age, male sex, and longer duration since the initiation of hemodialysis, as hyperhomocysteinemia is not an independent risk factor. Carotid plaque and IMT measurement by ultrasound can be also used to diagnose atherosclerosis in hemodialysis patients as well as in a normal population.

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ความสัมพันธ์ระหว่างระดับโฮโมซิสเตอีนในเลือด และภาวะหลอดเลือดแดงแข็ง ในผู้ป่วยที่ได้รับการฟอกเลือดด้วยเครื่องไตเทียม

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บทนำ: การมีระดับ homocysteine ในเลือดสูง เป็นปัจจัยเสี่ยงประการหนึ่งต่อการเกิด coronary artery heart disease และ atherosclerosis ในประชากรทั่วไป ผู้ป่วยไตวายเรื้อรังระยะสุดท้ายที่ได้รับการทำ hemodialysis มักพบว่า มีระดับ homocysteine ในเลือดสูงกว่าประชากรทั่วไป แต่อย่างไรก็ตาม บทบาทของ homocysteine ต่อการเกิด atherosclerosis ในผู้ป่วยเหล่านี้ ยังไม่ชัดเจน การวินิจฉัย atherosclerosis ด้วยการตรวจ ultrasound เพื่อดู carotid plaque และวัดความหนาของผนังหลอดเลือดชั้น intima (intima media thickness, IMT) เป็นวิธีมาตรฐานแบบ non-invasive วิธีหนึ่งในปัจจุบัน การศึกษานี้มีวัตถุประสงค์เพื่อตรวจหาระดับของ homocysteine และศึกษาความสัมพันธ์ของ homocysteine กับ atherosclerosis ในผู้ป่วยเหล่านี้

วัตถุประสงค์และวิธีการ: รวบรวมข้อมูลทางคลินิก และตรวจระดับสารต่าง ๆ ในเลือดที่เกี่ยวข้องกับการเกิด atherosclerosis ในผู้ป่วยที่ได้รับการทำ hemodialysis จำนวน 62 คน การวินิจฉัย atherosclerosis ในผู้ป่วยเหล่านี้ อาศัยจากประวัติการเป็น หรือเคยเป็น coronary artery heart disease, cerebrovascular disease หรือ peripheral vascular diseases และ/หรือตรวจพบ carotid plaque โดย ultrasound ผู้ป่วยส่วนหนึ่งจะได้รับการตรวจวัด IMT ของ common carotid artery ด้วย

ผลการศึกษา : ระดับ homocysteine ในเลือดของผู้ป่วยที่ได้รับการทำ hemodialysis มีค่าสูงกว่ากลุ่มควบคุม คือ 28.27 ± 8.32 และ $9.66 \pm 2.89 \mu\text{mol/l}$ ตามลำดับ ($p < 0.001$) จากการวิเคราะห์ univariate analysis พบว่าปัจจัยที่มีความสัมพันธ์กับ atherosclerosis ในผู้ป่วยเหล่านี้ ได้แก่ อายุที่มากขึ้น ($p < 0.001$), เพศชาย ($p = 0.05$), ระยะเวลาที่ได้รับการทำ hemodialysis ที่นานกว่า ($p = 0.05$), และระดับ homocysteine ในเลือดที่สูง ($p = 0.01$) แต่เมื่อวิเคราะห์ analysis of covariance แล้ว พบว่าระดับ homocysteine ในเลือด ไม่มีความสัมพันธ์กับ atherosclerosis อย่างมีนัยสำคัญทางสถิติ การศึกษานี้ยังพบความสัมพันธ์ระหว่าง IMT กับ atherosclerosis ($p < 0.001$) แต่ไม่พบความสัมพันธ์ระหว่าง IMT กับ ระดับ homocysteine ในเลือดของผู้ป่วยที่ได้รับการทำ hemodialysis

สรุป : ระดับ homocysteine ในเลือดสูง ไม่ได้เป็นปัจจัยเสี่ยงต่อการเกิด atherosclerosis ในผู้ป่วยที่ได้รับการทำ hemodialysis, อายุที่มากขึ้นมีความสัมพันธ์กับระดับ homocysteine ในเลือดที่สูง, การตรวจ ultrasound เพื่อดู carotid plaque และวัด IMT สามารถนำมาใช้วินิจฉัยภาวะ atherosclerosis ในผู้ป่วยเหล่านี้ได้ เช่นเดียวกับในประชากรทั่วไป
