

Association Between Macrominerals Intake and Changes in Internal Carotid Artery-Intima Media Thickness in Post Ischemic Stroke Patients

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Association of Macro-minerals Intake and Changes in Internal Carotid Artery-Intima Media Thickness in Post Ischemic Stroke Patients

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Abstract. Carotid Intima Media Thickness (C-IMT) has been widely used as marker for atherosclerosis. Previous studies on minerals intake and its association with C-IMT revealed various. Most of the studies showed inconsistent results. The aim of this study is to determine whether macro minerals intake is related to internal carotid-intima media thickness (IC-IMT). This is a longitudinal study, pre test post test design conducted in Neurology clinic, dr. Kariadi hospital, Semarang from June to December 2014. Subjects were 22 post ischemic stroke patients. Minerals intake and IC-IMT was measured using Food Frequency Questionnaire and Duplex Carotid Ultrasonography. Statistical analysis was performed using Chi-Square, Fisher Exact and Logistic Regression test. Subjects included in this study were 17 male subjects (77.3%) and 5 female subjects (22.7%). Mean of IC-IMT in female subjects was found to be higher than in male. Mean of total IC-IMT was increased after a period of six months (0.96 ± 0.80 to 0.97 ± 0.21 mm). There were significant association between calcium as well as sodium intakes and IC-IMT. In contrast, there were no association between magnesium as well as potassium intake and IC-IMT. Multivariate analysis suggest that sodium intake (OR=26.828) was the most influencing factor for IC-IMT, followed by calcium intake (OR=0.042). Calcium as well as potassium intake were independently associated with IC-IMT. Magnesium as well as sodium intake were not independently associated with IC-IMT changes. Sodium intake was the most influencing variable to IC-IMT changes, followed by calcium intake.

Keywords: calcium, potassium, sodium, magnesium, IC-IMT

1. Introduction

Atherosclerosis is the main pathway underlying stroke occurrences. Previous long term studies had identified risk factors for atherosclerosis including family history, age, sex, obesity, dyslipidemia, hypertension, diabetes, physical inactivity, and smoking [1][2][3][4][5]. Carotid intima media thickness (C-IMT), measured noninvasively using high resolution ultrasound imaging, had been widely used as a marker for atherosclerosis. A previous large scale study has revealed that increased C-IMT was a predictor for stroke occurrence [2][6][7][8][9]. Early detection as well as modification of risk factors for increased C-IMT can bring significant influence to prevention of atherosclerotic diseases such as stroke. Hypertension, diabetes mellitus (DM), dyslipidemia, and smoking have been associated with increased C-IMT, though it was incompletely explain how these risk factors cause high proportion in C-IMT difference [10].

Some studies concerning mineral intake and C-IMT still revealed various and showed inconsistent results. A study involving 5181 healthy subjects revealed that there was no association between



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magnesium intake and internal carotid-intima media thickness (IC-IMT). In contrast, there was association between magnesium intake and common carotid-intima media thickness (CC-IMT) [11]. Another study involving 351 healthy subjects revealed that sodium intake as well as ratio of sodium/potassium have negatively correlated with C-IMT[12][13]. A study involving 592 healthy subjects showed that magnesium intake was associated with C-IMT, however calcium, sodium and potassium intake were not associated with C-IMT[14]. Studies on mineral intake and the association with C-IMT changes were relatively scarce. Moreover, C-IMT studies in post ischemic stroke patients focusing measurements in internal carotid artery segment (as a site of advanced phase of atherosclerosis) were also scarce [15]. This study was aimed to determine the association between macro minerals intake and internal carotid intima media thickness (IC-IMT) changes in post ischemic stroke patients with IC-IMT above normal value on the first measurement.

2. Methods

This study was a research in the field of Neurology, Nutrition and Radiology. This study was performed using one group pretest-posttest design. Targeted population in this study was post ischemic stroke patients. Study population was post ischemic stroke patients who visited outward Neurology clinic, dr. Kariadi hospital from June to December 2014. Subjects were the same participants included in the study of Influence of Risk Factors to Atherosclerosis Progression in post ischemic stroke patients, performed in Dr.Kariadi hospital at the same period of time. Inclusion criterias were post ischemic stroke with the onset of more than 1 month and having IC-IMT above normal value on the first ultrasound examination. Exclusion criterias were renal dysfunction, diuretic consumption, history of steatorrhea, inflammatory bowel disease (IBD) and incomplete data. Study was performed after approval from Ethical commission of dr.Kariadi hospital. Interview was performed to all patients followed by physical examination, filling the food frequency questionnaire (FFQ), then Carotid ultrasonography, two times in the period of 6 months.

Mineral intake measurements

Measurement of minerals intake (in milligram) was performed using a semiquantitative food frequency questionnaire (FFQ) and Nutrisurvey Software Programme. FFQ was performed based on the study of 20 subjects who underwent food recall for 3x24 hours. Data showed the most common foods containing the macro minerals consumed based on the food recall.

The tunica intima media thickness measurement

Left and right carotid arteries of each subject were measured using ultrasonography Siemens sonoline Omnia FBE 0322®. The tunica intima media carotid artery was examined from the transverse projection and carotid artery along the cervical area starting from the supraclavicular region toward the cranial area of mandible angle. Tunica intima-media thickness of the internal carotid artery is the maximum thickness of 1 cm distal of bifurcation. The maximum left or right intima-media thickness of internal carotid artery (IC-IMT) were included to statistical analysis[9][16][17].

Statistical Analysis

Primary data obtained from patients after ischemic stroke include gender, age, history of hypertension, diabetes mellitus, dyslipidemia, smoking, overweight, intake of minerals (magnesium, calcium, sodium, potassium) and intima media thickness of the internal carotid artery. Statistical analysis to examine association of each factor of atherosclerosis were performed using Chi Square and Fisher Exact test, followed by logistic regression multivariate analysis. Significant result if p value <0.05 .

3. Results and Discussion

In this study, 22 subjects whose IC-IMT above normal level had the interview to fill FFQ form. Most of the subjects were male (17 subjects/77.3%). Only 5 subjects were female (22.7%). Mean of total IC-IMT on the first measurement was 0.96 mm. Mean of IC-IMT was 0.96 mm for male and 1 mm for female. On the second measurement, mean of total IC-IMT was 0.97 mm, 0.98 for male and 1.08 mm for female.

Mean of age of subjects included in this study was 62.8 years old. The youngest subject was 51 years old and the oldest one was 81 years old. Seven subjects (31.8%) were > 65 years old. In regards to risk factors for stroke, 15 subjects (68.2%) in this study had hypertension, 14 subjects (63.6%) had dyslipidemia, 9 subjects (40.9%) had diabetes mellitus, 11 subjects (50%) had history of smoking and 2 subjects (9.1%) were overweight. From all subjects included in this study, there were 10 subjects (45.5%) whose IC-IMT increased from first to second measurement (Table 1).

Table 1. Frequency Distribution of Subject's Characteristic

Age	Frequency	%
>= 65	7	31.8
< 65	15	68.2
Total	22	100.0
Sex		
male	17	77.3
female	5	22.7
Total	22	100.0
Hypertension		
Yes	15	68.2
No	7	31.8
Total	22	100.0
Dyslipidemia		
Yes	14	63.6
No	8	36.4
Total	22	100.0
DM type II		
Yes	9	40.9
No	13	59.1
Total	22	100.0
Smoking		
Yes	11	50.0
No	11	50.0
Total	22	100.0
Obesity		
Yes	2	9.1
No	20	90.9
Total	22	100.0

The description of minerals intake as well as IC-IMT of each subjects in this study were showed in Table 2.

Chi-Square bivariate test performed in this study suggested there was significant association between calcium intake and IC-IMT changes ($p=0.043$). Additionally, there was also significant association between potassium intake and IC-IMT changes ($p=0.031$). However, there was no association between magnesium intake and IC-IMT changes ($p=0.087$). There was also no association between sodium intake and IC-IMT changes ($p=0.074$) (Table 3).

Table 2. Frequency Distribution of minerals intake and IC-IMT

Macrominerals	Frequency	%
Kalium		
< 2516.7	8	36.4
>= 2516.7	14	63.6
Total	22	100.0
Natrium		
>= 1431.7	8	36.4
< 1431.7	14	63.6
Total	22	100.0
Calcium		
< 493.7	10	45.5
>= 493.7	12	54.5
Total	22	100.0
Magnesium		
< 276.5	11	50.0
>= 276.5	11	50.0
Total	22	100.0
IC-IMT 1		
≥ 0.8	22	100.0
< 0.8	0	0.0
Total	22	100.0
IC-IMT 2		
≥ 0.8	16	72.7
< 0.8	6	27.3
Total	22	100.0
Δ IMT		
Increase	10	45.5
Constant/decrease	12	54.5
Total	22	100.0

Table 3. Bivariate Analysis of Magnesium, Calcium, Sodium and Potassium With IC-IMT Changes.

Intake	Bivariate						
	Alteration IC-IMT		Statistic	P	RO	IK 95%	
	Increase (%)	Constant/ Decrease (%)				Min	Max
Magnesium							
< 276.5	7 (70)	4 (33.3)	$X^2=0.087$	0.087	4.667	0.765	28.466
≥ 276.5	3 (30)	8 (66.7)					
Calcium							
< 493.7	2 (20)	8 (66.7)	$X^2=0.043$	0.043	0.125	0.018	0.887
≥ 493.7	8 (80)	4 (33.3)					
Sodium							
≥ 1431.7	6 (60)	2 (16.7)	$X^2=0.074$	0.074	7.5	1.039	54.116
< 1431.7	4 (40)	10 (73.3)					
Potassium							
< 2516.7	1 (10)	7 (58.3)	$X^2=0.031$	0.031	0.079	0.007	0.843
≥ 2516.7	9 (90)	5 (41.7)					

Statistical analysis using Fisher's Exact and Chi Square test showed that there was no association between some traditional risk factors (as such hypertension, dyslipidemia, diabetes mellitus, smoking, obesity, age, and sex) and IC-IMT changes (see Table 4).

Table 4. Bivariate analysis association of traditional risk factors and IC-IMT changes.

Variables	Bivariate						
	IC-IMT		Statistic	<i>p</i>	OR	95% CI	
	Increase (%)	Constant/ Decrease (%)				Min	Max
Sex							
Male	7 (70)	10 (83.3)	Fisher= 0.624	0.624	0.467	0.061	3.565
Female	3 (30)	2 (16.7)					
Age							
≥ 65	2 (20)	5 (41.7)	Fisher = 0.381	0.381	0.350	0.051	2.407
< 65	8 (80)	7 (58.3)					
Hypertension							
Yes	6 (60)	9 (75)	Fisher= 0.652	0.652	0.5	0.081	3.082
No	4 (40)	3 (25)					
Dyslipidemia							
Yes	7 (70)	7 (58.3)	Fisher= 0.675	0.675	1.667	0.283	9.822
No	3 (30)	5 (41.7)					
DM type II							
Yes	7 (28)	19 (40)	Fisher= 0.296	0.296	0.573	0.201	1.637
No	18 (72)	28 (59.6)					
Smoking history							
Yes	3 (30)	8 (66.7)	$\chi^2 = 0.087$	0.087	0.214	0.035	1.307
No	7 (10)	4 (33.3)					
Overweight							
Yes	0 (0)	2 (16.7)	Fisher= 0.481	0.481	—	—	—
No	10 (100)	10 (83.3)					

Multivariate analysis was performed using logistic regression test. There were 5 variables included, history of smoking, magnesium intake, calcium intake, sodium intake, potassium intake. 2 variables influencing IC-IMT changes, including calcium intake ($p=0.037$) and sodium intake ($p=0.049$). The most influencing variable was sodium intake (OR=26.828) followed by calcium intake (OR=0.042). Subjects with sodium intake ≥ 1431.7 mg/day were 26.828 times more likely to have an increase in IC-IMT than subject with sodium intake < 1431.7 mg/day. Meanwhile, subjects with calcium intake < 493.7 mg/day were 0.042 times more likely to have an increase in IC-IMT than subjects with calcium intake ≥ 493.7 mg/day (table 5).

Table 5. Logistic regression analysis of association between risk factors and IC-IMT changes.

Variables	Bivariate				Multivariate			
	<i>p</i>	OR	95% CI		<i>Sig</i>	OR	95% CI	
			Min	Max			Min	Max
Sex	0.624	0.467	0.061	3.565				
Age ≥ 65	0.381	0.350	0.051	2.407				
Hypertension	0.652	0.5	0.081	3.082				
Dyslipidemia	0.675	1.667	0.283	9.822				
Diabetes mellitus	0.296	0.573	0.201	1.637				
Smoking history	0.087	0.214	0.035	1.307	0.162	0.106	0.005	2.464
Overweight	0.481	—	—	—				
Magnesium intake < 276.5 mg/day	0.087	4.667	0.765	28.466	0.055	19.784	0.936	418.26
Calcium intake < 493.7 mg/day	0.043	0.125	0.018	0.887	0.037	0.042	0.002	0.826
Sodium intake ≥ 1431.7 mg/day	0.074	7.5	1.039	54.116	0.049	26.828	1.015	0.826
Potassium intake < 2516.7 mg/day	0.031	0.079	0.007	0.843	0.507	0.333	0.013	8.584

In this study, though there was no association between sex and IC-IMT changes theoretically, data showed that mean of IC-IMT in female subjects was greater than male. On the first measurement, mean of IC-IMT in male subjects was 0.96 mm and female 1 mm. On the second measurement, performed 6 months later, mean of IC-IMT in male subjects was 0.96 mm and 1.08 in female subjects. This study differed from previous ones in term of subjects. In the previous study, the subjects were healthy subjects while in this study, the subjects were post ischemic stroke patients whose IC-IMT already above normal value [3][4][14].

Bivariate analysis performed in this study showed that there were no associations between some traditional risk factors, analyzed as confounding factors (such as hypertension, diabetes mellitus, dyslipidemia, smoking, obesity, age, and sex) and IC-IMT changes (table 2). This finding was different to other previous studies which revealed the association of the traditional risk factors with IC-IMT [5][14][18]. Explanation to this findings were that previous studies were conducted in huge number of healthy subjects, who were free from cerebrovascular disease. Variables were measured once (cross section) [4][5]. While this study was performed to 22 post ischemic stroke subjects whose IC-IMT already above normal value at first measurement. Measurement of IC-IMT was performed twice. The second measurement was performed six months later.

In this study, there was significant association between calcium intake and IC-IMT changes in post ischemic stroke patients ($p=0.043$). This finding was different to previous study by Masley et al, which was performed cross section in 592 healthy subjects and revealed that calcium intake was not associated to IC-IMT [8]. Some possibilities concerning this finding included that subjects in this study were already patients with atherosclerotic disease (post ischemic stroke patients and had abnormal IC-IMT in the first measurement).

Significance association were found between potassium intake and IC-IMT changes in post ischemic stroke patients in this study ($p=0.031$). This finding was similar to previous study by Ortiz et al in 351 subjects without cerebrovascular disease which revealed that association between potassium intake and C-IMT resembled J-shaped curve [12]. However, this finding was different to study by Masley et al which performed cross section in 592 healthy subjects. Masley et al concluded that potassium intake was not associated with C-IMT. Same consideration was revealed by writer, it was due to the situation that subjects in this study were already in atherosclerotic disease (post ischemic stroke patients whose IC-IMT already above normal value in first measurement) while in Masley's study the subjects were still "free" from atherosclerotic disease [8].

Similar to the finding of Otto et al, there was no association between magnesium intake and IC-IMT changes. However it was different to the result of Masley's study that revealed magnesium intake was associated with C-IMT [8][11].

There was also no association between sodium intake and IC-IMT changes in post ischemic stroke patients in this study ($p=0.074$). This result was different to study of Ortiz et al that concluded sodium intake was negatively correlated with C-IMT [12]. The Difference between this study and previous one was that previous study was done in 351 subjects without cardiovascular disease and C-IMT measurement was performed in common carotid artery, while in this study was performed to 22 post stroke patients and measurement was performed at the internal carotid artery segmented as the site for advanced phase of atherosclerosis.

Multivariate analysis using logistic regression test showed that the most influencing variable to IC-IMT changes was sodium intake, followed by calcium intake. This finding was similar to previous study that already confirmed sodium intake was negatively correlated with C-IMT [12]. Person with sodium intake ≥ 1431.7 mg/day tend to have increased IC-IMT changes 26.828 times compare to those with sodium intake < 1431.7 mg/day. This could be a warning to reduce sodium consumption in daily diet.

4. Conclusion

Calcium as well as potassium intake in post ischemic stroke patients were independently associated with IC-IMT changes. In contrast, magnesium as well as sodium intake are not independently

associated with IC-IMT changes. Sodium intake is the most influencing variable to IC-IMT changes, followed by calcium intake.

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