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Original Article

오메가 3 지방산이 뇌혈류 및 혈관저항에 미치는 영향: 예비연구

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The Effect of Omega-3 Fatty Acid Supplementation on Cerebral Blood Flow and Vascular Resistance: A Preliminary Study

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Background: The effects of omega-3 polyunsaturated fatty acids (PUFAs) on cerebral vessels have not been clarified until now. Thus we investigated the efficacy of omega-3 PUFAs supplementation on cerebral blood flow velocity and vascular resistance via transcranial doppler (TCD). **Methods:** Consecutive twenty patients (13 male and 7 female) with at least 1 cerebrovascular risk factor or a known cerebrovascular disease were enrolled. Patients were treated with omega-3 PUFAs (1 g, two times per day) for 12 weeks. Cerebral blood flow velocity, resistance index, and pulsatile index were checked before and after 12 weeks of treatment using TCD. **Results:** The change of resistance index in right MCA (from 0.58 ± 0.07 to 0.55 ± 0.07, p = 0.042) and left PCA (from 0.56 ± 0.07 to 0.53 ± 0.06, p = 0.037) showed significant improvement after 12 weeks of omega-3 PUFAs treatment. The changes in other vessels, however, failed to show any significant changes compared to the baseline. **Conclusions:** Omega-3 PUFAs treatment showed feasible efficacies for cerebral vascular resistances in this open label trial. To confirm these results, larger samples of patients and longer period of follow-up is warranted. (Korean J Clin Neurophysiol 2015;17:68-72)

Key Words: Omega-3 polyunsaturated fatty acids, Vascular resistance, Transcranial doppler

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Introduction

Omega-3 polyunsaturated fatty acids (PUFAs) supplements reduced mortality in secondary prevention studies.[1,2] Dietary supplementation with omega-3 PUFAs (1 g daily) in patients who had a history of myocardial infarction showed significant benefit in the risk of death and cardiovascular death.[1] Moreover, the myocardial infarction patients who were advised to eat fatty fish for polyunsaturated fat had a significant reduction in all cause mortality compared with those not so advised.[2] Recently, in a meta-analysis to clarify associations of fish consumption and omega-3 PUFAs with risk of cerebrovascular disease, the higher fish consumption is significantly associated

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with a reduced risk of incident cerebrovascular accident.[3]

However, the exact mechanism of action of omega-3 PUFAs remains elusive. Studies in patients with peripheral arterial disease and healthy adults failed to show significant improvement in endothelial function.[4,5] On the contrary, recent studies revealed that omega-3 PUFAs supplements improve endothelial vasomotor function in cigarette smokers and in subjects with metabolic syndrome.[6,7]

In this study, we planned to investigate the effect of omega-3 PUFAs on cerebral blood flow and vascular resistance in patients with cerebrovascular risk factors.

Materials and Methods

1. Subjects

Twenty patients with having cerebrovascular risk factors were recruited in a general hospital. The inclusion criteria were age older than 40 years and having at least 1 cerebrovascular risk factor or a known cerebrovascular disease, such as stroke history, hypertension, diabetes, dyslipidemia, and heart disease.[8] Poor temporal window for transcranial Doppler (TCD) were excluded from the study. The baseline characteristics for the patients are shown in Table 1. The lipid profiles were checked before beginning the study. All the patients were treated with omega-3 PUFAs (2 g per day, Omacor capsule, Kuhnil, Korea) for 12 weeks. Written informed consent were given to all the participants and the ethical approval was obtained from the Institutional Review Board (No. 2012-042).

2. Measurement of cerebral blood flow and vascular resistance

Cerebral blood flow velocity and vascular resistance were measured using TCD (Nicolet Pioneer TC8080). The anterior intracranial circulation was evaluated by measuring the systolic, diastolic, and mean blood flow velocity (cm/s) in the bilateral middle cerebral artery (MCA) at a depth of 52 mm and anterior cerebral artery (ACA) at a depth of 72 mm. For the posterior circulation, the posterior cerebral artery (PCA) was examined at a depth of 68mm. A Pourcelot resistance index (PRI) {(Vsystole-Vdiastole)/Vsystole} and Gosling pulsatile index (GPI) {(Vsystole-Vdiastole)/Vmean} were adopted for evaluating vascular resistance.[9,10] If there was a poor temporal window, the vessel was excluded from statistical analysis. A trained technician administered the tests, which were administered before and 12 weeks after omega-3 PUFAs treatment. We compared the results of cerebral blood flow velocity and vascular resistance (PRI and GPI) between baseline and 12 weeks after treatment using SPSS Ver 11.5 for Windows (SPSS Inc., Chicago, USA). The T-test for paired samples was used for the analysis and the two-tailed level of significance for all tests was set at 0.05.

Results

The mean age of the 20 patients (13 male) was 64.35 ± 10.34 years. The baseline characteristics are shown in Table 1. There was no change in blood pressure during 12 weeks, so systolic BP (mmHg) 129.32 ± 10.53 to 126.79 ± 17.36 (p = 0.635), diastolic BP (mmHg) 75.89 ± 6.79 to 77.32 ± 13.49 (p = 0.672). The cerebrovascular risk factors in the patients were stroke history (55%), hypertension (65%), diabetes (25%), dyslipidemia (40%), heart disease (5%), smoking (20%). Eighteen patients had been treated with antiplatelet (90%) and 15 patients with statin (75%).

Table 1. Baseline characteristics

Variables	Values
Age	64.35 ± 10.34
Sex (M:F)	13:7
Vascular risk factors, n (%)	
Stroke history	11 (55)
HTN	13 (65)
DM	5 (25)
Dyslipidemia	8 (40)
Heart disease	1 (5)
Smoking	4 (20)
Antiplatelet medication, n (%)	18 (90)
Statin medication, n (%)	15 (75)
Lipid profile (mg/dL)	
Total cholesterol	193.44±36.49
TG	216.67±149.80
HDL	45.17±9.87
LDL	115.78±33.89

Values are presented as mean±standard deviation (SD). DM; diabetic mellitus, F; female, HDL; high density lipoprotein, HTN; hypertension, LDL; low density lipoprotein, M; male, TG; triglyceride.

Table 2. Flow velocity and resistance index change

Variables	Rt			Lt		
	Baseline	12 weeks	*p*-value	Baseline	12 weeks	*p*-value
MCA (Depth 52 mm)						
Systolic velocity (cm/s)	83.29±18.81	79.41±10.86	0.383	85.40±24.30	83.53±13.87	0.795
Diastolic velocity (cm/s)	35.29±9.83	35.29±6.77	1.000	35.20±10.99	36.33±6.31	0.606
Mean velocity (cm/s)	54.06±13.05	52.24±7.45	0.522	54.67±16.26	55.07±8.22	0.929
PRI	**0.58±0.07**	**0.55±0.07**	**0.042**	0.58±0.08	0.56±0.07	0.134
GPI	0.90±0.19	0.85±0.17	0.062	0.93±0.20	0.86±0.17	0.058
ACA (Depth 72 mm)						
Systolic velocity (cm/s)	73.79±15.64	70.86±11.52	0.430	70.53±16.57	69.60±15.77	0.814
Diastolic velocity (cm/s)	32.71±8.66	31.79±5.81	0.479	30.93±7.53	31.93±7.07	0.394
Mean velocity (cm/s)	48.86±11.62	46.93±7.45	0.424	46.47±10.91	46.40±9.52	0.976
PRI	0.56±0.06	0.55±0.06	0.503	0.56±0.07	0.54±0.06	0.123
GPI	0.85±0.16	0.84±0.15	0.567	0.86±0.16	0.81±0.15	0.116
PCA (Depth 68 mm)						
Systolic velocity (cm/s)	47.00±10.09	47.56±7.41	0.838	46.60±8.72	44.40±8.98	0.346
Diastolic velocity (cm/s)	20.31±3.50	21.56±3.63	0.182	20.07±3.73	20.53±4.55	0.706
Mean velocity (cm/s)	30.88±5.86	32.44±4.76	0.314	31.00±5.30	30.13±6.21	0.613
PRI	0.56±0.66	0.54±0.06	0.345	**0.56±0.07**	**0.53±0.06**	**0.037**
GPI	0.85±0.16	0.80±0.14	0.199	0.85±0.17	0.79±0.15	0.090

Values are presented as mean±SD. ACA; anterior cerebral artery, GPI; Gosling pulsatile index, Lt; left, MCA; middle cerebral artery, PCA; posterior cerebral artery, PRI; Pourcelot resistance index, Rt; right.

There was a significant decrease in PRI with omega-3 PUFAs supplementation for 12 weeks in right MCA (from 0.58 ± 0.07 to 0.55 ± 0.07, p = 0.042) and left PCA (from 0.56 ± 0.07 to 0.53 ± 0.06, p = 0.037) (Table 2). However, PRI in other arteries failed to show any meaningful change. In GPI, though there was a decreasing trend in bilateral MCA (p = 0.062 at right, p = 0.058 at left), no significance were detected in all examined arteries.

In addition, omega-3 PUFAs did not have any effect on cerebral blood flow velocity in bilateral ACA, MCA, and PCA (Table 2).

Discussion

We evaluated the efficacy of omega-3 PUFAs on cerebral blood flow velocity and vascular resistance and found that omega-3 PUFAs treatment improved the cerebral arterial resistance index of right MCA and left PCA in patients with cerebrovascular risk factors.

Though the cerebral vascular resistance index or pulsatile index could be affected by various factors, such as calcification, liver cirrhosis, and so on, it could be assessed as a surrogate marker of cerebrovascular atherosclerosis.[11-13] In line with these studies, the resistance index has been regarded as a non-invasive evaluation method of the endothelial function.[14] The exact mechanism of omega-3 fatty acids on endothelial function is not fully understood, but several theories have been proposed.[7] Reduced production of the vasoconstrictor thromboxane A2 and increased synthesis of the vasodilator nitric oxide are thought to be one of the main action mechanisms in improving endothelial function.[7,15,16] Suggested hypothesis included affecting inflammation via modifying eicosanoid biosynthesis.[17] It also could be precursor to resolvins, protectins, and other inflammation resolving mediators having anti-inflammtory properties.[18] It has been proposed for the arterial stiffness, the incorporation of omega-3 PUFAs into atherosclerotic plaques can enhance stability by reducing macrophage infiltration and stabilizing plaque morphology.[19]

However, no effect of omega-3 fatty acid supplementation (Omacor fish oil 850-882 mg) on pulse wave velocity as arte-

rial stiffness was shown in patients with peripheral arterial disease.[4] The dietary intake of omega-3 PUFAs from fish also failed to show any efficacy on endothelial function and arterial stiffness in healthy non-smoking persons.[5] In addition, supplements long chain ω-3 fatty acids failed to show association with risk of cerebrovascular disease.[3] So they suggested that not a single nutrients but a wide range of nutrients abundant in fish mediated the beneficial effect of fish intake on cerebrovascular risk.[3] Contrary to this, Kim et al. investigated the plasma phospholipid fatty acid composition in ischemic stroke.[20] Low level of plasma DHA, reflecting dietary intake deficiency, is suggested to elevate the risk of ICAS (Intracerebral arterial stenosis).[20] Treatment with 2 g/day omega-3 PUFAs showed a significant improvement in FMD (flow-mediated dilation) as endothelial function and PWV (pulse wave velocity) as aortic stiffness in patients with metabolic syndrome.[7] The discrepancies among the result of previous studies could be due to differences in the inclusion criteria, omega-3 PUFAs doses, and used tools to estimate endothelial function.[6] We suggested that 2 g/day omega-3 PUFAs treatment in patients with cerebrovascular risk factors could have a positive efficacy on vascular resistance. The high percentage of stroke history and vascular risk factors in this study suggests the positive effect of omega-3 PUFAs on atherosclerotic vessels because of its anti-inflammatory and plaque stabilization effects.[6,7]

Though this is preliminary, the small sample number, relatively short duration, and no control group were the main limitations in our study. In addition, specific biological markers are needed to elucidate the action mechanism of omega-3 PUFAs on endothelium. These short comings warrant the further large-scale, long-term, detailed study.

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