

항산화 영양제의 보충이 관상동맥질환 환자의 지질산화 정도와 항산화계 효소의 활성도에 미치는 영향

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Effects of Antioxidant Supplementation on the Lipid Peroxidation and Antioxidative Enzyme Activities in Patients with Coronary Heart Disease

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ABSTRACT

Background and Objectives : The purpose of this study was to evaluate whether antioxidant supplementation with tocopherol, vitamin C, β -carotene, and selenium reduces lipid peroxide levels and increases antioxidative enzyme activities in patients with coronary heart disease. **Subjects and Methods :** Eighty nine patients participated in a randomized, double-blind, placebo-controlled trial. The antioxidant group (45 patients) was given daily doses of tocopherol (400 IU), vitamin C (500 mg), β -carotene (15 mg), and selenium (50 μ g) and the placebo group (44) received placebo. Thirty eight of the antioxidant group (84.4%) and thirty nine (88.6%) of the placebo group completed the 3-month supplementation. **Results :** Serum levels of α -tocopherol, vitamin C and β -carotene were significantly increased in the antioxidant group as compared to the placebo group ($p < 0.05$), however, retinol was not. Thiobarbituric acid-reactive substances (TBARS) decreased significantly (0.6 nmol MDA/mL) in the antioxidant group as compared with the level (0.09 nmol MDA/mL) seen in the placebo group ($p < 0.05$). Antioxidants did not affect the oxidized-LDL level. The activities of erythrocyte superoxide dismutase (SOD) significantly increased by 0.85 unit/mg hemoglobin in the antioxidant group versus 0.27 unit/mg hemoglobin in the placebo group ($p < 0.01$), and the activities of erythrocyte catalase significantly decreased by 0.04 unit/mg hemoglobin versus 3.37 unit/mg hemoglobin ($p < 0.01$). However, the activities of erythrocyte glutathione peroxidase (GPX) increased insignificantly by 0.09 unit/mg hemoglobin vs 0.1 unit/mg hemoglobin. **Conclusion :** These results suggest that antioxidant supplementation with tocopherol, vitamin C,

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-carotene and selenium in patients with coronary heart disease may provide a prophylactic effect against oxidative stress. (**Korean Circulation J 2001;31(11):1215-1224**)

KEY WORDS : Stent · Coronary artery disease · Intravascular ultrasound.

서 론

glutathione peroxidase(GPX)

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가 - tocopherol, C,

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(LDL)

LDL

endothelial dysfunction,

8 - 10)

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C, E, - carotene,

12)

- car -

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catalase, superoxide dismutase(SOD),

가 ()

3 (90)

thiobarbituric acid reactive substances(TBARS) thiobarbituric acid (TBARS) n - butanol excit - ation 515 nm, emission 533 nm Yagi ²³⁾ , - LDL kit(OLAB, biomedica Group Co.)

A, E, C - carotene

HPLC A E Bieri ²⁴⁾ retinyl acetate toco - phenyl acetate internal standard micro Bondapak C₁₈ column 292 nm UV detection C Otsuka ²⁵⁾ 5% , HPLC 8% , - carotene methan - olic KOH petroleum ether HPLC

superoxide dismutase activity 가 가 , pyrogallol oxidation method²⁶⁾가 가 가

. Glutathione peroxidase Paglia ²⁷⁾ Deagen ²⁸⁾ coupled enzyme procedure catalase Luck ²⁹⁾

SAS

paired t - test

(ANOCOVA ; Analysis of covariance)

결 과

연구대상자의 연구시작 시점에서의 특성 비교

76.3%	76.9%	
60		63.
2%	51.3%	
	가 25	
	26.3%	38.
5%		(Table 1).
		47.4%
30.8%		
		29.0%
18.0%		
1 3		
	29.0%	30.
	(Table 2).	

Table 1. General characteristics of study subjects at baseline level

General characteristics	Antioxidant		Placebo		p*
	No.	%	No.	%	
Gender					
Male	29	76.3	30	76.9	NS
Female	9	23.7	9	23.1	
Age					
<60	14	36.8	19	48.7	NS
60 -	24	63.2	20	51.3	
Body mass index (kg/m ²)					
<25	28	73.7	24	61.5	NS
25 -	10	26.3	15	38.5	

* : p value by Chi-square test, NS : not significant, No. : number

21.0% 15.4% 21.0% 12.8% (Table 3).

21.1% 20. 39.5% 46.1% (Table 4).

항산화영양제의 투여효과

44.7% 51.3% 21.1% 10.2% 36.8% 25. 6% 42.1% 38.4%

가 가 가 C 가 가

Table 2. Life styles of study subjects at baseline level

Life styles	Antioxidant		Placebo		p*
	No.	%	No.	%	
Alcohol					
Current	18	47.4	12	30.8	NS
Quit	9	23.7	10	25.6	
Never	11	28.9	17	43.6	
Smoking					
Current	11	29.0	17	18.0	NS
Quit	20	52.6	22	56.4	
Never	7	18.4	10	25.6	
Regular exercise					
>3 times/week	11	29.0	12	30.8	NS
1 - 2 times/week	1	2.6	6	15.4	
None	26	68.4	21	53.8	

* : p value by Chi-square test, NS : not significant, No. : number

Table 3. Food intake characteristics of study subjects at baseline level

Food intake	Antioxidant		Placebo		p*
	No.	%	No.	%	
Taking nutrient supplementation					
Yes	8	21.0	6	15.4	NS
No	30	79.0	33	84.6	
Taking healthy food					
Yes	8	21.0	5	12.8	NS
No	30	79.0	34	87.2	

* : p value by Chi-square test, NS : not significant, No. : number

Table 4. Disease and treatment characteristics of study subjects

Disease and treatment	Antioxidant		Placebo		p*
	No.	%	No.	%	
Disease type					
Old myocardial infarction	17	44.7	20	51.3	NS
Angina pectoris	21	55.3	19	48.7	
Diabete Mellitus					
with	8	21.1	4	10.2	NS
without	30	78.9	35	89.8	
Hypertension					
with	14	36.8	10	25.6	NS
without	24	63.2	29	74.4	
Hyperlipidemia					
with	16	42.1	15	38.4	NS
without	22	57.9	24	61.6	
Complications					
with	8	21.1	8	20.5	NS
without	30	78.9	31	79.5	
Taking lipid lowering agent					
Yes	15	39.5	18	46.1	NS
No	23	60.5	21	53.9	

* : p value by Chi-square test, NS : not significant, No. : number

retinol - carotene - tocopherol 18.72 $\mu\text{g/mL}$ 2.95 $\mu\text{g/mL}$ (p<0.05).

05). C 2.57 $\mu\text{g/mL}$ 0.27 $\mu\text{g/mL}$ (p<0.05).

- carotene 14.8 $\mu\text{g/mL}$ 2.37 $\mu\text{g/mL}$ (p<0.05).

retinol 0.03 $\mu\text{g/mL}$ 0.08 $\mu\text{g/mL}$ (Table 6).

(p<0.05).

retinol

Table 5. Daily mean dietary nutrient intakes of study subjects

Dietary nutrient intake	Antioxidant (n=37)			Placebo (n=39)			p*
	Before treatment	After treatment	Difference	Before treatment	After treatment	Difference	
Energy (kcal)	1458.7 \pm 490.5	1454.1 \pm 538.4	- 4.6 \pm 594.9	1523.3 \pm 788.7	1449.9 \pm 589.8	- 73.4 \pm 623.2	NS
Protein (g)	63.0 \pm 31.0	60.6 \pm 27.9	- 2.4 \pm 37.5	69.6 \pm 38.9	61.6 \pm 31.8	- 8.1 \pm 40.4	NS
Fat (g)	32.4 \pm 19.0	33.3 \pm 22.7	0.9 \pm 2.3	32.7 \pm 19.4	31.3 \pm 24.8	- 1.4 \pm 29.2	NS
Fiber (g)	6.3 \pm 4.3	6.2 \pm 5.4	- 0.1 \pm 6.2	7.0 \pm 5.7	5.3 \pm 2.4	- 1.7 \pm 5.9	NS
Vitamin A (RE)	611.7 \pm 760.6	736.9 \pm 1014.2	125.2 \pm 1285.8	559.8 \pm 452.4	702.0 \pm 697.3	142.2 \pm 861.1	NS
Retinol (μg)	56.7 \pm 78.7	47.1 \pm 73.9	- 9.5 \pm 107.5	88.2 \pm 242.6	118.3 \pm 450.2	30.1 \pm 511.4	NS
-carotene (μg)	3210.8 \pm 4557.9	3007.0 \pm 3846.8	- 203.9 \pm 6233.6	2762.6 \pm 2226.4	3266.7 \pm 3367.7	504.2 \pm 4269.8	NS
Vitamin C (mg)	90.6 \pm 64.7	86.9 \pm 60.0	- 3.7 \pm 73.7	100.0 \pm 71.4	86.0 \pm 41.0	- 14.0 \pm 83.4	NS

Mean \pm SD, * : significant mean difference of daily nutritient intakes between two groups by ANOCOVA, NS : not significant, ANOCOVA : analysis of variance

Table 6. Effects of antioxidant supplementation to serum antioxidant vitamins

Serum antioxidant vitamins	Antioxidant (n=38)			Placebo (n=39)			p [†]
	Before treatment	After treatment	Difference	Before treatment	After treatment	Difference	
Retinol ($\mu\text{g/mL}$)	0.49 \pm 0.2	0.46 \pm 0.2	- 0.03 \pm 0.3	0.59 \pm 0.3	0.51 \pm 0.2	- 0.08 \pm 0.2*	NS
-tocopherol ($\mu\text{g/mL}$)	17.17 \pm 11.6	35.89 \pm 17.4	18.72 \pm 21.6*	20.5 \pm 14.5	17.55 \pm 10.7	- 2.95 \pm 13.0	0.0001
Ascorbate ($\mu\text{g/mL}$)	6.52 \pm 3.5	9.09 \pm 2.9	2.57 \pm 3.9*	7.16 \pm 4.0	6.89 \pm 2.7	- 0.27 \pm 3.9	0.0003
-carotene ($\mu\text{g/dL}$)	19.26 \pm 11.2	34.05 \pm 16.9	14.8 \pm 18.8*	21.95 \pm 21.4	24.33 \pm 14.6	2.37 \pm 12.6	0.0006

Mean \pm SD, * : significant mean changes of antioxidant vitamin levels between before and after treatment by paired t-test, [†] : significant mean difference of antioxidant vitamin levels between two groups by ANOCOVA, NS : not significant, ANOCOVA : analysis of variance

Table 7. Effects of antioxidant supplementation to serum lipid peroxides

Serum lipid peroxides	Antioxidant (n=38)			Placebo (n=39)			p [†]
	Before treatment	After treatment	Difference	Before treatment	After treatment	Difference	
Thiobarbituric acid reaction substances (nmol MDA/mL)	2.4 ± 1.4	1.8 ± 0.9	-0.6 ± 1.7*	2.4 ± 1.4	2.3 ± 1.1	-0.09 ± 1.9	0.03
Oxidized LDL cholesterol (mU/mL)	538.5 ± 357.3	490.2 ± 314.9	-48.3 ± 221.1	456.2 ± 318.8	419.0 ± 290.8	-37.1 ± 303.5	NS

Mean ± SD, * : significant mean changes of lipid peroxidation status between before and after treatment by paired t-test, † : significant mean difference of lipid peroxidation status between two groups by ANOCOVA, NS : not significant, ANOCOVA : analysis of covariance, MDA : malonyl dialdehyde, LDL : low density lipoprotein

Table 8. Effects of antioxidant supplementation to antioxidant enzyme activities in red blood cell (Unit : Mean ± SD)

Antioxidant enzyme activities	Antioxidant (n=36)			Placebo (n=37)			p [†]
	Before treatment	After treatment	Difference	Before treatment	After treatment	Difference	
Superoxide dismutase (unit/mg hemoglobin)	15.50 ± 2.1	16.34 ± 2.5	0.85 ± 1.5*	14.86 ± 2.4	15.13 ± 3.5	0.27 ± 3.1	0.0006
Catalase (unit/mg hemoglobin)	9.94 ± 5.3	9.90 ± 5.9	-0.04 ± 7.6	9.67 ± 5.7	6.30 ± 4.8	-3.37 ± 5.0*	0.005
Glutathione peroxidase (unit/mg hemoglobin)	3.04 ± 0.7	3.13 ± 1.0	0.09 ± 1.1	2.76 ± 0.4	2.86 ± 0.4	0.10 ± 0.3	NS

Mean ± SD, * : significant mean changes of antioxidant enzyme activities between before and after treatment by paired t-test, † : significant mean difference of antioxidant enzyme activities between two groups by ANOCOVA, NS : Not significant, ANOCOVA : analysis of covariances

MDA/mL, TBARS가 0.6 nmol (p<0.05), SOD 0.85 unit/mg hemoglobin, 가 0.27 unit/mg hemoglobin (p<0.01), catalase 0.04 unit/mg hemoglobin, 3.37 unit/mg he - moglobin (p<0.05), 가 (Table 7). 0.01)(Table 8).

고 찰

. SOD 0.85 unit/mg hemoglobin 가 C, , tocopherol, (p<0.05), 0.27 unit/mg he - moglobin 가 , 가 catalase 0.04 unit/mg hemoglobin 가 가 3.37 unit/mg hemoglobin LDL (p<0.05). , GPX 가 가 (TBARS) - LDL

. TBARS LDL 가 , Jialal ³¹⁾ 3
 가 tocopherol(800 IU)
 (30 mg) C(1000 mg),
 tocopherol
 SOD cata - LDL
 lase 가 - LDL
 - tocopherol, C
 - carotene 가 - LDL
 . LDL
 3 - LDL
 , - LDL LDL
 가 , ³²⁾
 retinol , C, -
 tocopherol, - carotene 가
³⁰⁾ retinol , 가
 retinol , - LDL
 , TBARS TBARS
 가 가
³¹⁾³³⁾ 가
 가 가
 , TBARS, SOD, catalase, GPX, - tocopherol,
 C - carotene catalase, SOD, GPX
 가
 가 84.4% 88.6%
 - LDL , TBARS 가
 LDL , Fuller ¹²⁾ tocopherol 2
 tocopherol 가 SOD 가 가

가 (p<0.05),
 30 - 33) 가
 33) 가
 가
 reactive substances 0.6 nmol
 MDA/mL 0.09
 nmol MDA/mL (p<0.
 05), 가 - LDL 가
 . Superoxide dismutase
 0.85 unit/mg hemoglobin
 가 0.27 unit/mg hemoglobin
 가 (p<0.01). catalase
 0.04 unit/mg he -
 가 , 가 - LDL moglobin 3.37 unit/mg
 hemoglobin 가 (p<0.01).
 SOD catalase 가 TB - glutathione peroxidase
 ARS 0.09 unit/mg hemoglobin, 0.1 unit/mg
 가 hemoglobin 가
 가
 결 론 :

요 약

배경 및 목적 :

가 가 , - LDL
 SOD catalase
 tocopherol, 가 TBARS
 C, , 가
 , ,
 가

방 법 :

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44 45
 . 3
 38 (84.

4%) 39 (88.6%)
 - carotene(15 mg), C
 (500 mg), tocopherol(400 IU), (50 µg)

결 과 :

, - tocopherol,
 C, - carotene

중심 단어 : ; ; ;

1998

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