

주정금단 후 혈중 Superoxide Dismutase 활성도의 변화

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Changes in Blood Superoxide Dismutase Activities after Alcohol Withdrawal

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ABSTRACT

Objectives : The aims of this study were to evaluate changes in plasma superoxide dismutase(SOD) activities in alcohol dependence, to find out variables to influence on the SOD activities, and finally to identify the correlation of SOD activities with the alcohol-associated cognitive disorders.

Methods : For 24 male alcoholics and 21 healthy male controls, plasma SOD activities were measured by spectrophotometry on 1-2 wks after alcohol withdrawal. Structured interviews and laboratory tests were also performed.

Results : 1) Upon comparing SOD activities between controls and alcoholics, the SOD activities were significantly ($p < 0.01$) lower in alcoholics (0.308 ± 0.140 units/mL) than in healthy controls (0.313 ± 0.086 units/mL).

2) Upon comparing SOD activities according to the presence of alcohol-related cognitive disorders, the SOD activities were significantly ($p < 0.05$) lower in alcoholics with cognitive disorders (0.247 ± 0.049 units/mL) than in alcoholics without cognitive disorders (0.317 ± 0.148 units/mL).

3) Upon comparing SOD activities according to the presence of alcoholic polyneuropathy or alcohol withdrawal seizure, the SOD activities showed no significant differences between alcoholics with polyneuropathy or epilepsy and those without.

4) Upon analyzing variables influencing on the SOD activities in alcoholics, the SOD activities had the negative correlation with hemoglobin ($r = -0.433$) and severity of alcohol withdrawal symptoms ($r = -0.375$).

5) Upon comparing variables according to the presence of alcohol-related cognitive disorders, the occurrence of alcoholic polyneuropathy ($p < 0.05$) and blood phosphorus concentrations ($p < 0.01$) were significantly higher in alcoholics with cognitive disorders than those without.

6) Upon analyzing an association between SOD activities and variables in alcoholics with cognitive disorders, the SOD activities were positively correlated with the onset age ($r = 0.995$), and negatively correlated with the severity of alcohol withdrawal symptoms ($r = -0.996$).

Conclusions : Lower SOD activities in alcohol dependence suggested alcohol-associated cognitive disorders and alcohol withdrawal symptoms might be caused by oxidative stress.

KEY WORDS : Alcohol dependence · Superoxide dismutase activities · Cognitive disorder · Hemoglobin · Severity of alcohol withdrawal symptoms · Blood phosphorus concentration.

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서론

50 70% , 10% 가, 12.5% Wernicke - Korsakoff (Dufour 1993). B 가 (free radical reaction) 가 (Hunt 1993). lipid peroxidation , superoxide dismutase(SOD) antioxidant (excitotoxicity) (Crews Chandler 1993). peroxide dismutase(SOD) 가 SOD 가

대상 및 방법

1. 연구대상
1998 12 1999 8
DSM - (American Psychiatric Association 1994) 24
21
44.8 ± 8.0 (35 63)
42.6 ± 6.2 (31 53)
가 (p=0.356).
10.9 ± 2.9
22.7 ± 7.7

24.4 ± 9.5 (5).
가
20 (83.3%)
7 (29.2%)
(3).
2. 연구방법
1 2
5 6cc , SOD spectrophotometry (Flo' <ting 1984). , 4 2500g 5 extraction rea - gent 400 μL 250 μL , 4 3000 g 10 , 0 4 assay (1). (Selzer 1971) Michigan Alcoholism Screening Test - Korean Version(MAST - K)(1985) 가 , Clinical Institute Withdrawal Assessment Scale(CIWA - A)(Naranjo Sellers 1986), Mini - Mental State Examination (MMSE - K)(1989 ; 1989) 가 . , triglyceride, SGOT, SGPT, -GTP,

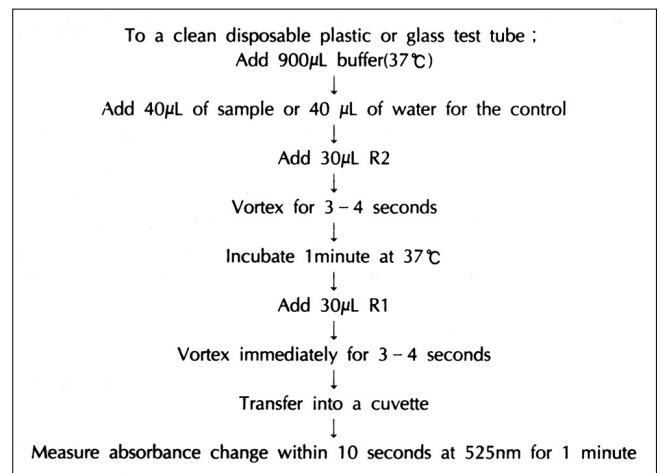


Fig. 1. Superoxide dismutase assays.

결 과

1. 대조군과 주정지존군에서 Superoxide Dismutase 활성도의 비교

(1). , SOD 0.313 ± 0.086 units/mL(0.23 0.56units/mL) , SOD 0.308 ± 0.140units/mL(0.09 0.60units/mL) (p=0.009).

2. 알코올성 인지장애 유무에 따른 Superoxide Dismutase 활성도의 비교

MMSE - K 가 , 24 가 , 25 가 SOD 0.247 ± 0.049units/mL, 가 SOD 0.317 ± 0.148units/mL 가 SOD 가 (p=0.046).

3. 알코올성 말초신경염, 알코올금단성 간질 유무에 따른 Superoxide Dismutase 활성도의 비교

SOD 3 (3). , SOD 0.310 ± 0.141units/mL, SOD 0.303 ± 0.159 units/mL SOD

Table 1. Comparison of plasma superoxide dismutase activities between healthy controls and alcoholics

	Superoxide dismutase activities(units/mL)			
	Controls(N=21)		Alcoholics(N=24)	
Range	0.23	0.56	0.09	0.60
Mean ± S.D.	0.313 ± 0.086		0.308 ± 0.140*	

*p=0.009

Table 2. Comparison of superoxide dismutase activities according to the alcohol-related cognitive disorders(N=21)

Cognitive disorder	No.(%)	Superoxide dismutase activities (units/mL)	p-Value
No (MMSE-K 25)	21 (87.5)	0.317 ± 0.148	p=0.046
Yes (MMSE-K 24)	3(12.5)	0.247 ± 0.049	

(p=0.955).

SOD 0.347 ± 0.176units/mL, SOD 0.292 ± 0.126units/mL SOD (p=0.353).

4. 주정지존군에서 Superoxide Dismutase 활성도에 영향 미치는 요인

SOD 4 (4). , SOD , , , (

Table 3. Comparison of superoxide dismutase activities according to the alcoholic polyneuropathy and alcohol withdrawal seizure(N=21)

	No.(%)	Superoxide dismutase activities (units/mL)	p-Value
Alcoholic polyneuropathy			
No	4(16.7)	0.303 ± 0.159	p=0.955
Yes	20(83.3)	0.310 ± 0.141	
Alcohol withdrawal seizure			
No	17(70.8)	0.292 ± 0.126	p=0.353
Yes	7(29.2)	0.347 ± 0.176	

Table 4. Correlation coefficients between SOD activities and variables in the 24 male alcoholics

Variables	Pearson's correlation coefficients ()	p-Value
Age	-0.116	0.590
Education	0.125	0.561
Onset age	-0.024	0.912
Duration	-0.138	0.519
Polyneuropathy	0.019	0.930
Epilepsy	0.181	0.397
WBC	-0.179	0.403
Hemoglobin	-0.433	0.035
Platelet	0.142	0.507
Cholesterol	-0.164	0.445
Triglyceride	0.130	0.543
- GTP	0.104	0.628
SGOT	-0.097	0.651
SGPT	-0.092	0.667
Ammonia	-0.056	0.796
Magnesium	-0.151	0.481
Calcium	0.128	0.550
Phosphorus	-0.056	0.793
MMSE-K ¹	0.169	0.431
MAST-K ²	0.041	0.849
CIWA-A ³	-0.375	0.071

1 : Mini-Mental State Examination-Korean Version

2 : Michigan Alcoholism Screening Test-Korean Version

3 : Clinical Institute Withdrawal Assessment Scale

Table 5. Comparison of variables (Mean ± S.D.) between alcoholics with cognitive disorders (MMSE-K 24) and those without cognitive disorders (MMSE-K 25)

Variables	Total (N=24)	MMSE-K 24 (N=3)	MMSE-K25 (N=21)	p-Value
Age (Yrs)	44.8 ± 8.0	39.0 ± 3.5	45.7 ± 8.2	p=0.213
Education (Yrs)	10.9 ± 2.9	8.0 ± 3.5	11.3 ± 2.7	p=0.535
Onset age (Yrs)	22.7 ± 7.7	19.0 ± 1.7	23.2 ± 8.0	p=0.320
Duration (Yrs)	24.4 ± 9.5	20.0 ± 3.0	25.1 ± 10.0	p=0.092
Polyneuropathy*	1.8 ± 0.4	2.0 ± 0.0	1.8 ± 0.4	p=0.047
Epilepsy*	1.3 ± 0.5	1.0 ± 0.0	1.3 ± 0.5	p=0.000
WBC (/ul)	7122.9 ± 2733.3	7676.7 ± 380.0	7043.8 ± 2919.7	p=0.084
Hemoglobin (mg%)	13.6 ± 2.3	14.1 ± 3.5	13.6 ± 2.3	p=0.354
Platelet (× 10 ³ /ul)	250.4 ± 207.3	165.6 ± 127.5	262.5 ± 215.8	p=0.662
Cholesterol (mg/dl)	141.8 ± 38.9	146.3 ± 15.2	141.2 ± 41.4	p=0.279
Triglyceride (mg/dl)	150.7 ± 85.7	210.0 ± 119.2	142.2 ± 80.2	p=0.360
g-GTP (U/L)	317.2 ± 392.1	482.3 ± 697.0	293.6 ± 351.5	p=0.068
SGOT (IU/L)	111.1 ± 124.9	64.3 ± 20.3	117.8 ± 132.4	p=0.206
SGPT (IU/L)	58.4 ± 78.7	49.0 ± 18.5	59.7 ± 84.1	p=0.386
Ammonia (ug/dl)	75.2 ± 78.5	70.0 ± 16.0	76.0 ± 84.0	p=0.532
Magnesium (mg/L)	1.9 ± 0.3	1.8 ± 0.4	1.9 ± 0.3	p=0.854
Calcium (mg/L)	8.7 ± 0.7	8.1 ± 0.9	8.8 ± 0.6	p=0.438
Phosphorus (mg/L)	3.8 ± 0.9	4.1 ± 1.9	3.8 ± 0.7	p=0.008
MMSE-K ¹	27.4 ± 3.0	20.7 ± 1.2	28.4 ± 1.6	p=0.247
MAST-K ²	30.5 ± 9.6	34.0 ± 9.2	30.0 ± 9.7	p=0.692
CIWA-A ³	26.9 ± 3.3	30.0 ± 2.7	26.5 ± 3.0	p=0.742
SOD activity	0.308 ± 0.140	0.247 ± 0.049	0.317 ± 0.148	p=0.046

*No=1, Yes=2

2 : Michigan Alcoholism Screening Test-Korean Version

1 : Mini-Mental State Examination-Korean Version

3 : Clinical Institute Withdrawal Assessment Scale

, triglyceride), (-GTP, SGOT, SGPT, am-
 monia), (magnesium, calcium, phosphorus),
 (MMSE - K) (MAST -
 K) 가 . SOD
 (p=0.035)
 (= - 0.433). (CIWA - A)
 (p=0.071), SOD
 (= - 0.375).

5. 인지장애 유무에 따른 변인의 비교

5 (5). ,
 ,
 가 가
 가 .
 가 (p=0.047),
 가
 (p=0.000). 가 (4.1 ± 1.9
 mg/L) 가 (3.8 ± 0.7mg/L)
 (p=0.008).

Table 6. Correlation coefficients between SOD activities and variables in the male alcoholics with cognitive disorders

Variables	Pearson's correlation coefficients ()	p-Value
Age	0.410	0.731
Education	0.410	0.731
Onset age	0.995	0.065
Duration	-0.101	0.935
WBC	0.706	0.501
Hemoglobin	-0.776	0.435
Platelet	0.950	0.203
Cholesterol	0.890	0.301
Triglyceride	0.968	0.161
-GTP	0.601	0.589
SGOT	-0.498	0.669
SGPT	0.575	0.610
Ammonia	-0.811	0.398
Magnesium	0.760	0.450
Calcium	-0.782	0.429
Phosphorus	0.345	0.775
MMSE-K ¹	0.585	0.602
MAST-K ²	-0.818	0.390
CIWA-A ³	-0.996	0.056

1 : Mini-Mental State Examination-Korean Version

2 : Michigan Alcoholism Screening Test-Korean Version

3 : Clinical Institute Withdrawal Assessment Scale

6. 인지장애를 동반한 주정의존군의 여러 변인과 Super-oxide Dismutase 활성도의 연관성

가 SOD 가
6 (6). , 가
SOD
, 가 SOD
(=0.995, p=0.065),
(= -0.996, p=0.056).

고 찰

, We - rnicke - Korsakoff
(1984 ; 1986), gl - utamate(Glu), - aminobutyric acid(GABA) rec - eptorgated ion channel
(Tsai 1995).
, serotonin(5 - HT) dopamine(DA)
(1997), norepinephrine(NE), Glu, aspartate
(ASP), GABA , N - methyl - D - aspartate(NMDA)
(Tsai 1995). Glycine NMDA coagonist
Glu NMDA (Foster
Kemp 1989 ; Wood 1995). Lustig (1992)
NMDA
MK - 801
long - term potentiation(LTP) , Glu
NMDA (Lovinger
1989 ; Blitzer 1990 ; Morrisett Swartzwelder 1993 ;
Grunze 1996). Sinclair Lo(1986) CA1
LTP

NMDA
(lorio 1992). Morgan (1992)
NMDA Glu
NMDA
가
(Grant 1990 ; Valverius 1990 ; Hoffman 1992 ;
Snell 1993 ; Trevisan 1994). SepAlveda (1995)
(dentate gy - rus) NMDA - NE
NMDA Glu
acamprosate가
(Sass
1996 ; Spanagel Zieglensberger 1997).
(Hunt 1993). alcohol dehydrogenase
ethanol - inducible cyt - ochrome P450 catalase
(Albano 1991).
ethanol ,
ethanol - hydrogen hydroxyl hy - droxyethyl , nitric oxide
, nitric oxide superoxide
peroxynitrite , hydroxyl nitroxide
(Halliwell 1992).
lipid peroxidation , SOD,
- tocopherol, ascorbate, selenium , glut - athione , lipid pe - roxidation
(Ahmad 1988 ; Pellmar 1993 ; Puttfarcken 1993a).
Zidenberg - Cherr (1990)
copper - zinc SOD(CuZnSOD)
glutathione peroxide
NMDA 가
long - term potentiation(LTP) , Glu
NMDA (Lovinger
1989 ; Blitzer 1990 ; Morrisett Swartzwelder 1993 ;
Grunze 1996). Sinclair Lo(1986) CA1
LTP
voltage - sensitive calcium channel 가
channel 가가
(Crews Chandler 1993). Volterra (1994)

SOD, 가
(= 0.995),
(= - 0.996)
SOD
가
가
중심 단어 : Superoxide dismutase

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