

알코올의존 환자의 Aldehyde Dehydrogenase 2 유전자 변이에 따른 음주 후 반응 및 성격특성

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Acute Alcohol Responses and Personality Traits by Aldehyde Dehydrogenase 2 Genotype Variances in Patients with Alcohol Dependence

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ABSTRACT

Objectives : The purpose of this study is to evaluate the pathophysiology of alcoholics by investigating the differences in frequency of Aldehyde Dehydrogenase 2(ALDH2) genotypes and ALDH2 alleles between patients with alcohol dependence and controls, and the differences of drinking and personality traits in Korean male alcoholics with ALDH2 genotype variances.

Methods : The authors selected 98 patients with alcohol dependence and 53 controls. Self - report questionnaires for acute responses after alcohol ingestion, the AUI(Alcohol Use Inventory), and the NEO - PI - R(NEO Personality Inventory Revised) were given to all patients with alcohol dependence. ALDH2 genotypes were typed with Mbo RFLP(Restriction Fragment Length Polymorphism) method in 53 controls and 98 patients with alcohol dependence. The authors divided alcoholic patients into two groups according to the presence of variant ALDH2² allele ; normal ALDH2 alcoholics(N=87) and variant ALDH2 alcoholics(N=11).

Results : 1) The genotypic frequencies of subjects with ALDH2^{1/1} were higher and those with ALDH2^{1/2} and

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98
53
가
138
(Alcohol Use Inventory, AUI),
가
DSM-가
10
rater reliability)
0.791(p<0.01)
R(NEO Personality Inventory Revised)
가
DSM-가
가
DSM-가
40
98
DSM-
Spearman's rank correlation
0.735(p<0.05)
2
liability) 0.816(p<0.01), 가
0.805(p<0.01)
가 DSM-가 DSM-
가 0.704(p<0.01)
(internal consistency)
0.8889, 0.8140
가 가
가 가
Cloninger¹²⁾가
25 가 가
가 1

2. 연구도구

Rhi TJ¹³⁾ 7
17
가
2
physiologic responses) 3
5
Cronbach 0.87
0.92 Horn¹⁴⁾ AUI
31 0 6 7
6가 Cronbach
0.792~0.910 NEO-PI-R Costa
McCrae¹⁵⁾가
240 5
Neuroticism, Extraversion, Openness,
Agreeableness, Conscientiousness
6
Openness values, actions
가 (0.26, 0.44)
28
0.57~0.81 0.83~0.91
0.56~0.92
0.67~0.95

3. 실험방법

1) Polymerase chain reaction-Restriction fragment length polymorphism(PCR-RFLP)
primer GenBank accession
number M20455 J03043 가

mitochondrial ALDH2 exon
 12 , primer Primer
 Detective program(ClonTech)
 sense primer 5' - HEX(fluorescence)CTA TGA
 TGT GTT TGG AGC CCA GT - 3 , anti-
 sense primer 5' - TAA TAC GAC TCA CTA TAG
 CCA CAC TCA CAG TTT TCT TCT T - 3 '
 PCR - RFLP

2) 통계처리 및 분석

SPSS 8.0 for Windows
 ALDH2
² - test Fisher's
 exact probability test
 ALDH2
 AUI, , NEO -
 PI - R Mann - Whitney
 U test Fisher's exact probability test
 p<0.05

결 과

1. 알코올의존 환자군과 대조군에서의 ALDH2 유전자형 및 대립유전자 빈도

98 ALDH2^{1/1}, ALDH2^{1/2},
 ALDH2^{2/2} 87 (88.8%), 4 (4.1%), 7
 (7.1%) 53 30
 (56%), 20 (38%), 3 (6%)
 ALDH2^{1/1} 가 ALDH2^{1/2}, ALDH2^{2/2}
 (² =29.22, df=2, p<0.01).
 ALDH2¹ 90.8%
 ALDH2² 9.2%
 75.5%, 24.5% 가

(² =13.01, df=2, p<0.01)(1).

2. ALDH2 유전자형에 따른 사회인구학적 특성

98 ALDH2 가
 87 ALDH2²
 가 ALDH2 가
 11 , ,
 , , ,
 가 (2).

3. ALDH2 유전자형에 따른 임상양상

ALDH2 ALDH2
 가
 가 Cloninger¹²⁾ ALDH2
 가 ,
 , , ALDH2
 ,
 ALDH2 가
 50%가 가 21
 (24.1%), 21 (24.1%),
 가 45
 (51.72%) ALDH2 가
 가 5 (45.5%),
 가 4 (36.4%), 가 2 (18.2%)
 ALDH2 가
 ALDH2
 (3).

4. ALDH2 유전자형에 따른 알코올 사용적도에서의 차이 (AUI)

, ,

Table 1. Genotype and allele frequencies of ALDH2 polymorphism in alcoholic patients and controls

	N	Genotype			Allele frequency	
		ALDH2 ^{1/1} (%)	ALDH2 ^{1/2} (%)	ALDH2 ^{2/2} (%)	ALDH2 ¹ (%)	ALDH2 ² (%)
Alcoholic patients	98	87(88.8)	4(4.1)	7(7.1)	178(90.8)	18(9.2)
Controls	53	30(56.6)	20(37.7)	3(5.7)	80(75.5)	26(24.5)
²			29.22			13.01
p			0.0000*			0.0000**

N : number of individuals, * : df=2, ** : df=1

Table 2. Demographic characteristics of alcoholic patients with normal or variant ALDH2 gene

Alcoholic patients	with Normal ALDH2 gene(N=87) Mean(SD)	with Variant ALDH2 gene(N=11) Mean(SD)	U	P
Ages(years)	42.37(.89)	42.09(.01)	449.0	.739
Education(years)	11.10(3.08)	11.45(1.81)	450.0	.738
	N(%)	N(%)	²	P
Marital status			1.761	.808
Unmarried	20(23.0)	3(27.3)		
Married	35(40.2)	3(27.3)		
Divorced	24(27.6)	4(36.4)		
Death	2(2.3)	1(9.1)		
Separated	5(5.8)	0(0.0)		
Cohabiting	1(1.2)	0(0.0)		
Religion			1.918	.681
Catholic 1	7(19.5)	1(9.1)		
Protestant	22(25.3)	3(27.3)		
Buddhist	12(13.8)	3(27.3)		
Others	1(1.2)	0(0.0)		
No	35(40.2)	4(36.4)		
Occupation			11.569	.269
Managers	5(5.8)	0(0.0)		
Office worker	10(11.5)	0(0.0)		
Salesman	11(12.6)	1(9.1)		
Service	4(4.6)	3(27.8)		
Agriculture	12(13.8)	3(27.8)		
Labourer	21(13.8)	3(27.8)		
Army, police	1(1.2)	0(0.0)		
Others	1(1.2)	0(0.0)		
No	22(25.3)	1(9.1)		
Socioeconomic status			3.331	.443
Low	24(27.6)	2(18.2)		
Low-middle	22(25.3)	5(45.5)		
Middle	35(40.2)	3(27.3)		
Middle-high	3(3.5)	1(9.1)		
High	3(3.5)	0(0.0)		

Two-tailed Mann-Whitney U test and Fisher's exact probability test

N : number of individuals

5. ALDH2 유전자형에 따른 음주 후 급성 신체, 심리반
 응적도에서의 차이

ALDH2 가 (5.99 ± 3.85) ALDH2 가 (3.93 ± 2.70)
 ALDH2 가 (9.64 ± 3.32) ALDH2 가 (7.27 ± 1.95)
 (U=208.5, p=0.002) (U=145.00, p<0.01).

(4).

가 ALDH2 (5). 6. ALDH2 유전자형에 따른 NEO-PI-R 척도에서의 차이
NEO - PI - R Neuroticism, Extraversion, Openness, Agreeableness, Conscientiousness 5

Table 3. Clinical characteristics of patients with alcohol dependence

	Normal ALDH2 alcoholics(N=87) Mean(SD)	Variant ALDH2 alcoholics(N=11) Mean(SD)	U	P
Age of onset(yrs)	18.64(3.40)	19.55(3.93)	411.00	.442
Loss of control(yrs)	32.20(7.78)	35.36(7.20)	354.50	.162
Duration of illness(yrs)	24.39(6.76)	23.55(7.24)	444.00	.697
Amount(bottles)				
Average	2.69(1.60)	3.45(2.54)	423.50	.521
Maximum	6.27(4.15)	6.91(3.05)	385.50	.291
Frequency(days/month)	22.57(7.29)	25.00(4.47)	412.00	.445
Severity	4.64(0.59)	4.73(0.47)	442.00	.631
	N(%)	N(%)	2	P
Course			0.518	.665
Persistent	76(87.4)	9(81.8)		
Episodic	10(11.5)	2(18.2)		
Unspecified	1(1.2)	0(0.0)		
Tolerance			4.536	.105
Same	21(24.1)	4(36.4)		
Decreased(after increased)	45(51.7)	2(18.2)		
Increased	21(24.1)	5(45.5)		
Family loading			0.001	1.000
Yes	47(54.0)	6(54.6)		
No	40(46.0)	5(45.5)		
Type			1.823	.436
I	24(27.6)	1(9.1)		
II	34(39.1)	5(45.5)		
Mixed	29(33.3)	5(45.5)		

Two-tailed Mann-Whitney U test and Fisher exact probability test
N : number of individuals, yrs : years

Table 4. Comparisons of AUI between normal and variant ALDH2 alcoholics

	Normal ALDH2 alcoholics(N=87) Mean(SD)	Variant ALDH2 alcoholics(N=11) Mean(SD)	U	P
AUI 1	23.75(9.59)	24.09(9.45)	477.50	.991
AUI 2	17.83(7.74)	21.45(7.66)	347.50	.140
AUI 3	26.20(8.34)	25.18(8.39)	453.50	.778
AUI 4	17.25(8.42)	15.91(8.85)	429.50	.501
AUI 5	5.99(3.85)	9.64(3.32)	208.50	.002*
AUI 6	17.95(4.88)	19.00(6.07)	340.00	.117

* : statistically significant by two-tailed Mann-Whitney U test

AUI : Alcohol Use Inventory

1 : Psychological benefits of alcohol use, 2 : Disruptive consequences of alcohol use, 3 : Compulsive drinking, 4 : Pathological drinking style, 5 : Marital dysfunction, 6 : Anxious concern of drinking and treatment readiness

Table 5. Comparisons of acute responses after alcohol ingestion between normal and variant ALDH2 alcoholics

	Normal ALDH2 alcoholics(N=87)	Variant ALDH2 alcoholics(N=11)	U	P
	Mean(SD)	Mean(SD)		
Total response	48.82(16.91)	46.36(15.78)	409.00	.434
Response 1	3.93(2.70)	7.27(1.95)	145.00	.000*
Response 2	17.44(9.37)	10.08(8.39)	436.50	.636
Response 3	21.37(10.95)	26.55(10.67)	360.50	.184
Response 4	7.62(5.37)	7.82(4.24)	470.00	.923
Response 5	13.94(6.83)	12.27(4.65)	409.50	.437

* : statistically significant by two-tailed Mann-Whitney U test

Response 1 : Flushing and cardiovascular responses, Response 2 : Other physiologic responses

Response 3 : Flushing and other physiologic responses(Response 1 +Response 2)

Response 4 : Negative psychological responses, Response 5 : Positive psychological responses

ALDH2 가 AL-

Aggreableness DH2^{2/2} 98 7 (7.1%)

6 altruism ALDH2 ALDH2^{2/2} 2 (1.4%) 19)

가 (25.73 ± 2.90) ALDH2^{2/2}

(U=295.00, p=0.038). ALDH2

Conscientiousness dutifulness

ALDH2 (28.53 ± 3.94)

(26.55 ± 3.14)

ALDH2²

ALDH2 (6).

24.5~25.7%,²⁰⁾²¹⁾

24~25%,²²⁾²³⁾ 15~24%¹⁸⁾¹⁹⁾

25%

고 찰

ALDH2^{1/1} 가 ALDH2^{1/2}, ALDH2^{2/2} ALDH2 ALDH2^{2/2} Higuchi²⁰⁾

가 ALDH2 ALDH2^{1/1} homozygote

ALDH2^{2/2}

AL-

4.1% ALDH2^{1/2} ALDH2^{1/2} DH2^{1/2} 가

¹⁶⁻¹⁸⁾ 13~16.7%

ALDH2^{1/2} 가 ALDH2^{2/2} 가

2)

ALDH2^{1/2} ALDH2² 12%, 10%

acetaldehyde monoamines 가
tetrahydroisoquinoline(TIQ), salsolinol, tetrahydro- ALDH2 가
dropapaveroline(THP) , acetaldehyde가
morphine alkaloid ALDH2
acetaldehyde가 가
(27)28) serotonin, ALDH2 가
dopamine, GABA 가 , ,
가 (29 - 32) 38 - 40)
ALDH2²
(33 - 35) ALDH2 가
(36) - ,
가 ALDH2 가
ALDH2 가
ALDH2 가
1979 , 1986 , 1992
ALDH2^{1/2} 가 2.5%, 8.0%, 13.0%
ALDH2² 가
(37) - 가
ALDH2 가
가 - - ALDH2
ALDH2^{2/2} 가
ALDH2² 가
ALDH2 가 ,
comfort() 가
가
ALDH2 가 가
(23)24) 가
가
ALDH2 NEO - PI - R 5
가
ALDH2 ALDH2
가 altruism()
dutifulness()
ALDH2
가 가

가 가

ALDH2 가 가

ALDH2

가 , 가

가 , 가

가

ALDH2

가

ALDH2

ALDH2² 가

중심 단어 : ALDH2

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