

정신분열병 환자에서 Cytochrome P450 2D6 유형에 따른 부작용에 대한 연구

이 민 수*† · 남 종 원*

Antipsychotics Induced Extrapyramidal Symptoms in Schizophrenics in Relation to Cytochrome P450 2D6 Genotype

Min Soo Lee, M.D.,*† Jong Won Nam, M.D.*

ABSTRACT

The genetically determined CYP2D6 activity may be considered to be associated with antipsychotic induced extrapyramidal side effects with inter-individual variation. Genetic polymorphism of CYP2D6 was determined by polymerase chain reaction(PCR) and MspI restriction fragment length polymorphisms(RFLP) for 194 schizophrenics. Subjects with a 334bp band were classified a1a1, those with 229bp and 105bp bands a2a2, and those with all three bands a1 - a2. We did not identify schizophrenic subject with poor metabolizer. 194 schizophrenic patients previously treated neuroleptic medication, were assessed by Extrapyramidal Symptom Rating Scale(ESRS).The cases were composed of 33 akathisia, 47 parkinsonism, 21 tardive dyskinesia.

These results are similar to the previous understanding that the poor metabolizer is very rare in Orientals compared to Caucasians, therefore, it considered that CYP2D6 genotypes have maybe no association with schizophrenia and extrapyramidal side effects in Koreans.

KEY WORDS : CYP2D6 · Schizophrenia · EPS · Antipsychotics.

서 론

CYP2D6 (substrate) 가 (1w -

cytochrom P - 450 (Andreason 1997 ; Arms -

가 (1999 ; Schatzberg Nemeroff trong 1997). CYP2D6

1998). CYP2D6

CYP2D6 가 , 20

slow me - tabolizer (Richelson 1998). Slow metaboli - 가 가

ahashi 1994), CYP2D6

1997). CYP2D6

CY -

Department of Neuropsychiatry, College of Medicine, Korea University, Seoul, Korea

† : , 136 - 705 5가 126 - 1) (02) 920 - 5354,) (02) 923 - 3507

P2D6

CYP2D6

대상 및 방법

1. 연구대상

DSM -

가

194

Extrapyramidal Symptom Rating Scale (ESRS) (Chouinard 1995).

2. 연구방법

1) Genomic DNA의 정제

1.5ml 13,000rpm 1

pellet ACE shocking solution(NH4Cl 8g,

Na2EDTAH2O 1g, KH2PO4 0.1g 1L)

500 µl 3

2

pellet 400 µl nucleic

lysis Buffer[Tris(pH 8.0) 10mM, NaCl 400mM, EDTA 2mM]

pellet 10% SDS 27 µl pr-

oteinase K 10 µl 가 56 2

saturated NaCl 135 µl 15

13000rpm 1

2 DNA

DNA 70%

100 µl

2) 중합효소연쇄반응(Polymerase Chain Reaction : PCR)

을 이용한 유전자형의 판별

Cytochrome P450 CYP2D6 gene 506 G

A transition (Go-

ugh 1990).

CYP2D6

5' - GCC TCC GCC AAC CAC TCC G - 3'

5' - AAA TCC TGC TCT TCC GAG GC - 3'

PCR 50 µl

Taq pol buffer 50mM KCl/10mM TrisCl(pH 8.3)

MgCl2 1.5mM

each Primer each 20pmol/50 µl

dNTP 200 µM

Taq polymerase 3U

Template DNA 200ng

- 50 µl

94 5 , 94 30
60 30 , 72 30 35 .

3) 증폭된 생성물의 분석

Cytochrome P450 CYP2D6 locus G A transi-
tion PCR (334bp) BstNI

5%, polyacrylamide gel

ethidium bromide

(ultraviolet transilluminator)

polaroid

(polaroid, film 667)

4) Determination of PCR product

Size of product : 334bp

Cutting with MspI : Allele 1 334bp

Allele 2 29bp 105bp

3. 통계학적 분석

spss 7.0

2

p<.05

결 과

39.0±7.8

107

87

47

(24%),

33 (17%),

21

(11%) (1).

Genomic DNA PCR

MspI

334bp band

a1a1 , 229bp band 105bp band

a2a2 , 3 band a1a2

a2a2

HOM H(homozygote wild type)

193 , a1a2 HEM HET(heterozygote) 1

a1a1 HOM PM(homozygote
mutants) poor metabolizer

(1). HEM HET(heterozygote) 1 ES-

RS

토 의

CYP2D6

가

Table 1. Distribution of Extrapyramidal Symptom in patients with schizophrenia

	Male	female	p
Tardive dyskinesia	7	14	0.357
Parkinsonism	27	20	0.782
Akathisia	10	33	0.748

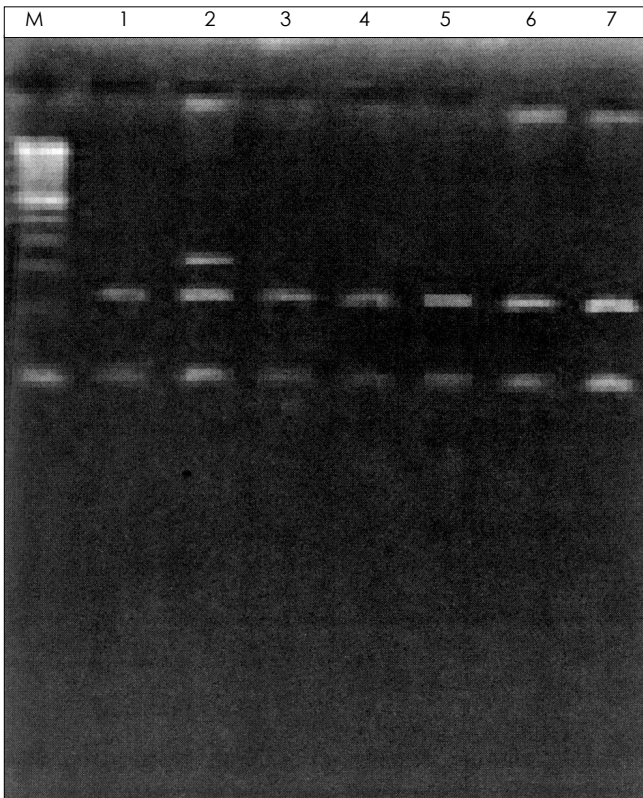


Fig. 1. PCR analysis BstNI RFLP in CYP2D6 alleles. 1 : a2a2, 2 : a1a2, 3 : a2a2, 4 : a2a2, 5 : a2a2, 6 : a2a2, 7 : a2a2.

CYP2D6
 CYP2D6
 poor metabolizer
 3 10%, 0 2%
 (Kroemer Eichlbaum 1995 ;
 Masimirembwa 1993).
 poor metabolizer poor
 metabolizer
 (1998)
 poor metabolizer가
 CYP2D6
 extensive metabolizer CYP2D6
 가

중심 단어 : CYP2D6

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CYP2D6
 가 poor metaboli-
 zer
 CYP2D6 B
 가가 (Kurth Kurth 1993).
 CYP2D6 CY -
 P2D6 가
 CYP2D6
 가 poor metabolizer
 (Andreassen 1997 ; Arm-
 strong 1997 ; Iwahashi 1994),
 (Kawanishi 1997 ; Ueno 1996)
 CYP2D6
 CYP2D6가 dopamine
 transporter CYP2D6
 Andreassen (1997) CYP2D6

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