

Fluoxetine 투여 후 Amitriptyline의 혈장농도 변화

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Plasma Level of Amitriptyline after Fluoxetine Addition

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ABSTRACT

Objective : The purpose of this study was to compare the plasma amitriptyline and nortriptyline level between before and after fluoxetine addition with patients who were currently taking amitriptyline.

Method : From the inpatient and outpatient unit of Soon Chun Hyang University Hospital, Chunan, fourteen subjects who were taking amitriptyline 25mg more than 1 week at least were given fluoxetine 20mg. Before and 2 weeks after fluoxetine addition, the plasma level of amitriptyline and nortriptyline are analyzed simultaneously by High Performance Liquid Chromatography(HPLC). At the same times, HAM - D(Hamilton Rating Scale for Depression) score and the UKU(Uldvalg for Kliniske Undersøgelser) side effect scale were checked.

Results : After fluoxetine addition to the patients who were taking amitriptyline, the plasma level of amitriptyline, nortriptyline and sum of amitriptyline and nortriptyline had risen. The mean plasma amitriptyline level increased from 168.9 ± 89.4 ng/ml to 183.0 ± 102.0 ng/ml after fluoxetine addition($p=0.011$), but the change was not statistically significant. The mean plasma nortriptyline level increased significantly from 114.3 ± 70.2 ng/ml to 168.0 ± 86.2 ng/ml after fluoxetine addition($p=0.011$). In addition, the mean plasma level of total amitriptyline and nortriptyline increased significantly from 283.1 ± 125.3 ng/ml to 350.9 ± 78.4 ng/ml after fluoxetine addition($p=0.016$). After fluoxetine addition, no significant change was noted in the UKU side effect scale score.

Conclusion : As consequence of comparison of plasma amitriptyline and nortriptyline level before and after fluoxetine addition, mean amitriptyline, nortriptyline and total plasma level was increased after fluoxetine addition. This suggests that coadministration of amitriptyline and fluoxetine may induce improvement of depressive symptom in depressive patients by way of increased plasma level of amitriptyline.

KEY WORDS : Amitriptyline · Nortriptyline · Fluoxetine · Plasma level of amitriptyline.

서 론

take inhibitors ; SSRI) fluoxetine 1988

(selective serotonin reup-

(tricyclic antidepressants ;

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TCA) 가 , , 가 , , CYP2D6 (Kaplan Sadock (; haloperidol, risperidone, propranolol, carbamazepine, codein) 1998). Weilburg (1989) SSRI SSRI 가 . Levitt (1999) TCA fluoxetine 가 TCA 가 . Nemeroff (1996) cytochrome P450(CYP)2D6 TCA 가 fluoxetine norfluoxetine CYP2D6 12 SSRI fluoxetine TCA 가 TCA 가 TCA fluoxetine (Bergstrom 1992). Fluoxetine TCA 가 (Aranow 1989). (Therapeutic Drug Monitoring) (Stephanie 1990).

TCA SSRI TCA

연구대상 및 방법

1. 연구대상

2001 6 8 fluoxetine amitriptyline 25mg 1 14 (8 , 6) , 50.8 ± 14.0 가 6 가 5 가 3 (1). Amitriptyline 25mg (Sheldon Preskon 1993). fluoxetine

2. 연구방법

1) 혈장농도측정

fluoxetine amitriptyline nortriptyline , fluoxetine 20 mg 2 amitriptyline nortriptyline . Amitriptyline nortriptyline 12 , High Performance Liquid Chromatography(HPLC) (Thomas 1979). (Heparinized vacutainer tube) 4~5cc , 3000RPM HPLC amitriptyline nortriptyline

2) 임상증상의 평가

가 fluoxetine 2 Hamilton Rating Scale for Depression(HAM - D) (Hamilton 1960). 가 HAM - D 50%

3) 부작용의 평가

Amitriptyline fluoxetine 가 fluoxetine 2 Uldvalg for Kliniske Undersøgelser(UKU) (psychic), (neurologic), (autonomic), (other) (Lingjaerde 1987). 0 3 가 가

4) 통계처리

SPSS/PC+ 10.0 fluoxetine 2 amitriptyline nortriptyline Wilcoxon signed rank test fluoxetine HAM - D UKU

결 과

1. Amitriptyline과 nortriptyline의 혈장농도

Amitriptyline 25mg amitriptyline (1). 1) Amitriptyline 168.9 ± 89.4ng/ml 가 2) Nortriptyline 114.3 ± 70.2ng/ml (p=0.011) 가 3) Amitriptyline 350.9 ± 78.4ng/ml (2). 4) Amitriptyline/nortriptyline 2.8 ± 3.4 (3).	fluoxetine 20mg nortriptyline fluoxetine 183.0 ± 102.0ng/ml (2). fluoxetine 168.0 ± 86.2ng/ml (2). fl- 283.1 ± 125.3ng/ml (p=0.016) 가 fluoxetine 2.3 ± 3.0 (3).
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Table 1. Demographic data of subject

No. of patient	14(M : 8, F : 6)
Age (Mean ± S.D)	50.8 ± 14.0
Diagnosis	Major depressive disorder : 6 Dysthymic disorder : 5 Somatoform disorder : 3

Table 2. Mean plasma level and change of amitriptyline, nortriptyline and amitriptyline plus nortriptyline before and 2 weeks after fluoxetine 20mg addition

	Baseline	2 Week	Change of	p*
	(ng/ml)	(ng/ml)	value	
	Mean ± S.D	Mean ± S.D	Mean ± S.D	
Amitriptyline	168.9 ± 89.4	183.0 ± 102.0	23.7 ± 73.2	0.331
Nortriptyline	114.3 ± 70.2	168.0 ± 86.2	54.1 ± 63.7	0.011
Amitriptyline +Nortriptyline	283.1 ± 125.3	350.9 ± 78.4	67.9 ± 101.0	0.016

* : Statistically significant by Wilcoxon signed rank test

Table 3. Change of amitriptyline/nortriptyline ratio, HAM-D and UKU side effect scale score before and 2 weeks after fluoxetine 20mg addition

	Baseline	2 Week	p*
	(Mean ± S.D)	(Mean ± S.D)	
Ratio	2.8 ± 3.4	2.3 ± 3.0	ns
HAM-D	14.9 ± 5.1	14.7 ± 5.0	ns
UKU side effect scale	2.9 ± 1.2	3.2 ± 1.5	ns

* : Statistically significant by Wilcoxon signed rank test

HAM-D : Hamilton Rating Scale For Depression

UKU : Uldvalg for Kliniske Undersøgelser

2. 항우울 효과와 부작용

1)	HAM - D	fluoxetine	
	14.9 ± 5.1	14.7 ± 5.0	(3).
2)	UKU	fluoxetine	
	2.9 ± 1.2	3.2 ± 1.5	(3).
가			

고 찰			
TCA	fluoxetine	TCA	
(1992)	11	(Harvey Preskorn 1996).	Vandel fluoxetine
TCA	10	TCA	
9	3	2	가 가
fluoxetine	4	3	2 가
	60%	가	.
fluoxetine		3	amitriptyline
2	nortriptyline	가	20% 90% 가
		TCA	가
	. Stephanie(1990)		fluoxetine
time	desipramine	nortriptyline	7
		desipramine	nortriptyline
		2~11	가
	nortriptyline		4 가
	. Adnan (1995)	amitriptyline 50mg	fluoxetine 20mg
		15	amitriptyline 50mg
		10	
	amitriptyline	nortriptyline	가 amitriptyline
	2	nortriptyline	9
	fluoxetine	가	amitriptyline
	nortriptyline	가	.
	fluoxetine	amitriptyline	nortriptyline
	Adnan (1995)		amitriptyline
		(amitriptyline : 44.2ng/ml,	nortriptyline 5.7ng/ml)
		31.1	50.8
가		가	
amitriptyline	nortriptyline	가	(Burch 1983).
가			
fluoxetine	가	nortriptyline	가
			nortriptyline
가	amitriptyline		

가

Baumann(1996) TCA fluoxetine ,
TCA 가 TCA (Nelson 1991 ; Weilburg 1989).
. TCA Nelson (1991) TCA 52
(Biotransformation) , TCA fluoxetine 17
(isoenzyme) CYP2D6가 , 2 TCA
(rate - limiting enzyme) (Stephanie HAM - D 35%
1990). SSRI fluoxetine norfluoxetine HAM - D 62%
CYP2D6 TCA SSRI 가 가
TCA (Lemb- fluoxetine HAM - D
erger 1985). Amitriptyline Nelson
nortriptyline , amitriptyline nortripty- (1991) 가
line (hydroxylation) 10 - hydro- amitriptyline
xyamitriptyline 10 - hydroxynortriptyline 가
(Sheldon 1993). Skjelbo Brosen(1992) fluoxe-
tine norfluoxetine TCA

amitriptyline fluoxetine Amitriptyline fluoxetine
nortriptyline amitriptyline
4 Vaughan(1988) nortriptyline 100mg fluoxetine 20mg
CYP2D6 가 nortriptyline 가
amitriptyline
nortriptyline 가 TCA fluoxetine , ,
(Adnan 1995). , Hirokane (2001) amitrip- 가 TCA
tyline nortriptyline CYP2C19 가 fluoxetine , TCA
, nortriptyline CYP2D6가 fluoxetine (fluoxetine : 2~4 , nor-
CYP2D6 가 fluoxetine
amitriptyline/nortriptyline TCA fluoxetine
가 nortriptyline/hydroxynor- 20mg Westermeyer (1991) TCA fluoxetine
triptyline 가 fluoxetine amitriptyline
amitriptyline nortriptyline nortriptyline
TCA fluoxetine
, amitriptyline Weilburg (1989)
amitriptyline/nortriptyline fluoxetine fluoxetine
line fluoxetine amitripty- CYP 가
(PM ; Poor metabolizer, EM ; Extensive metabolizer)
CYP2D6 가가
TCA SSRI TCA SSRI CYP2D6 가
가 , TCA SSRI CYP
(Levitt 1999). TCA SSRI TCA - TCA 가 30 가
가 가 (Sheldon 1993),
(Kurtz 1997). TCA SSRI 25mg amitriptyline

amitriptyline
가 Benzodiazepine
가
결론
Amitriptyline 25mg 14
fluoxetine 20mg amitriptyline nortriptyline
1) Amitriptyline fluoxetine 가
2) Nortriptyline fluoxetine 가
3) Amitriptyline nortriptyline fluoxetine 가
4) Amitriptyline/nortriptyline fluoxetine 가
amitriptyline
amitriptyline
fluoxetine amitriptyline nortriptyline 가 가
amitriptyline fluoxetine 가
amitriptyline
fluoxetine

중심 단어 : Amitriptyline · Nortriptyline · Fluoxetine · Plasma level of amitriptyline

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