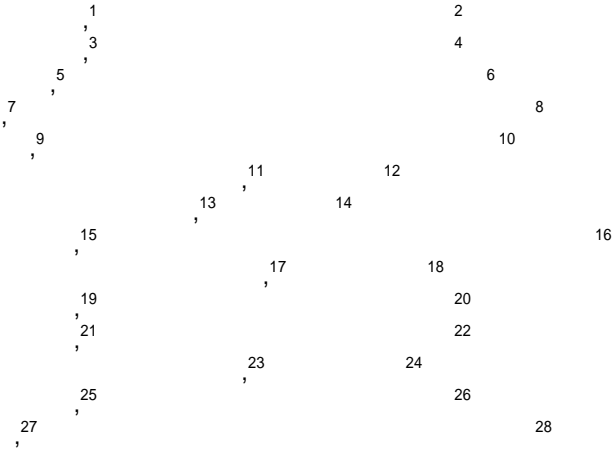


우울장애 환자에서 Nefazodone의 항우울효과, 항불안효과 및 수면·성기능·삶의 질 등에 미치는 영향에 관한 다기관 연구

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ABSTRACT

A Multicenter Study on Effects of Nefazodone(SerzoneTM) on Depression, Anxiety, Sleep, Sexual Functions, and Quality of Life in Patients with Depression

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Nefazodone

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Objective : The aim of this study is to determine effects of nefazodone on depression, anxiety, sleep and sexual function in depressive patients. **Subjects and Methods :** This is an open, non-comparative, multi-center study. Antidepressant and other clinical effects of nefazodone were evaluated in 230 patients of 26 centers, aged 14 years or more, who met DSM-IV criteria to major depressive disorder or dysthymic disorder and didn't have other psychiatric disorders and were physically healthy. The clinical efficacy was assessed at week 1, 2, 4 and 8 using Clinical Global Improvement (CGI), Hamilton Depression Scale (HAM-D), Beck Depression Inventory (BDI), State and Trait Anxiety Inventory-State Anxiety (STAI-SA). Other clinical effects were assessed with Weekly Sleep Questionnaire, Sexual Functioning Questionnaire and GHQ-QOL-12, a scale for quality of life. Adverse drug reactions were checked with a questionnaire. Post-treatment effects of drug were compared with pre-treatment baseline condition. **Results :** The response rates by Clinical Global Improvement and HAM-D after 8 weeks treatment were 62.4% and 75.2% respectively. Comparing to baseline, nefazodone was proved to have significantly higher antidepressant and antianxiety effects in depressive patients and it improved also sleep, sexual functions and quality of life. Both patients and physicians satisfied with the effects of drug. Adverse drug reactions were a few and not serious, and most of them disappeared as treatment continued. **Conclusion :** These results suggest that not only nefazodone has antidepressant effects and antianxiety effects, but also it improves sleep disturbance, sexual dysfunction and the quality of life in depressive patients. Adverse drug reactions were a few and not serious. **(Korean J Psychopharmacol 2001;12(3):211-221)**

KEY WORDS : Nefazodone · Antidepressant effect · Anxiety · Sleep disturbance · Sexual dysfunction.

서 론

4% 2%가 가 1,2)
 5 10%가

(17)) 14 , (3)
 , (4) 가 ,
^{4,5)} (mortality) , ,
 (morbidity) ^{6,7)} (wash - out) 가 (MA -
 가 . OI
 1980 2 가 , fluoxetine
 , monoamine oxidase inhibitor(MAOI) fluoxetine 가
 , , , , ,) , (5) 14 (가
 , MAOI tyramine 72 가 , (6) 가
 . ⁸⁾ 1980 가 , (6) 가
 , fluvoxamine, fluoxetine, sertraline, par -
 oxetine, citalopram selective se -
 rotonin reuptake inhibitor(SSRI)가 (1) , , ,
 SSRI 가 가 ⁸⁾ (2) 1 가 ,
 가 ^{9,10)} . .
 nefazodone serotonin noradrenergic reuptake
 inhibitor(SNRI) , trazodone 가 , (3)
 (,) , , , , , , , , , ,
⁸⁾ Nefazodone , (4) DSM - IV
 가 ¹¹⁻¹⁴⁾ , Axis II 가 ,
 SSRI¹⁵⁻²¹⁾ 가 (5) 3 , (6)
 nefazodone imipramine
^{22,23)} nefazodone 2 ,
²⁴⁾ nefazodone (7) nefazodone
¹⁸⁾ , (8) , (9)
²⁴⁾ 12
 DSM - IV²⁵⁾ , (10) , ,
 nefazodone 8 가 .

2. 약물투여

nefazodone 100 mg
 200 mg . 100 mg/
 day 1 100 mg/day
 , 600 mg/day 가 , 1 2
 가
 ; (1) 가 3 8 300 600 mg/day
 , DSM - IV . 100 mg/
 , (2) HAM - D ²⁶⁾ day 가 ,

연구 대상 및 방법

1. 연구대상

26

Nefazodone

nefazodone 100 mg/day
 (, , ,)
 lorazepam 1 2 mg/day
 가
 MAOIs,
 (: lithium, buspirone, pin-
 dolol, tryptophan, T3 - thyroxine)
 (: triazolam, terfenadine, astemi-
 zole, cisapride, lovastatin, simvastatin, atrovastatin)

3. 임상효과 및 평가

1) 항우울효과
 가 , 2, 4, 8
 가 Clinical Global Improve-
 ment(CGI), 17 - item Hamilton Rating Scale(HAM-
 D)^{26,27)} Beck 's Depression In-
 ventory(BDI)²⁸⁾ . CGI “ ”
 “ ” 5 가
 . 8 CGI 가
 HAM - D 가
 . CGI “ ” 가
 , HAM - D(17 items)
 50% 가
 HAM - D(17 items) 가 10

2) 불안증상, 수면, 성기능 및 삶의 질에 미치는 영향
 , 1, 2, 4,
 8 가 ,
 8 가 . 가
 Spielberger 20
 , 20
 State and Trait Anxiety Inventory - State
 Anxiety(STAI - SA)
 STAI - SA ²⁹⁾

, DSM - IV
 5
 2
 7 “ ”
 (Weekly Sleep Questionnaire) 가 가
 .
 ()
 가 () 6 ‘
 가 가 ‘
 가 General Health Questio-
 nnaire 12
 “ - 12 ^{30,31)} 가
 가

4. 안전성
 inten -
 tion - to - treat
 가 .

5. 통계처리

1) 유효성 분석
 (1) 가 HAM - D, CGI
 , 가
 가
 가 HAM - D BDI score
 (repeated measure of
 ANOVA) . (2)
 STAI - SA
 HAM - D 9, 10, 11
 . (3)
 (weekly sleep questionnaire)
 HAM - D 4,
 . (4)

5, 6

가 가 paired t - test .

. (5) “ 가 가

- 12 ” 가 230 , 2 가가 가

paired t - test . 200 , 4 가가 가

2) 안전성 분석 188 , 8 가가 가

가 . 가 166 . 8

가 가 가 166 CGI HAM - D

8 1 8

GIS HAM - D 165

가 가 가 가

가 가 가

가 230 29.6%(68/

230), 70.4%(162/230)

45.4 (16 81) .

가 51.3%(118/230) ,

48.7%(112/230) .

가 43.0%(99/

230) , 57.0%(131/230

) . 239 .

benzodiaze -

pine alprazolam 22.2%(53/239) , lo -

razepam 18.8%(45/239) , diazepam 3.3%(8/239

) . 75.7%(174/230

) , 24.3%(56/230) .

66%(37/56)가

가 73.9%

(170/230) , 26.1%

(60/230) . Nefazodone 1

1 346 mg .

2. 항우울효과

8 CGI “ ”

CGI 62.4%(103/165) , HAM -

D(17 items) 50% 가

HAM - D(17 items)

가 10 75.2%

(124/165) (Table 1).

HAM - D 17 24.02 ± 5.88

가 가 paired t - test

. (5) “ 가 가

- 12 ” 가 230 , 2 가가 가

paired t - test . 200 , 4 가가 가

2) 안전성 분석 188 , 8 가가 가

가 . 가 166 . 8

가 가 가 166 CGI HAM - D

8 1 8

GIS HAM - D 165

가 가 가 가

가 가 가

가 230 29.6%(68/

230) , 70.4%(162/230)

45.4 (16 81) .

가 51.3%(118/230) ,

48.7%(112/230) .

가 43.0%(99/

230) , 57.0%(131/230

) . 239 .

benzodiaze -

pine alprazolam 22.2%(53/239) , lo -

razepam 18.8%(45/239) , diazepam 3.3%(8/239

) . 75.7%(174/230

) , 24.3%(56/230) .

66%(37/56)가

가 73.9%

(170/230) , 26.1%

(60/230) . Nefazodone 1

1 346 mg .

2. 항우울효과

8 CGI “ ”

CGI 62.4%(103/165) , HAM -

D(17 items) 50% 가

HAM - D(17 items)

가 10 75.2%

(124/165) (Table 1).

HAM - D 17 24.02 ± 5.88

1. 연구대상환자

26 230 8

166

1 64

Nefazodone

Table 1. Patients rated as "much improved" in Clinical Global Improvement (CGI) and patients under 10 point in Hamilton Depression Scale (HAM-D) at 2 weeks, 4 weeks, and 8 weeks treatment period with nefazodone

Week	Clinical Global Improvement number of patients* (%)	HAM-D number of patients (%)
Week 2	59/200 (29.5%)	57/199 (28.6%)
Week 4	90/187 (48.1%)	106/188 (56.4%)
Week 8	103/165 (62.4%)	124/165 (75.2%)

* : responder/total

2, 4, 8 15.90 ± 6.82, 12.22 ± 6.55, 8.98 ± 5.51

(p = 0.0001).

BDI 21 20.86 ± 9.66, 16.98 ± 9.98, 13.64 ± 9.21

(p = 0.0001)(Table 2).

CGI 67.2%(45/67), 76.3%(45/59), 33.3%(13/39), HAM-D 77.3%(51/55), 78.3%(47/60), 66.7%(26/39)

CGI

3. 항불안효과

STAI-SA (63.14 ± 10.28) 1, 2, 4, 8 (57.11 ± 11.13, 54.00 ± 10.82, 50.85 ± 11.39, 47.27 ± 11.46)

(p = 0.0001), HAM-D

9, 10, 11 (5.59 ± 1.82) 2, 4, 8 (3.60 ± 1.77, 2.88 ± 1.78, 2.09 ± 1.46)가 (p = 0.0001)(Table 2).

4. 수면에 미치는 영향

(20.10 ± 4.76) 1, 2, 4, 8 (16.32 ± 5.29, 14.76 ± 5.74, 13.25 ± 5.43, 11.87 ± 5.71)

(p = 0.0001), HAM-D

4, 5, 6

(3.68 ± 1.65) 2, 4, 8 (2.25 ± 1.84, 1.62 ± 1.55, 1.10 ± 1.32)가 (p = 0.0001)(Table 2).

5

2

가, nefazodone

(Table 2).

5. 병용약제인 진정 수면제가 항불안 효과 및 수면에 미치는 영향

8 STAI-SA (benzodiazepine, zolpidem, trazodone) 58.3%(88/151), 41.7%(63/151)

8 STAI-SA 0 8 63.70 ± 10.41, 49.97 ± 10.69

20.45 ± 4.88, 11.90 ± 5.79

63 STAI-SA 0 8 63.78 ± 8.98, 53.35 ± 10.24, 11.83 ± 5.66

0 8 STAI-SA -8.63 ± 7.15, -8.05 ± 6.33

paired t-test

(p = 0.6087),

-13.73 ± 11.10, -10.43 ± 8.99

(p = 0.0530).

8 88 38.6%(34/88)가

4.5%(4/88) 34 STAI-SA 0 8 65.27 ± 8.88, 48.30 ± 11.41, 21.78 ± 3.51, 20.50 ± 3.02

가 4 STAI-SA 0 50 ± 6.40
 8 64.67 ± 12.60, 46.00 ± 10. (p=0.5071).
 18 , 0 8
 20.50 ± 3.02, 11.75 ± 2.75 . 6. 성기능에 미치는 영향
 가 가
 8 STAI-SA - 20.62 ± (N=179, 17.24 ± 4.48) 8
 12.77, - 19.50 ± 16.42 paired t - test (N=130, 14.85 ± 4.50) 2.41 ± 5.24
 (p=0.8728), paired t - test
 - 10.79 ± 6.48, - 8. (p=0.0001)(Table 2).

Table 2. Changes in depression, anxiety, sleep, sexual function, and quality of life in depressive patients with nefazodone treatment*

Variable**	Baseline	Week of study			
		week 1	week 2	week 4	week 8
HAM-D ¹⁾	N = 230 24.02 ± 5.88		N = 199 15.90 ± 6.82 [†]	N = 188 12.22 ± 6.55 [†]	N = 165 8.98 ± 5.51 [†]
BDI ¹⁾	N = 208 28.22 ± 10.12		N = 179 20.86 ± 9.66 [†]	N = 168 16.98 ± 9.98 [†]	N = 149 13.64 ± 9.21 [†]
STAI-SA ¹⁾	N = 208 63.14 ± 10.28	N = 188 57.11 ± 11.13 [‡]	N = 179 54.00 ± 10.82 [†]	N = 168 50.85 ± 11.39 [†]	N = 150 47.27 ± 11.46 [†]
HAM-D (9 + 10 + 11) ¹⁾	N = 230 5.59 ± 1.82		N = 199 3.60 ± 1.77 [†]	N = 188 2.88 ± 1.78 [†]	N = 165 2.09 ± 1.46 [†]
Weekly Sleep Q ¹⁾	N = 207 20.10 ± 4.76	N = 189 16.32 ± 5.29 [†]	N = 180 14.76 ± 5.74 [†]	N = 168 13.25 ± 5.43 [†]	N = 151 11.87 ± 5.71 [†]
HAM-D (4 + 5 + 6) ¹⁾	N = 230 3.68 ± 1.65		N = 199 2.25 ± 1.84 [†]	N = 188 1.62 ± 1.55 [†]	N = 165 1.10 ± 1.32 [†]
Weekly Sleep Q ²⁾ (1 - 5)	N = 207 14.83 ± 4.28	N = 189 11.50 ± 4.62 [†]	N = 180 10.18 ± 4.87 [†]	N = 168 8.96 ± 4.50 [†]	N = 151 7.91 ± 4.44 [†]
Weekly Sleep Q ³⁾ (6 + 7)	N = 207 5.27 ± 1.61	N = 189 4.82 ± 1.74 [‡]	N = 180 4.58 ± 1.80 [†]	N = 168 4.29 ± 1.83 [†]	N = 151 3.95 ± 2.06 [†]
Sexual Functioning Q	N = 179 17.24 ± 4.48				N = 130 14.85 ± 4.50 [†]
GHQ-QOL-12	N = 206 27.51 ± 6.95				N = 150 20.91 ± 7.46 [†]

* : Values represent Mean ± SD

** : HAM-D : Hamilton Depression Scale, BDI : Beck Depression Inventory, STAI-SA : Spielberger Trait Anxiety Inventory, HAM-D (9 + 10 + 11) : Items 9, 10, 11 of HAM-D, Weekly Sleep Q : Weekly Sleep Questionnaire, HAM-D (4 + 5 + 6) : Items 4, 5, 6 of HAM-D, Weekly Sleep Q (1 - 5) : Items 1, 2, 3, 4, 5 of Weekly Sleep Questionnaire, Weekly Sleep Q (6 + 7) : Items 6, 7 of Weekly Sleep Questionnaire, Sexual Functioning Q : Sexual Functioning Questionnaire, GHQ-QOL-12 : 12 items for quality of life in General Health Questionnaire

† : The values are significantly different compared to baseline (p = 0.0001)

‡ : The values are significantly different compared to baseline (p = 0.0002)

1) Significant difference (p = 0.0001) between week 2 & 4, 2 & 8 and 4 & 8

2) Significant difference (p = 0.009) between week 4 & 8, Significant difference (p = 0.0001) between week 2 & 1, 4 & 1, 8 & 1, 2 & 4, 2 & 8 and 4 & 8

3) Significant difference (p < 0.01) between week 4 & 1, 8 & 1, 8 & 2 and 8 & 4, No significant difference (p > 0.05) between week 2 & 1 and 2 & 4

Nefazodone

Table 3. Post-treatment satisfaction with nefazodone

Post-treatment satisfaction	Patient N (%)	Investigator N (%)
Very much dissatisfied	0 (0)	2 (1.1)
Very dissatisfied	4 (2.8)	3 (1.7)
Dissatisfied	8 (5.5)	8 (4.6)
Neither dissatisfied nor satisfied	26 (17.9)	33 (19.0)
Satisfied	43 (29.7)	45 (25.9)
Very satisfied	51 (35.2)	64 (36.8)
Very much satisfied	13 (9.0)	19 (10.9)

7. 삶의 질에 미치는 영향

(N=206, 27.51 ± 6.95)
 8 (N=150, 20.91 ± 7.46)
 6.86 ± 8.46 paired t - test
 (p=0.0001)

(Table 2).

8. 환자 및 의사만족도

가 73.9%, 73.6%
 (Table 3).

9. 이상반응

28.3%(65/230) 41.7%(96/230)
 Nefazodone 가 가
 nefazodone 가
 24.8%(57/230)
 35.2%(81/230)
 Nefazodone 1%
 11.7%(27/230), 3.0%(7/230),
 2.2%(5/230), 2.2%(5/230),
 2.2%(5/230), 1.7%(4/230), 1.7%
 (4/230), 0.9%(2/230), 0.9%(2/230)
 (fe - mur neck fracture),

가 0.4%(1/230)
 고 찰
 single open study
 nefazodone
 nefazo - done

가
 1980
 , MAOI, lithium
 noradrenergic serotonergic
 muscarinic, choli -
 nergic, H₁ - histaminergic, alpha₁ adrenergic

MAOI tyramine
 reversible MAO inhibitor(RIMA)

MAOI
 MAOI
 1980 fluvoxamine, fluoxetine, sertr -
 aline, paroxetine, citalopram SSRI
 가 MAOI

SSRI 가 가
 8)
 8) 가 ben -
 zodiazepine 가 9,10)
 Nefazodone SNRI SSRI
 Nefazodone 5HT₂ rece -
 ptor 5 - HT_{1A} 가 , 5 - HT_{1A} -

mediated neurotransmission 가 가 ,
serotonin 가 SSRI ,
SSRI 가
8) Nefazodone trazodone , , , , ,
1 - adrenergic receptor 2, 4, 8
Nefazodone 2 -adr - HAM - D , BDI
energetic, -adrenergic, 5-HT₂ receptors CGI 62.4%,
H₁ - histaminergic, muscarinic, cho - HAM - D 75.2% nefazodone
linergic, dopaminergic 19-21)
8) 21) nefazodone 491 503 mg/day 가
Nefazodone ,
가 11-14) 11-15) SSRI¹⁶⁻¹⁸⁾ double depr -
가 amitri - ession 가 nefazodone
ptyline¹⁹⁾ (50 200 mg/day) , ne - 가 ²²⁻²⁴⁾
fazodone 가 nefazodone
nefazodone 1 200 mg
nefazodone 300 STAI - SA HAM -
600 mg/day , D 가
²⁰⁾ 126 HAM - D
(85% 가 nefazodone
(melancholic)) 6
nefazodone 2 fluoxetine
²¹⁾ nefazodone imipramine 가 , nefazodone
1 가 ,
^{22,23)}
double - blind placebo - substitution nefazodone
131 . Feighiner ³²⁾ nefazodone
(17 - item HAM - D 18 , , , , , , , ,
) placebo 18.3% nefazodone 1.8%
²⁴⁾ Fluoxetine ¹⁸⁾
nefazodone , , , , , , , ,
sertraline double blind par - nefazodone
allel group nefazodone benzodiazepine 가
¹⁷⁾ 53.0% ,
nefazodone(200 300 mg/1day) 가 STAI - SA 가
pine benzodiazie -
가

Nefazodone

8 STAI - SA 가 가 75.2%(124/165) . ne - nefazodone nefazodone TCA SSRI 결 론 : nefazodone nefazodone Feighner ¹⁷⁾ nefazodone sertraline done 중심 단어 : Nefazodone nefazodone ser - traline

요 약

목 적 : Nefazodone

방 법 : 가 26 , 230 가 가 . DSM - IV , 14 가 가 . 가 CGI(Clinical Global Improvement), 17 - items Hamilton Depression Scale (HAM - D), Beck Depression Inventory(BDI), State and Trait Anxiety Inventory - State Anxiety(ST - AI - SA), (weekly sleep questionnaire), 가 가 , . 1 346 mg 8 . 가 , 1, 2, 4, 8 . 가 .

결 과 : 8 CGI 가 62.4%(103/165) , HAM - D(17 items) 50%

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