

Clozapine으로 치료 중인 만성 정신분열병 환자의 수면양상

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Sleep Patterns in Chronic Schizophrenic Patients Treated with Clozapine

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ABSTRACT

Objectives : Daytime drowsiness or sedation and changes in night sleep are commonly seen in patients treated with clozapine. There is, however, very limited information on their degree and nature during the course of treatment. The purpose of this study was to understand the sleep patterns in chronic schizophrenic patients with clozapine treatment over a period of 24 weeks.

Method : The sleep pattern was evaluated using a set of 5-point scale questionnaire, to record subjective impressions of the night sleep induction, maintenance and quality, and daytime drowsiness and fatigue. In addition, unusual experiences associated with night sleep were recorded. The sleep questionnaire was repeatedly administered at baseline and at 1, 2, 4, 8, 12 and 24 weeks of drug treatment. At present, data on 12 patients has been collected.

Results : All the components of night sleep were significantly improved in the 1st through the 12th week after treatment with clozapine. Daytime drowsiness was significantly higher in the 1st to the 2nd week after the treatment and fatigue was also significantly higher in the 1st to the 4th week after the treatment. Eight patients experienced noticeable increases in salivation during night sleep, and of these, one also reported frequent nocturnal urination and even enuresis. However, all these adverse factors did not affect the major sleep patterns.

Conclusions : These findings suggest that the beneficial effects of clozapine on night sleep might last much longer than the undesirable effect of daytime drowsiness and fatigue. In other words, tolerance of the hypnotic action of clozapine might develop late and tolerance of the daytime drowsiness and fatigue might be evident earlier.

KEY WORDS : Clozapine · Chronic schizophrenia · Sleep.

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8

(1998).

) (062) 220 - 6146,) (062) 225 - 2351

가

Clozapine

clozapine

가

(Angst 1971 ; Ca-

sey 1989 ; Kane 1988 ; Meltzer 1989).

연구대상 및 방법

D₂ D₁ D₄

(5HT₂, 5HT_{1c}, 5HT₃),

1. 연구대상

(H₁), (), (M₁)

(Baldessarini Frankenburg 1991 ; Coward 1992 ;

clozapine 1)

Fitton Heel 1990 ; Kane 1988 ; Meltzer 1992).

clozapine

, 2) 4 (DSM

(1989) (H₁) () Liberman -)(APA 1994)

3) 2가 2

가

Clozapine

가 , 4)

18 65

9 43%(Lieberman

, 5) clozapine

1989 ; Kane 1988 ; Dev Krupp 1995), 19

clozapine 3

83%(1993a ; 1993b ; 1995)

1) , , 2)

가

, 3)

(Lieberman 1989 ; Marinkovic

, 4) 가 5000/mm³

1994 ; Chatterton 1995)

가 2500/mm³ , 5)

(1995)

, 6) , ,

1 3 52% 12

8) , 7)

81%

, 9)

, 10) 4

가 , 12)

(polysomnogram : PSG) clozapine

8

depot

가 cl-

ozapine 25mg 3 (Touyz 1977)

2. 연구방법

12.5mg 15 (Touyz 1978) clo-

1) 약물투여

zapine 가

clozapine

clozapine (Braun - Scharm Martinius 1991 ;

Tandon 1995 ; Wetter 1996 ; Heinz - Selch 1997)

(Weiden 1997), 3

REM , non - REM

가 ,

가

lorazepam

, clozapine

Clozapine

Clozapine

가

clozapine

clozapine 가

12.5mg

가

2 3 12.5 25mg

가

200mg, 7, 100mg, 14, 가, 0 (,)
 one sample t - test . CGI - SI
 50mg, paired t - test
 600mg, 200mg, 1, clozapine,
 1/3, 2/3) 0.05
 Clozapine 24 가 SPSS 8.0 for windows

lorazepam, 가, amit -
 riptyline 10 25mg,
 valproate

결 과

2) 평가 및 조사내용
 1, 2, 4, 8, 12, 24
 가
 (1)
 1 (- , 2
) (-) . 12
 가 가 가 (-) 1, clozapine 2
 , 0 () 4
 , 가
 (2)
 1 (-)
) (-)
 가 가 가 . -2 +2
 5 , 0 ()
 , 가
 (3)
 1 clozapine
 . 1 clozapine
 (4) (clinical global impression of severity
 of illness : CGI - SI)
) 7 () 7 가 1 (

1. 연구대상의 인구학적 및 임상적 특성
 16 (8 ,
 8) , 4 (1 ,
 3) 24 가 가
 12 . clozapine
 1 , 1 , 1
 2
 . 12
 1 , clozapine 2
 4
 24
 2. 약물투여 및 CGI-SI의 변화
 Clozapine CGI - SI 3
 Clozapine 1 68.75mg ,
 12 260.42mg , 24
 236.36mg . CGI - SI cloza -
 pine 5.71 ,
 24 2.92 . Paired t - test
 CGI - SI 2 , 4 , 8 , 12
 24
 clozapine 4
 clozapine
 8 (baseline week) lorazepam 0.5
 3mg/day . Clozapine 1
 clozapine 8 clozapine
 3 가 1 3 lorazepam 0.5 2
 mg/day . 2 4 8
 5 1 1 2 lorazepam 0.5 1mg/day
 . 1 lorazepam 0.5 1mg/day
 . Lorazepam ,
 . Haloperidol 3

3. 자료분석

가

3. 수면양상의 변화

(1.5 3.0mg) clozapine
 3 . Benztropine 2 5
 1 2mg . Amitriptyline , , 1, 2, 4,
 8 1 , 12 24 2 8, 12 .
 10 25mg . 12 2 24 .
 paroxetine 40 50mg . 8 ,
 clozapine 450mg 1 24 val - 1
 proate 400mg . , 가 .

Table 1. Demographic and clinical characteristics of patients

No./sex/age (years)	Age at onset (years)	Number of previous hospitalization	Schizophrenic subtypes (DSM-)
1/F/31	15	3	Paranoid
2/F/43	20	5	Paranoid
3/M/26	24	1	Paranoid
4/F/30	22	5	Paranoid
5/F/36	19	7	Undifferentiated
6/M/27	21	2	Undifferentiated
7/M/31	23	0	Undifferentiated
8/M/32	24	0	Residual
9/F/34	19	0	Disorganized
10/F/26	23	3	Paranoid
11/M/33	29	3	Paranoid
12/M/44	41	2	Undifferentiated

Table 2. Clinical conditions and major reasons for clozapine trial

Patient No.
1 - 6. Having been treated with two or more conventional neuroleptics, showing no favourable response to them.
7, 8. Having been treated with conventional neuroleptics, which showed intolerance to them because of severe adverse effects (mainly extrapyramidal symptoms).
9 - 12. Exacerbation of psychotic symptoms in the drug-free state, having previous history of an unfavourable response and/or intolerance to the conventional neuroleptics.

Table 3. Time course of clozapine dosage and CGI-SI scores

	Weeks						
	Baseline	1	2	4	8	12	24
Clozapine doses (mg/day) ^a							
Mean(SD)	0	68.75(27.95)	137.50(44.27)	222.92(87.55)	260.42(118.92)	260.42(113.05)	236.36(119.04)
Range	0	37.5 - 125	62.5 - 200	125 - 400	125 - 450	125 - 450	75 - 500
CGI-SI scores ^b							
Mean(SD)	5.71(0.58)	4.83(0.94)	4.42(0.90)**	4.00(1.04)**	3.67(0.98)***	3.42(1.00)***	2.92(1.00)***
Range	4 - 6	4 - 6	3 - 6	3 - 6	2 - 5	2 - 5	2 - 6

^aA dose up to 200mg per day was administered as single dose at bedtime. A dose of more than 200mg per day was divided into two doses and the larger portion (approximately two of the third) was administered at bedtime with the smaller one in the morning.

^bCGI-SI denotes a clinical global impression for severity of illness, and is rated by the following criteria : 1 not ill, 2 very mild, 3 mild, 4 moderate, 5 moderately severe, 6 severe and 7 extremely severe.

, *Significant difference from baseline at p<01, p<001, respectively, by paired t-test.

Table 4. Number(%) of patients receiving lorazepam and/or other psychotropic drugs concomitantly^a

Drug class	Weeks						
	Baseline	1	2	4	8	12	24
Lorazepam	8(67)	11(92)	8(67)	5(42)	1(8)	1(8)	1(8)
Haloperidol	3(25)	1(8)	-	-	-	-	1(8)
Benztropine	2(17)	-	-	-	-	-	-
Amitriptyline	-	-	-	-	1(8)	2(17)	2(17)
Paroxetine	-	-	-	-	-	2(17)	2(17)
Valproate	-	-	-	-	-	-	1(8)

^aA patient may receive more than one class of drug at a particular point of time. Eleven patients received lorazepam and/or other psychotropic drugs at least once or more over the baseline and the following 24 weeks of treatment with clozapine.

Table 5. Sleep patterns^a

Items ^b	Weeks						
	Baseline	1	2	4	8	12	24
Night sleep							
Sleep induction	-0.50(1.38)	1.58(0.67)***	1.08(1.00)**	0.92(1.16)*	0.92(1.44)*	0.83(0.94)**	-0.25(1.14)
Sleep maintenance	0.25(1.29)	1.17(1.03)**	1.25(1.14)**	1.00(1.04)**	1.08(0.90)**	1.00(0.60)***	0.08(1.08)
Sleep quality	-0.33(1.23)	1.17(0.72)***	0.83(0.72)**	0.50(0.52)**	0.75(0.75)**	0.50(0.67)*	0.58(1.08)
Daytime status							
Drowsiness	-0.17(1.19)	1.00(0.74)***	0.83(1.19)*	0.42(1.16)	0.00(0.85)	-0.17(0.72)	-0.42(0.67)
Fatigue	0.00(1.41)	1.25(0.75)***	0.92(0.67)***	0.75(0.75)**	0.08(1.08)	0.00(0.85)	-0.08(0.90)

^aData are means(standard deviations) of scores from self-rating scales for sleep patterns.

^bFor individual items, the direction and magnitude of the response was graded on a positive-negative continuum, using a 5 point scale from +2 (very positive or satisfactory) through zero (equally good and bad or not remarkable, i.e. the ordinary level) to -2(very negative or unsatisfactory).

*, **, ***Significant differences from the zero state of the each week at p<0.05, p<0.01, p<0.001, respectively, by one-sample t-test.

clozapine 2 4 apine lorazepam 4

clozapine 가 clozapine lorazepam 4 12

가 , 가 , clozapine clozapine

가 , 가 , clozapine 가 (20 30%) (Baldessarini Frankenburg 1991 ; 가 8

, (1995) , clozapine Fitton Heel 1990). 가 ,

12 81% . clozapine 1 가 . Cloz -

apine , 가 (Young 1998).

clozapine 가 가

Lorazepam clozapine 4 , , 가 .

clozapine 가 clozapine 가

가 , cloz - Clozapine ephedrine(Fu -

ller 1996), desmopressin(Katz Rosenthal 1994 ; Spi-
gset 1996 ; Steingard 1994) oxybutynin(Frankenburg
1996) clozapine
(Aronowitz 1995). clozapine
clozapine
가
1 desmopressin

Clozapine amitriptyline(Copp 1991),
benztropine(Bourgeois 1991)
(M₁) pirenzepine(Fritze Elliger
1995), 2- clonidine(Grabowski 1992)
가
Clozapine

Druss Mazure 1993),
Hinze - Selch (1995) clozapine
1
REM 가
가

(Lewander 1994). 가
(H₁), (α₁), (M₁), (D₁)
(Lader 1989 ; Ongini Longo 1989 ;
Martin 1993). ()
(Lewander 1994 ;
Peacock Gerlash 1996) D₂

clozapine haloperidol
clozapine
Factor Br -

own(1992) (1999)
clozapine
clozapine

가
Clozapine
clozapine

PSG
중심 단어 : Clozapine

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