

# 만성 정신분열증 환자에서 Clozapine의 치료반응과 혈장 Homovanillic Acid 및 5-Hydroxyindoleacetic Acid 농도와의 관계

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## Relationship between Clozapine-Induced Therapeutic Responses and Plasma Homovanillic Acid and 5-Hydroxyindoleacetic Acid Levels in Patients with Chronic Schizophrenia

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### ABSTRACT

This study was done to examine changes of plasma homovanillic acid(HVA), 5-hydroxyindoleacetic acid(5-HIAA), and HVA/5-HIAA ratio during an 8-week clozapine trial and to investigate the relationship between the plasma monoamine metabolites and treatment responses.

Twenty-seven chronic schizophrenic patients were treated for 8 weeks with clozapine. The psychopathology was assessed at baseline just clozapine trial and then every 2 weeks until the end of 8-week clozapine treatment using the Positive and Negative Syndrome Scale(PANSS) and the Clinical Global Impression scale(CGI). The plasma HVA and 5-HIAA levels were measured also biweekly using high performance liquid chromatography with electrochemical detection method.

Plasma HVA and 5-HIAA levels were significantly decreased during a 8-week clozapine treatment, although plasma HVA/5-HIAA ratio showed no significant change. The changes of plasma HVA levels were in significant correlations with the changes of PANSS positive scores, of general psychopathology scores, and changes of total scores. The changes of plasma 5-HIAA levels were in significant correlations with the changes of PANSS negative scores. But the changes of plasma HVA/5-HIAA ratio had no significant correlation with any PANSS subscale score changes. 48% of the patients treated with clozapine was categorized as responders, who showed at least a 20% decrease in PANSS total score and a CGI severity score of mildly ill or less (3) at the end point of the study. The baseline plasma HVA levels and HVA/5-HIAA ratio were significantly higher in responders(N=13) than in nonresponders(N=14). But no significant difference in baseline levels of plasma 5-HIAA was found between responders and nonresponders. At the end point of the study, there was significant difference in the change of plasma HVA between responders(40.3% decrement) and nonresponders(3.1% increment). But no significant differences in the change of plasma 5-HIAA and the change of plasma HVA/5-HIAA ratio between responders and nonresponders were observed.

These results suggest that the antipsychotic effect of clozapine on positive symptoms may be associated with dopaminergic blocking activity, and that on negative symptoms may be associated with serotonergic blocking activity. The baseline plasma HVA levels and the change of HVA levels from baseline may be useful predictors of treatment response with clozapine.

**KEY WORDS** : Clozapine · Therapeutic response · Plasma HVA · Plasma 5-HIAA · Chronic schizophrenia.

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서론

1950 chlorpromazine 가 가 paradigms (An - den 1970 ; Carlsson Lindqvist 1963) D<sub>2</sub> Clozapine dibenzodiazepine 가 (atypical) clozapine 가 (Creese 1976 ; Seeman 1975) (overactivity) (Juul - Povlsen 1985 ; Meltzer 1989). 가 clozapine 가 ( 1993 ; Kane 1988 ; Meltzer 1989) . Clozapine chlorpromazine haloperidol catalepsy , prototype (Meltzer 1989). clozapine homovanillic acid( HVA) (Bowers Heninger 1981 ; Post 1975 ; Sharma 1989) 가 HVA 가 (Berger 1980 ; Rimon 1971), (Sharma 1989). 1980 가 가 (typical antipsychotic drugs) 1993). 가 (Meltzer 1989 ; Szymanski 1993). 가 HVA 가 가 (Davidson 1987 ; Davila 1988), HVA/5 - HIAA(5 - hydroxyindoleacetic acid) HVA/ MHPG 가 (Bowers 1989 ; Chang 1990 ; Davidson 1991 ; Pickar 1986), HVA (positive) (Pickar 1990) 가 (Hsiao 1993 ; Szyman - ski 1993). Hsiao (1993) HVA 5 - HIAA HVA/5 - HIAA (Crow 1979 ; Haberland Hetey 1987) (Widerlov 1988) D<sub>2</sub> 20 30% (Davis 1980 ; Kane 1989), 가 (Andreasen Olsen 1982) 가 가 가

clozapine HVA 8  
 5 - HIAA HVA/5 - HIAA  
 가 가 , ,  
 HIAA HVA/5 - HIAA  
 가 가 , clozapine  
 , HVA , 5 - HIAA  
 HVA/5 - HIAA , clozapine 8  
 HVA , 5 - HIAA ,  
 HVA/5 - HIAA 가 가  
 가 clozapine  
 가

apine 가 2  
 가 가 .  
 PANSS 가  
 “ Positive and Negative Sy -  
 ndrome Scale”( PANSS ) 가 . PANSS  
 가 Kay (1987)  
 Kay PANSS  
 video tape  
 가 가 (inter - rater reliability)가 0.8  
 CGI 가  
 CGI(Clinical Global Impression ; Guy 1976)  
 가

**대상 및 방법**

**1. 연구대상**

, 1) , 2)  
 18 45 , 3) 2  
 , 4) DSM - III - R(American Psychiatric Associa -  
 tion 1987)  
 , 1) , , 2)  
 가 , 3) 가 5000/mm<sup>3</sup>  
 가 2500/mm<sup>3</sup> , 4)  
 , 5)  
 , 6) , 7)  
 , 8) (8 ) depot

**2. 연구방법**

**1) 치료약물 투여**

clozapine  
 가 가  
 clozapine . Clozapine  
 25mg 1 2 50mg bid 2 ,  
 75mg tid 2 , 100mg tid 2 ,  
 ( 2 )  
 8

**2) 임상증상의 평가**

가 1 cloz -

Kane (1988)

PANSS 가 20%  
 CGI 가 (mild)

**3) 혈장 HVA 및 5-HIAA 농도측정**

tryptophan  
 2 ,  
 8 ( )  
 (15cc) EDTA - tube  
 - 70  
 HVA 5 - HIAA Seegal (1986)  
 (electrochemical deceptor)가  
 (high pressure liquid chromato -  
 graphy ; HPLC)  
 HPLC  
 HPLC Waters (Waters Associates, Milford, MA,  
 USA) model 510 pump, model 717 plus autosampler,  
 model M460 amperometric detector, Temperature control  
 module(TCM)  
 Bus LAC/E card Millenium™ 2010 Chr -  
 omatography Manager software가 IBM PC  
 column Shiseido (Tokyo, Japan) 250  
 × 4.6mm I.D., 5 μm particle size, reversed phase C<sub>18</sub> colu -  
 mn column temperature 30  
 sodium phosphate  
 (monobasic), citric acid, 1 - outane sulfonic acid(sodium salt),  
 isovanillic acid, EDTA(ethylene diamine tetra - acetic acid)  
 Sigma (St. Louis, MO, USA), methyl alcohol, tetrahy -

drofuran Burdick and Jackson (Muskegon, MI, USA), lyophilized serum Biorad (Segrate, Italy), perchloric acid Wako Pure Chemical (Osaka, Japan), phosphoric acid E. Merck (Darmstadt, Germany), Milli-A water system(Millippre Corp, Bedford, MA, USA)

3 Sigma HVA  
5 - HIAA , Stock 2  
1mg/ml - 70

가

HVA 5 - HIAA

HVA 5 - HIAA perchloric acid

1ml sample 4

, internal standard isovanillic acid 100

vortex mixing , 100 µl perchloric acid

vortex mixing 30 4

13,000×g 15 4

40 µl HPLC

system

0.08M sodium phosphate, 0.01M citric

acid, 5mM 1 - Octane sulfonic acid, 0.1mM EDTA가

phosphate buffer 945ml 50ml methyl alcohol 5ml

tetrahydrofuran 1L pH 3.1

0.22 µm pore size filter ultra - son -

icator 30 1.2ml/

min , amperometric detector +

850mV vs Ag/AgCl electrode potential 1.5×1nA

HVA, 5 - HIAA

int -

ernal standard가 가 drug free serum

(ratio)

#### 4) 자료분석

Clozapine PANSS , HVA ,  
5 - HIAA , 5 - HIAA , HVA/5 - HIAA

가 Bonferroni's t - test

. Clozapine HVA ,

5 - HIAA , HVA/5 - HIAA

PANSS , PANSS

, PANSS

Pearson's correlation test

(%) [( - )/  
× 100]

, (PANSS  
, PANSS , PANSS , CGI ),

( HVA , 5 - HIAA

, HVA/5 - HIAA ) Student's t - test

Clozapine 8

Student's t - test

SPSS/PC<sup>+</sup>(ver 5.0)

0.05

## 결 과

### 1. 인구사회학적 자료

29 clozapine 2

1 1

27 22

, 5 27.3±6.6 .

18.7±4.4 , 8.6±5.6 . DSM -

III - R 18 (68%) 가

4 , 3 , 1

1 (Table 1).

### 2. Clozapine 치료에 따른 혈장 HVA 농도, 5-HIAA 농도 및 HVA/5-HIAA 농도비의 변화

Clozapine HVA 5 - HIAA  
가

, HVA/5 - HIAA 가 . Bo -

nferroni's t - test HVA

8 가 ,

5 - HIAA 6 , 8

**Table 1.** Demographic data and schizophrenic subtypes(N=27)

| Variables                  | Value      |
|----------------------------|------------|
| Age(years)                 | 27.3± 6.6  |
| Sex(frequency)             |            |
| Male                       | 22         |
| Female                     | 5          |
| Onset age(years)           | 18.7± 4.4  |
| Duration of illness(years) | 8.6± 5.6   |
| Number of hospitalization  | 3.9± 2.8   |
| Weight(kg)                 | 66.8± 11.4 |
| Subtype of schizophrenia   |            |
| Undifferentiated type      | 18         |
| Residual type              | 4          |
| Paranoid type              | 3          |
| Catatonic type             | 1          |
| Disorganized type          | 1          |

3. Clozapine 치료에 따른 PANSS 하위척도점수의 변화

Clozapine PANSS 가 (Table 2).  
 Bonferroni's t-test  
 PANSS 2 8 가  
 PANSS 8 가 (Table 3).  
 4. Clozapine 치료에 따른 혈장 대사물의 변화율과 치료반응과의 상관관계  
 Clozapine 8 PANSS  
 HVA 5 - HIAA HVA/  
 5 - HIAA HVA  
 PANSS (r=0.587, p=0.002),  
 PANSS (r=0.539, p=0.004), PA -  
 NSS (r=0.648, p<0.001)

**Table 2.** Changes of plasma monoamine metabolite levels during an 8-week clozapine treatment in chronic schizophrenia

|               | Duration of clozapine treatment(week) |                |                |                             |                             | p <sup>a</sup> |
|---------------|---------------------------------------|----------------|----------------|-----------------------------|-----------------------------|----------------|
|               | Baseline                              | 2nd week       | 4th week       | 6th week                    | 8th week                    |                |
| HVA(ng/ml)    | 10.37<br>(2.54)                       | 8.71<br>(2.53) | 8.88<br>(2.15) | 8.96<br>(3.41)              | 7.45<br>(2.64) <sup>b</sup> | 0.018          |
| 5-HIAA(ng/ml) | 6.36<br>(1.62)                        | 5.84<br>(1.54) | 5.37<br>(1.31) | 4.57<br>(1.81) <sup>b</sup> | 4.58<br>(1.87) <sup>b</sup> | 0.005          |
| HVA/5-HIAA    | 1.75<br>(0.73)                        | 1.52<br>(0.57) | 1.75<br>(0.50) | 2.13<br>(1.17)              | 2.10<br>(2.62)              | 0.225          |

Each value represents mean(standard deviation)

<sup>a</sup> : Repeated measures one-way ANOVA

<sup>b</sup> : p<0.05 compared to baseline by post-hoc Bonferroni's t-test

**Table 3.** Changes of PANSS scores during an 8-week clozapine treatment in chronic schizophrenia

|                       | Duration of clozapine treatment(week) |                   |                   |                  |                  |
|-----------------------|---------------------------------------|-------------------|-------------------|------------------|------------------|
|                       | Baseline                              | 2nd week          | 4th week          | 6th week         | 8th week         |
| PANSS scores          |                                       |                   |                   |                  |                  |
| Positive <sup>a</sup> | 26.26<br>( 6.65)                      | 21.22<br>( 7.44)  | 19.15<br>( 5.70)  | 17.74<br>( 4.70) | 17.15<br>( 4.56) |
| Negative <sup>b</sup> | 36.19<br>( 7.71)                      | 33.59<br>( 7.88)  | 31.19<br>(11.64)  | 27.26<br>( 6.65) | 27.37<br>( 6.18) |
| General <sup>a</sup>  | 65.52<br>(10.04)                      | 56.41<br>( 1.54)  | 50.67<br>( 9.10)  | 45.11<br>( 8.50) | 44.26<br>( 7.25) |
| Total <sup>a</sup>    | 127.96<br>(20.11)                     | 111.22<br>(21.58) | 101.00<br>(22.19) | 90.11<br>(17.13) | 88.78<br>(14.18) |

Each value represents mean(standard deviation)

<sup>a</sup> : p<0.05 by repeated measures one-way ANOVA and p<0.05 compared to baseline from 2nd week through 8th week by post-hoc Bonferroni's t-test

<sup>b</sup> : p<0.05 by repeated measures one-way ANOVA and p<0.05 compared to baseline from 4th week through 8th week by post-hoc Bonferroni's t-test

(Table 4). 5 - HIAA PAN -  
 SS (r=0.659, p<  
 0.001)(Table 4).

Clozapine 8 HVA 5 - HIAA  
 HVA/5 - HIAA PA -  
 NSS  
 HVA PANSS (r=0.  
 394, p=0.046), (r=0.713, p<0.001), PA -  
 NSS  
 (r=0.516, p=0.007)  
 5 - HIAA PANSS  
 (r=0.481, p=0.013), (r=  
 0.644, p<0.001) HVA/5 -  
 HIAA PANSS  
 (Table 5).

5. 치료반응군과 치료비반응군 간의 clozapine 투여전 인구  
 사회학적 자료 및 기준 임상변수의 비교

Clozapine 8 13 (48%),  
 14 (52%) Clozapine  
 가  
 (5.2 ± 3.2 )  
 (2.5 ± 1.3 ) (p = 0.008)(Table 6).  
 22 11 5 2  
 clo -  
 zapine PANSS  
 가 (Table 6).

6. 치료반응군과 치료비반응군 간의 clozapine 투여전 기준  
 대사물 농도와 clozapine 투여 8주 후 대사물 농도 변화  
 율의 비교

Clozapine  
 HVA HVA/5 - HIAA  
 5 - HIAA

**Table 4.** Correlation between the percentile changes of plasma monoamine metabolites levels and the percentile change of PANSS subscale scores from baseline at the end of study

|              | HVA                       | 5-HIAA                    | HVA/5-HIAA    |
|--------------|---------------------------|---------------------------|---------------|
| PANSS scores |                           |                           |               |
| Positive     | 0.587(0.002) <sup>a</sup> | -0.029(0.889)             | -0.052(0.805) |
| Negative     | 0.372(0.061)              | 0.659(0.000) <sup>a</sup> | 0.135(0.520)  |
| General      | 0.539(0.004) <sup>a</sup> | -0.074(0.721)             | -0.331(0.106) |
| Total        | 0.647(0.000) <sup>a</sup> | 0.148(0.472)              | -0.166(0.427) |

Each value represents correlation coefficient(P value)

<sup>a</sup> : p<0.05 by pearson's correlation test

**Table 5.** Correlation between the percentile changes of plasma monoamine metabolites levels and the percentile change of PANSS each item scores from baseline at the end of study

|  | HVA                     | 5-HIAA                  | HVA/5-HIAA  |
|--|-------------------------|-------------------------|-------------|
| Positive subscale                            |                         |                         |             |
| Delusion                                     | 0.3940.046 <sup>a</sup> | 0.0530.796              | 0.0520.806  |
| Conceptual disorganization                   | 0.2990.138              | -0.3590.071             | -0.1580.450 |
| Hallucinatory behavior                       | 0.7130.000 <sup>a</sup> | 0.0170.934              | -0.1930.355 |
| Excitement                                   | 0.2010.324              | 0.2460.226              | 0.1750.040  |
| Grandiosity                                  | 0.1170.570              | -0.0360.862             | 0.1640.433  |
| Suspiciousness/persecution                   | 0.2960.142              | 0.0150.940              | 0.1560.458  |
| Hostility                                    | 0.2560.206              | 0.0790.701              | -0.1430.495 |
| Negative subscale                            |                         |                         |             |
| Blunted affect                               | 0.3320.098              | 0.4810.013 <sup>a</sup> | 0.2400.249  |
| Emotional withdrawal                         | 0.0920.654              | 0.1430.487              | -0.0300.887 |
| Poor rapport                                 | 0.0850.680              | 0.6440.000 <sup>a</sup> | 0.1670.425  |
| Passive/apathetic social withdrawal          | 0.3480.082              | 0.3070.128              | 0.1500.475  |
| Difficulty in abstract thinking              | -0.0260.900             | -0.1730.398             | -0.2700.192 |
| Lack of spontaneity and flow of conversation | 0.5160.007 <sup>a</sup> | 0.2830.162              | -0.2810.174 |
| Stereotyped thinking                         | 0.3860.052              | 0.3560.075              | 0.0750.723  |

Each value represents correlation coefficient (P value)  
<sup>a</sup> : p < 0.05 by Pearson's correlation test

**Table 6.** Comparison between responders and non-responders in demographic data and baseline clinical assessment scores

| Variables                           | Responders (N=13) | Non-responders (N=14) | p <sup>a</sup> |
|-------------------------------------|-------------------|-----------------------|----------------|
| Demographic data                    |                   |                       |                |
| Age (years)                         | 26.2 ± 6.4        | 28.4 ± 6.8            | 0.413          |
| Sex (frequency)                     |                   |                       | -              |
| Male                                | 11                | 11                    |                |
| Female                              | 2                 | 3                     |                |
| Onset age (years)                   | 19.7 ± 5.0        | 17.9 ± 3.8            | 0.288          |
| Duration of illness (years)         | 6.5 ± 5.7         | 10.5 ± 4.8            | 0.062          |
| No. of hospitalization              | 2.5 ± 1.3         | 5.2 ± 3.2             | 0.008          |
| Baseline clinical assessment scores |                   |                       |                |
| PANSS positive                      | 35.0 ± 8.6        | 38.1 ± 6.2            | 0.284          |
| PANSS negative                      | 27.6 ± 6.1        | 25.0 ± 7.1            | 0.317          |
| PANSS total                         | 128.6 ± 18.2      | 128.2 ± 22.0          | 0.959          |
| CGI severity                        | 6.2 ± 1.0         | 6.2 ± 1.1             | 0.879          |

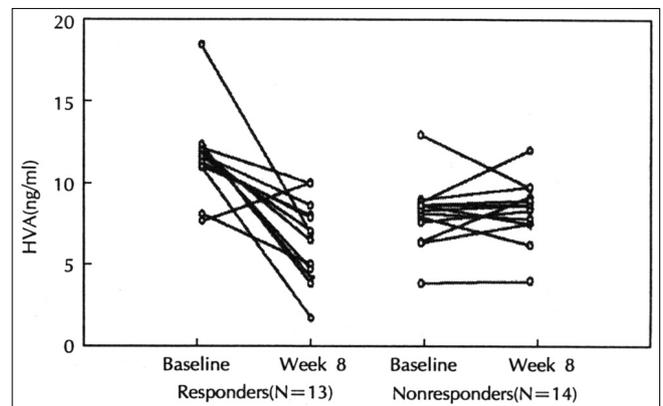
Each value represents mean ± S.D. of frequency  
<sup>a</sup> : p value by Student's t-test

가 (Table 7).  
 8 HVA 가 40.3% ,  
 HVA 가 3.1% 가  
 (Table 7, Fig. 1). 5 - HIAA  
 (16.5% ) (11.9% )

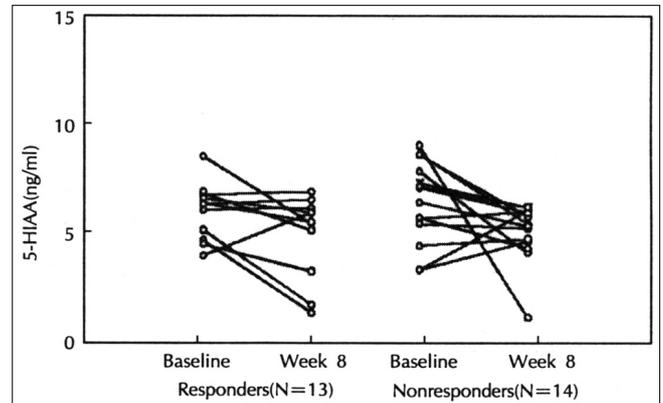
**Table 7.** Comparison between responders and non-responders in baseline plasma monoamine metabolites levels and the percentile change of monoamine metabolites levels

| Variables                   | Responders  | Non-responders | p <sup>a</sup> |
|-----------------------------|-------------|----------------|----------------|
| Baseline metabolites levels |             |                |                |
| HVA level (ng/ml)           | 11.7 ± 2.5  | 8.4 ± 2.1      | <0.001         |
| 5-HIAA level (ng/ml)        | 6.1 ± 1.3   | 6.6 ± 1.9      | 0.423          |
| HVA/5-HIAA                  | 2.0 ± 0.5   | 1.4 ± 0.7      | 0.037          |
| 8 monoamine metabolites     |             |                |                |
| HVA                         | 40.3 ± 28.8 | 3.1 ± 19.1     | <0.001         |
| 5-HIAA                      | 16.5 ± 34.7 | 11.9 ± 39.2    | 0.755          |
| HVA/5-HIAA                  | 22.7 ± 33.0 | -70.9 ± 85.5   | 0.099          |

Each value represents mean ± S.D.  
<sup>a</sup> : p value by Student's t-test



**Fig. 1.** Mean plasma homovanillic acid at baseline and at end of study (week 8) for responders and nonresponders.



**Fig. 2.** Mean plasma 5-HIAA at baseline and at end of study (week 8) for responders and nonresponders.

가 (Table 7, Fig. 2). HVA/5 - HIAA

가

(Table 7).

고 찰

clozapine, clozapine 38

. Clozapine 8 PANSS 가 20% 63% D<sub>2</sub> . Clozapine  
 CGI 가 (mild) D<sub>1</sub> D<sub>2</sub>  
 27 13 (48.1%) D<sub>1</sub>

30 50% clozapine D<sub>2</sub> D<sub>4</sub>  
 (Kane 1988 ; Lindström 1988 ; Na-ber 1989 ; Small 1987) (Van Tol 1991).  
 Clozapine HVA 5 - HIAA D<sub>2</sub> HVA 가  
 HVA 가 (Meltzer 1989 ; Pickar 1992 ; Potter 1989) HVA D<sub>2</sub> D<sub>1</sub>  
 HVA, 5 - HIAA가 가 HVA, 5 - HIAA D<sub>4</sub> .  
 가 가 HVA, 5 - HIAA가 가 5 - HIAA  
 가 가 가 (Meltzer 1989), Nordström (1993)  
 가 가 가 PET colapine 5 - HT  
 가 가 가 HT HT 5 - HT  
 HVA 5 - HIAA  
 (Bacopoulos 1979 ; Kendler Davis 1984) 5 - HIAA  
 uine 가 debrisq - ( 1995 ; Alfredsson  
 HVA Wiesel 1989) 5 - HIAA  
 (Massemd 1993) HVA (Degrell Nagy 1990) ,  
 HVA 5 - HIAA  
 HVA (Kahn Davidson 1993) 가 clozapine, risperidone - (se-  
 가 가 가 rotonin - dopamine antagonists ; SDAs)  
 Haloperidol, fluphenazine HVA 가 HVA/5 - HIAA 가  
 (Bowers 1989 ; Pickar 1986) cloza- (Pickar 1992 ; Szymanski  
 pine HVA 1993), haloperidol (Hsiao  
 HVA/5 - HIAA 1993)  
 HVA 가 HVA, 5 -  
 (Bowers 1984 ; Chang 1988) HIAA HVA/5 - HIAA clozapine  
 clozapine HVA 가 clozapine  
 가  
 clozapine (positron emi-  
 sion tomography ; PET) (Farde 1992) 가 가  
 70 80% D<sub>2</sub> 가 (Hsiao 1987). 가

(HVA, 5-HIAA MHPG) PANSS, HVA  
 (bala- 5-HIAA)  
 nce) HVA/5-HIAA HVA/MHPG  
 가  
 가 HVA PANSS  
 (Hsiao 1993).  
 HVA/5-HIAA가  
 (Lieberman 1994),  
 HVA/5-HIAA 가 clozapine  
 가 HVA/5-HI-  
 AA 가 HVA/5-HIAA  
 가 가 가  
 HVA/5-HIAA HVA/5-HIAA PA-  
 가 가 NSS, CGI 가  
 가 PANSS  
 가 clozapine  
 가  
 1980 HVA  
 HVA/5-HIAA 가 5-  
 가 (Andreasen Olsen 1982 ; Crow HIAA 가  
 1980). clozapine 8  
 HVA 가 5-  
 (delusion), (hallucination), HIAA HVA/5-HIAA 가  
 (bizzar, agitated behavior), HVA 가  
 (conceptual disorganization) (productive)  
 (blunted affect), HVA 가 clozapine  
 (poor contents of speech and thought), 5-HI-  
 (apathy), (anhedonia), (blocking), AA 가  
 (lack of motivation), (social withdrawal),  
 (cognitive defect) (deficit)  
 clozapine HVA/5-HIAA  
 가 가 가 HVA/5-HIAA가  
 (Crow 1980 ; Johnstone 1978 ; Meltzer (Pickar 1992 ; Szymanski 1993)  
 1986). Clozapine (Kane clozapine HVA/5-HIAA  
 1988 ; Meltzer 1989) 가 HVA가  
 HVA PANSS  
 , 5-HIAA PANSS  
 cloz- 가 5-HT 가 5-HIAA  
 apine

clozapine 가 . Clozapine 8 HVA  
 가 40.3% , HVA 가 3.  
 clozapine 1% 가 . Clozapine  
 HVA HVA/5 - HIAA 8 5 - HIAA HVA/5 - HIAA  
 가 , 가  
 HVA/5 - HIAA 가  
 가 HVA/5 - HIAA 가  
 가  
 요 약  
 27  
 clozapine 8  
 (PANSS CGI ) ( HVA ,  
 5 - HIAA HVA/5 - HIAA )  
 , clozapine  
 clozapine 8  
 가 clozapine  
 가 가  
 , 5 - HIAA 가 , HVA/  
 5 - HIAA 가 . HVA/  
 clozapine 8 HVA , 5 - HIAA  
 , HVA/5 - HIAA 8  
 (PANSS , ,  
 , ) HVA  
 PANSS , ,  
 5 - HIAA PANSS  
 , clozapine  
 8 HVA PANSS  
 , PANSS  
 5 - HIAA PANSS  
 . Clozapine 8 PANSS 가 20%  
 CGI 가  
 , 27 48%(13 )가  
 . Clozapine (N = 13 )  
 (N = 14 ) HVA  
 HVA/5 - HIAA  
 , 5 - HIAA 가

중심 단어 : Clozapine . HVA . 5 - HIAA .

참고문헌

김승현 · 이민수 · 광동일(1995) : 정신분열증 환자에서 *Haloperidol* 투여에 따른 임상효과와 혈장 *Homovanillic Acid*의 농도 및 혈장 *5-Hydroxyindoleacetic Acid* 농도와의 관계. *생물정신의학* 2 : 77-90

이홍식 · 이희상 · 남궁기 · 김찬형 · 최낙경 · 도정호 · 전지용 · 황영신 · 유계준 · 이호영(1939) : 치료저항 정신분열증 환자에서의 *clozapine*효과. *대한정신약물학회지* 4 : 161-168

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