

정신분열병 환자에서 Interleukin-12와 Transforming Growth Factor Beta 1의 치료 전후의 변화*

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Changes of Interleukin-12 and Transforming Growth Factor Beta 1 before and after Antipsychotic Treatments in Schizophrenic Patients*

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ABSTRACT

Background : Several reports have suggested that cytokine alterations could be related to the pathophysiology of schizophrenia. In this study, we measured plasma level of interleukin - 12(IL - 12), a pro-inflammatory T helper 1(Th1) cytokine and transforming growth factor - 1(TGF - 1), an anti-inflammatory Th3 cytokine before and after antipsychotic treatment in schizophrenic patients.

Methods : The plasma concentrations of IL - 12 and TGF - 1 were measured by using quantitative ELISA in 23 schizophrenic patients and 31 normal controls at admission and 8 weeks later. The psychopathology was measured by Brief Psychiatric Rating Scale(BPRS).

Results : IL - 12 and TGF - 1 levels were significantly higher in schizophrenic patients than in controls before treatment. At the 8 week of treatment, the TGF - 1 levels returned to control values, while IL - 12 levels were not significantly changed. There were no significant correlations between the changes of BPRS scores and the changes of IL - 12 or TGF - 1 levels in schizophrenic patients.

Conclusion : Cytokine abnormalities in schizophrenia might be involved in the pathophysiology of the illness. It is possible that TGF - 1 plays an important role in the schizophrenia.

KEY WORDS : Cytokine · Interleukin · TGF · Schizophrenia.

서 론

(inflammatory reaction system)

가¹⁾²⁾

가

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가 (cytokine) , 3-5) (glia) (macrophage) 가 6) 가 7) 8)9) 10) 11) (hypothalamic - pituitary - adrenocortical system), (,) , 12)13) (monocytic) Th1, Th2, Th3 14) (pro-inflammatory) (, IL - 1, IL - 6, IL - 12, IL - 18, TNF -) (nonspecific innate immunity) . Th1 (, IL - 2, IFN -) 1 T (Type 1 T helper cell) (Cell - mediated immunity, CMI) , Th2 (, IL - 4, IL - 5, IL - 9, IL - 10, IL - 13, LIF) 2 T (type 2 T helper cell) (humoral immune reaction) , (anti - inflammatory effect) Th3 T (regulatory T cell)가 , (transforming growth factor - beta - 1 ; TGF - 1) . TGF - 1

가 . TGF - 1 (pro - inflammatory) Th1 IL - 4 IL - 10 T 가 TGF - 1 15) Th2 , TGF - 1 16) 가 Th1 (type 1 T helper cell - specific cellular immunity) Th2 Th1 - Th2 18) 가, 가, IL - 1, IL - 6, IL - 18, Tumor necrosis factor(TNF) - 가 19 - 23) Th1 IL - 2 interferon(IFN) - *in vitro* 5)24)25) Th2 IL - 4 IL - 10 가 26)27) Th1 가, 28) 29)30) IL - 2 가 , IL - 2 IFN - *in vitro* 31) *in vivo* IL - 2 *in vitro* IL - 2 T 가 T 가 Th1 IL - 12 TGF - 1 IL - 12 TGF - 1 8 IL - 12 TGF - 1

방 법

1. 연구 대상

23 . Diagnostic and Statistical Manual of Mental Disorders(DSM - IV) 32) Structured

Clinical Interview for DSM - IV³³⁾
가 .
가 .
4
(IRB)
Brief Psychiatric Rating Scale(BPRS)³⁴⁾
가 . 8
15 risperidone(5.2mg ;
2~10mg), 3 olanzapine(13.3
mg ; 10~20mg), 2 clozapine(
75mg ; 50~100mg), 1 haloperidol(21
mg), 2 neponide(16.5mg ;
15~18mg)
가
AST, ALT,
hemoglobin, hematocrit, urea
creatinine Venereal
Disease Research Laboratory(VDRL), (EKG)
(EEG)
31
(body mass index, BMI)
가
가
2
()
VDRL X
1 44

2. 혈장 IL-12 및 TGF-β1의 측정

8 9 10ml lit-
hium heparin 3800rpm
10
-70
8 , IL - 12
TGF - 1 R & D Sys-
tems quantitative high sensitive human
IL - 2, TGF - 1 kit quantitative colori-
metric sandwich ELISA . TGF -
1 (latent form)
가 .
100 μL 100 μL of 2.5N acetic acid/
10M Urea가 가 10 100
μL 2.7N NaOH/1M HEPES 가 .
IL - 2 TGF - 1
monoclonal antibody가 coating 96well

Table 1. Demographic data of subjects

	Schizophrenia (n=23)	Normal controls (n=31)
Sex(male/female)	9/14	8/23
Age(years)	34.4 ± 8.5 (19 - 54)	34.7 ± 10.3 (19 - 66)
BMI(kg/m ²)	22.8 ± 3.2	22.1 ± 2.2
Age of onset(years)	29.6 ± 8.3 (16 - 50)	
Duration of total illness (months)	56.4 ± 55.3 (6 - 180)	
Numbers of previous admission(n)	0.9 ± 1.6 (0 - 4)	
Family history(yes/no)	2/21	
Medication status on admission		
Medication-naive	17	
Medication-free	6	
Subtypes		
Paranoid	13	
Undifferentiated	7	
Disorganized	3	
Psychopathology score*		
BPRS at admission	26.5 ± 10.2	
BPRS at 8 weeks	12.5 ± 9.6	

* : The psychopathological scores were based on the Brief Psychiatric Rating Scale(BPRS)

microplate 100 μ L
 , 2 , well 400ul
 washing buffer 3 . 200ul IL - 12,
 TGF- 1 가 horseradish peroxidase
 well 2 .
 200 μ L , 20 50 μ L
 2N sulfuric acid . Plate O.D
 Organon teknika microwell system 450nm
 . IL - 12, TGF - 1
 가 (minimal detectable dose) 2pg/ml, 50pg/ml
 , - (intra and inter
 assay coefficient of variance) 10% .

3. 통계적 분석

two - tailed
 t - test . chi - sq-
 uare test .
 가
 Pearson δ product moment correlation
 coefficients . 가 $p < 0.05$
 , SPSS 11.01 .

결 과

1. 대상자들의 인구학적 자료

($\chi^2 =$
 1.087, df=1, $p=0.297$), (t= -0.154, df=51.456,
 $p=0.878$), (t=0.893, df=52, $p=0.376$)
 가 (1).

8

2. 정신분열병 환자와 정상 대조군에서 혈장 IL-12와 TGF- β 1 농도

IL - 12
 TGF - 1 . IL - 12 TGF -
 (2). , IL - 12 TGF -

Table 2. Plasma IL-12 and TGF- 1 levels in the study subjects

	Schizophrenia (n=23)	Controls (n=31)	Statistics
IL-12 (pg/ml)	13.5 \pm 13.5	5.8 \pm 2.4	t=3.1 ; df=52, $p < 0.05$
TGF- 1 (ng/ml)	23.6 \pm 11.4	16.4 \pm 11.4	t=2.3 ; df=48, $p < 0.05$

Table 3. Changes of plasma IL-12 and TGF- 1 levels before and after 8 weeks of treatment

	Before treatment	After treatment	Statistics
IL-12(pg/ml)	13.5 \pm 13.5	11.6 \pm 3.0	t=0.8 ; df=22, n.s.*
TGF- 1 (ng/ml)	23.6 \pm 11.4	16.3 \pm 8.4	t=2.4 ; df=22, $p < 0.05$
IL-12/TGF- 1	0.7 \pm 0.9	1.0 \pm 0.7	t= - 1.0, df=22, n.s.

*n.s. : not significant

1 (ratio) , Th1/Th3

IL -
 12 TGF - 1 ,
 , BPRS 가
 . 가

3. 8주간의 치료 전후의 IL-12 and TGF- β 1 농도 변화

23 가 8

paired t - test

8 IL - 12
 TGF - 1 TGF -
 1
 , IL - 12 (3,
 1). , 8

IL - 12 IL - 12
 (t=7.581, df=41.782, $p <$

0.001) TGF - 1

(t= -0.039, df=51.998, $p=0.969$). IL - 12 TGF -
 1 , Th1/Th3
 (3).

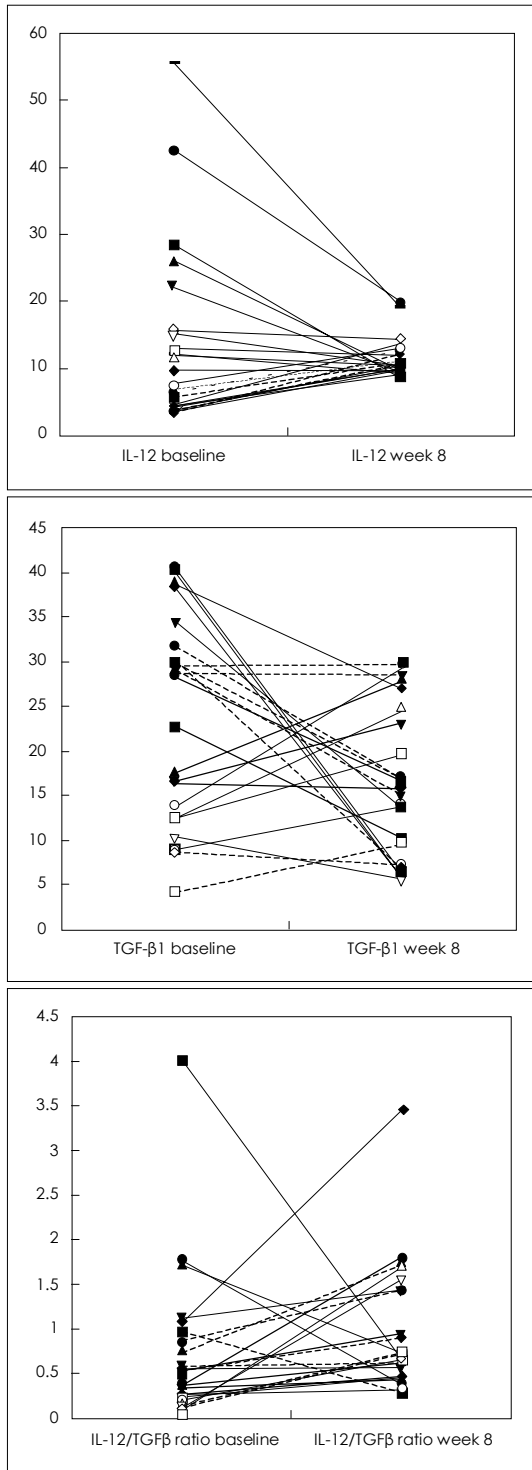


Fig. 1. Changes of plasma IL-12, TGF- 1 levels and IL-12/TGF- 1 ratio before and after 8 weeks of treatment.

고 찰

가
 , Th1 IL - 12 Th3
 TGF - 1
 가
 IL - 12
 가
 Th1/Th2
 Th3
 TGF -
 1
 Th3
 TGF - 1
 , IL - 12
 haloperidol IL - 1
 IL - 2, IL - 6, INF -
 가
 risperidone clozapine
 가
 IL - 6, INF - TNF -
 , 가
 leukemia inhibitory factor receptor
 가
 가
 IL - 12

가 가 . 가 .
, 8 IL - 12 가 가
가 가 가 . ,
IL - 12
, IL - 12
가
가 가 Th3 TGF - 1
. 39 - 41)
가 .
Th1/Th2 요 약
²⁵⁾²⁸⁾³¹⁾⁴⁴⁾ Th1 Th2
가 . Schwartz
Th2 가
가 ⁴⁵⁾ Kim type 1 T
Th1 Th2 ⁴⁶⁾ helper cell(Th1), type 2 T helper cell(Th2), type 3
T helper cell(Th3)
Th1/Th2 가
Th1/Th3 Th1 interleukin - 12(IL - 12), Th3
transforming growth factor - 1(TGF -
Th3 1)
Th1 방 법 :
가 TGF - 1 가 IL - 12 TGF - 1 31
Th3 TGF - 1 8 IL - 12
IL - 12 Th1/Th2 TGF - 1 .
8 , 2 Brief
, psychiatric rating scale(BPRS)
결 과 :
Th3 IL - 12 TGF - 1 . 8
가 TGF - 1
8 , IL - 12
. BPRS
가 IL - 12 TGF - 1

가
결 론 :

, TGF - 1

중심 단어 : TGF

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