

정신분열병 환자에서 Ziprasidone의 인지기능에 대한 효과

박 성 혁¹ · 김 찬 형^{2,3}

¹, ², ³

ABSTRACT

Effects of Ziprasidone on Cognitive Function in Patients with Schizophrenia

Sung-Hyouk Park, MD¹ and Chan-Hyung Kim, MD, PhD^{2,3}

¹Seoul National Hospital, Seoul, ²Department of Psychiatry, ³Institute of Behavioral Science in Medicine, Yonsei University College of Medicine, Seoul, Korea

Cognitive impairments are a fundamental characteristic of schizophrenia which can limit patients' function in daily lives. Cognitive impairments are among the most important determinant of functional disability of schizophrenia. Typical antipsychotics seem to have minimal effect on the enhancement of cognitive functioning in patients with schizophrenia. It seems that atypical antipsychotics have benefit of improving the cognitive function to a greater degree than typical antipsychotics. In 3 studies where patients were switched to ziprasidone because of suboptimal efficacy or adverse effects, patients demonstrated significant improvements of multiple cognitive domains. Path analysis of switch study showed that improvement of cognitive function and affective symptom were associated improvement of social function. In comparison of cognitive effects of ziprasidone versus olanzapine, both demonstrated substantial and comparable cognitive enhancing effects relative to previous treatment. (Korean J Psychopharmacol 2005;16(Supplement 3):28-34)

KEY WORDS : Ziprasidone · Schizophrenia · Cognitive function · Functional disability.

서 론

(cognitive functioning)

가 가 ¹⁾
(cognitive impairment)

²⁾

(high risk child) ³⁾

⁴⁾

(first epi-

sode)

⁵⁾

(functional disability)

가 , (negative symptom)

(positive symptom)

⁶⁾

⁷⁾

(episo-

dic memory), (vigilance), (executive function),

(working memory),

교신저자 : , 135 - 720 146 - 92

: (02) 3497 - 3340 · : (02) 3462 - 4304
E - mail : spr88@yumc.yonsei.ac.kr

(verbal fluency) 가 , HT_{2A} (prefrontal cortex)
 가 , dopamine 가 ,¹⁹⁾ 5-HT_{2A/D2}
 .⁷⁾ Green acetylcholine
 7) (verbal memory) 가 ,²⁰⁾
 (social problem solving) (skill acquisition) , ziprasidone 5-HT_{1A}, 5-HT_{1D},
 (card sorting) community functioning 5-HT_{2c} . 5-HT_{1A}
 가 (partial agonist)
 dopamine 가
 .¹⁸⁾ , synapse
 serotonin norepinephrine
 .²¹⁾ ziprasidone
 3가
 olanzapine 가
 ziprasidone
 (functional outcome)
 (typical antipsychotics)
 가 .⁸⁾
 가 가
 .⁹⁾
 (atypical antipsychotics)
 clozapine,^{10,11)} risperidone¹²⁾ olanzapine¹³⁾
 .
 .¹⁴⁾
 (differential benefit)
 (double blind)
 15) olanzapine risperidone
 ,^{16,17)} olanza-
 pine risperidone
 Ziprasidone 2005
 . ziprasidone
 가 D₂ 5-HT_{2A}
 (antagonism) .¹⁸⁾ 5-

HT_{2A} (prefrontal cortex)
 dopamine 가 ,¹⁹⁾ 5-HT_{2A/D2}
 acetylcholine
 가 ,²⁰⁾
 ziprasidone 5-HT_{1A}, 5-HT_{1D},
 5-HT_{2c} . 5-HT_{1A}
 (partial agonist)
 dopamine 가
 .¹⁸⁾ , synapse
 serotonin norepinephrine
 .²¹⁾ ziprasidone
 3가
 olanzapine 가
 ziprasidone

본 론

1. 약물 변경 연구(Switch studies)

1) 약물 변경 연구

Harvey²²⁾ 270 ,
 (N=108,
 PANSS : 67.5), olanzapine(N=104, PANSS
 : 65.6), risperidone(N=58, PANSS
 : 71.0) ziprasidone
 6 , (multicenter),
 (open label) 가

18 55
 ziprasidone 20~80 mg b. i. d
 (anticholinergics) (benzodiaze-
 pine) 12
 (baseline)
 6 / (learning/memory : Rey Au-
 ditory Verbal Learning Test[RAVLT], Spatial Working
 Memory Test), / (attention/vigilance :
 Continuous Performance Test Identical Pairs version
 [CPT - IP], Digit Span Distraction Test[DSDT]),

Ziprasidone

Table 1. Ziprasidone으로 약물 변경 후 인지 기능의 변화²²⁾

Cognitive test	Conventional to ziprasidone		Olanzapine to ziprasidone		Risperidone to ziprasidone	
	Change from baseline (Mean ± SD)	Effect size	Change from baseline (Mean ± SD)	Effect size	Change from baseline (Mean ± SD)	Effect size
RAVLT						
Total learning	2.893 ± 0.866**	0.26	4.494 ± 0.951***	0.39	3.935 ± 1.374**	0.32
Long-delay recall	1.110 ± 0.321***	0.29	1.256 ± 0.287***	0.34	1.422 ± 0.302***	0.37
Recognition/discrimination	0.038 ± 0.014**	0.31	0.037 ± 0.010***	0.36	0.038 ± 0.017*	0.33
Spatial working memory						
5-s delay	- 1.169 ± 0.930	0.28	0.342 ± 0.818	0.06	1.763 ± 1.057	0.21
15-s delay	- 0.086 ± 0.668	0.02	0.388 ± 0.553	0.08	0.738 ± 0.620	0.11
DSDT	5.442 ± 2.466*	0.23	2.114 ± 2.169	0.10	4.422 ± 1.960*	0.22
TMT						
Part A	- 6.638 ± 2.674*	0.21	- 0.224 ± 1.941	0.01	- 1.047 ± 1.946	0.06
Part B	- 18.630 ± 6.098**	0.23	0.482 ± 4.709	0.00	- 6.826 ± 5.314	0.12
WCST						
Categories attained	- 0.246 ± 0.198	0.09	0.273 ± 0.165	0.09	0.756 ± 0.268**	0.34
Total errors	- 0.696 ± 2.545	0.02	- 3.118 ± 2.092	0.12	- 9.711 ± 2.557***	0.35
Category fluency test	1.263 ± 1.263	0.12	1.576 ± 0.735*	0.12	0.617 ± 0.972	0.04
Letter Fluency test	2.658 ± 0.873**	0.24	0.262 ± 0.807	0.02	2.370 ± 1.060*	0.21

* : p<0.05, ** : p<0.01, *** : p<0.001

(visuomotor speed : Trail Making Test[TMT] parts A and B), (executive function : Wisconsin Card sorting Test[WCST]), (verbal fluency : Category Fluency Test, Letter Fluency Test) 5가 가 . risperidone . 18가 global cognitive score 3 risperidone verbal skill Positive and Negative Syndrome Scale(PANSS) 12가 7 가 . olanzapine global cognitive score (effect size)가 0.20 (small improvement) . olanzapine ziprasidone PANSS 가 . 22) 3가 ziprasidone 가 0.20 . (factor analysis) 18가 (verbal skill), / (attention/short - term memory) (random assignment)

Table 2. Ziprasidone 약물변경연구에 사용된 PANSS subscale^{23,24)}

PANSS cognitive subscale	
N5	Difficulty in abstract thinking
N7	Stereotyped thinking
G4	Tension
G5	Mannerisms and posturing
G11	Poor attention
G12	Lack of judgement and insight
PANSS anxiety-depression cluster ²⁴⁾	
G1	Somatic concern
G2	Anxiety
G3	Guilt feeling
G6	Depression
G15	Preoccupation
PANSS prosocial subscale ²⁵⁾	
P3	Hallucinatory behavior
P6	Suspiciousness/persecution
N2	Emotional withdrawal
N4	Passive social withdrawal
N7	Stereotyped thinking
G16	Active social avoidance

(multiple study arms) .¹⁾

가 , (motivation)

가 .¹⁾

²²⁾ 3가 ziprasidone 가 , ziprasidone

ziprasidone

. olanzapine

risperidone

, olanzapine PANSS

가 가 , 6 PANSS

가 가 .²²⁾ ,
olanzapine
가 (93.4 kg), 가
(p<0.0001, vs) . , olanzapine

가 .²²⁾

2) 약물변경연구에 대한 경로 분석

Loebel ²⁶⁾ ziprasidone
(affective symptom)
가 (social function)
가 Lindenmayer ²⁴⁾
5가 (factor) 2가 cognitive
factor anxiety/depression factor ,
(social function) 가 Purnine ²⁵⁾
prosocial factor PANSS
(2). prosocial factor

. cog-
nitive subscale (p<0.05) rispe-
ridone(p<0.01)

. anxiety - depression cluster score

risperidone(p<0.005)

. prosocial score(proso-
cial factor) 3가 (

, olanzapine p<0.05 ; risperidone

p<0.001) . cognitive subscale

anxiety - depression cluster score (path coef-
ficient 0.512 ; p<0.001) prosocial subscale
(path coefficient 0.623 ; p<0.001)

. anxiety - depression cluster score

prosocial improvement (path coeffi-
cient 0.280, p=0.0001) . cognitive subscale

anxiety - depression subscale

, prosocial improvement (path
coefficient 0.512*0.280=0.143) . , cog-

nitive subscale improvement가 prosocial improvement
(path coefficient 0.623+0.143=0.766, p=0.001)

Ziprasidone

, prosocial improvement 50% (1). anxiety - depression cluster score pro-social improvement ziprasidone

가
가
26)

2. Ziprasidone과 olanzapine이 인지기능에 미치는 영향 비교

Harvey 27) ziprasidone olanzapine 6 olanzapine 1

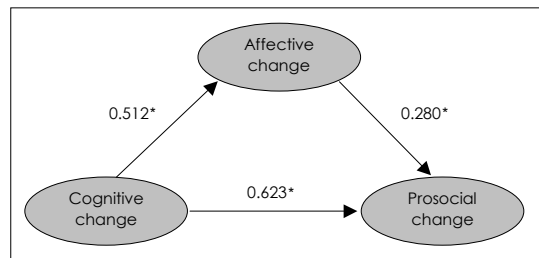


Figure 1. PANSS prosocial subscale에 대한 영향.23,24)

, screening Clinical Global Impressions - Severity (CGI - S) 1 4 CGI - S가 4 Clinical Global Impressions - Improvement

Table 3. Ziprasidone과 olanzapine의 인지기능에 대한 비교27)

	Ziprasidone				Olanzapine			
	N	Change from baseline (Mean ± SD)	P	Effect size	N	Change from baseline (Mean ± SD)	P	Effect size
Attention domain								
CPT d'	49	0.24 ± 0.592	0.007	0.36	60	0.28 ± 0.67	0.002	0.42
TMT part A	65	-13.65 ± 39.97	0.007	0.24	79	-10.29 ± 35.51	0.012	0.18
Memory domain								
RAVLT								
Learning trials 1 - 5	73	4.93 ± 9.40	0.000	0.38	89	6.46 ± 8.36	0.000	0.50
Delayed recall	69	1.22 ± 2.16	0.000	0.31	86	1.48 ± 3.14	0.000	0.37
Digit span								
Nondistracton (%)	64	-1.45 ± 16.28	0.48	-	78	0.12 ± 20.00	0.95	-
Distraction (%)	64	2.23 ± 21.15	0.40	-	78	1.03 ± 21.88	0.68	-
Executive function								
WCST								
Categories completed	60	-0.18 ± 1.761	0.42	-	78	0.38 ± 1.723	0.052	-
Perseverative errors	51	-1.75 ± 12.330	0.31	-	66	-1.18 ± 13.881	0.49	-
TMT part B	67	-9.51 ± 61.10	0.21	0.07	87	-25.70 ± 61.147	0.000	0.18
Verbal fluency								
Letter fluency	69	0.78 ± 7.53	0.39	-	87	0.91 ± 8.70	0.33	-
Category fluency	71	-0.23 ± 8.74	0.82	0.01	87	1.89 ± 7.17	0.016	0.06

(CGI - I) 3 269 (176 , sidone olanzapine
93) ziprasidone
(N=136) olanzapine (N=133) t - test olanzapine category flu-
1 (fixed dose) ency ziprasidone
ziprasidone 2 40 mg b.i.d. , olanzapine risperidone
5 80 mg b.i.d. olanzapine 2 5 olanzapine category fluency
mg q.d. 5 10 mg q.d. .2 .17,27) olanzapine category fluency
ziprasidone 40, 60, 80 mg b.i.d., olanz- nzapine category fluency 가
apine 5, 10, 15 mg q.d. (flexible .17,27) ziprasidone / ,
dose)
, 12
6
(3). ziprasidone (48.5%) 가
olanzapine (36.8%) 가 가 .1)
(8.8%, 8.3%, p=0.6350) .
.1) ziprasidone

RAVLT learning delayed recall
DSDT
olanzapine TMT part B
WCST
olanzapine category
fluency letter
ter fluency 가
multivariate analy-
sis of variance(MANOVA) (baseline
to endpoint, LOCF),
(Wilks Lambda=0.81, Pillais Approx F12,93=1.19,
p=0.31). MANOVA ziprasidone
(sample size)가 t - test(exploratory t -
test) . Bonferroni cor- ziprasidone
rection category fluency olanz- . olanza-
zapine ziprasidone pine olanzapine
(p<0.004).
Ziprasidone(40~80 mg bid)
olanzapine(5~15 ziprasidone
mg qd) zipra-

Ziprasidone

ziprasidone

가

중심 단어 : Ziprasidone

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