

## 리스페리돈 장기 지속형 주사제의 효용과 안정성 : 12주 다기관 경구 항정신병약물로부터 교체연구

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이상열<sup>7</sup> · 이양현<sup>8</sup> · 홍경수<sup>9</sup> · 김대호<sup>10</sup> · 김영훈<sup>11</sup> · 김창윤<sup>1</sup>

1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 가

### ABSTRACT

#### Effectiveness and Tolerability of Long-Acting Risperidone : A 12 Weeks, Multi-center Switching Study from Oral Antipsychotics

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**Objective** : To evaluate maintained effectiveness and tolerability when treated with long-acting risperidone compared to the previous antipsychotics in patients with schizophrenia or other psychotic disorders and to compare maintained effectiveness between oral risperidone and non-risperidone subgroups.

**Methods** : Subjects aged at least 18 years who required long-term antipsychotic therapy and who have been symptomatically stable on a stable dose of antipsychotics during the last month were enrolled in the non-rando-

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mized, single-arm, multi-center, 12 weeks duration study. Antipsychotic medications were switched from oral antipsychotics to long-acting risperidone. Injections were administered every 2 weeks. Most patients were started on 25mg long-acting risperidone injection or 37.5mg in some patients. The dosage were adjusted according to the patients' symptoms and responses to treatment at the discretion of investigators. Oral antipsychotics were continued at the same dose as before for 2 weeks and then were stopped or tapered off within next 7days.

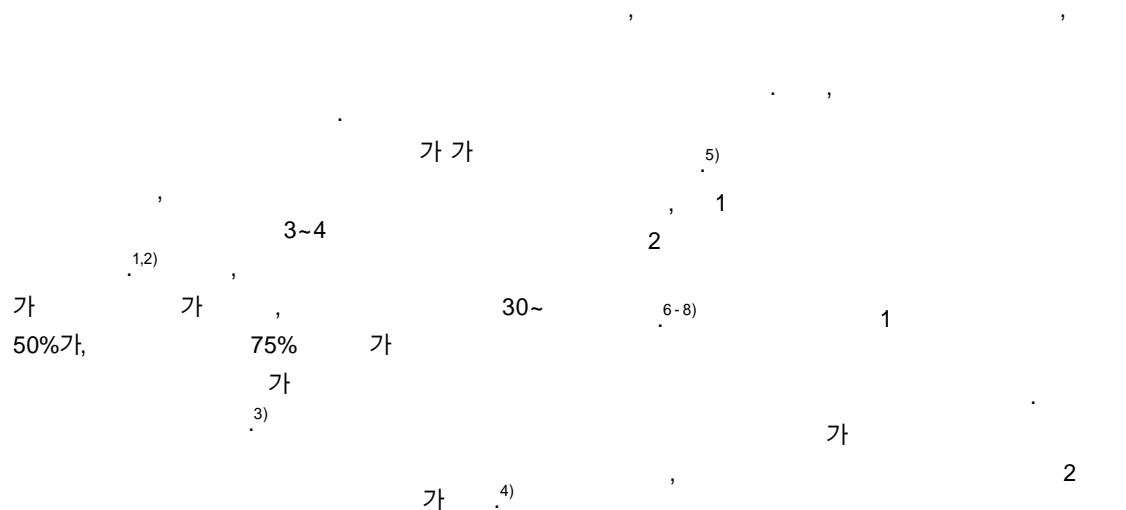
**Results :** A total of 204 patients with schizophrenia (N=192) and other psychotic disorder (N=12) from 20 sites in Korea were enrolled. The drop-out rate was 22.5% at 12 weeks. LOCF analysis has been performed. At 12 weeks after switching from oral antipsychotics to long-acting risperidone, statistically significant improvement was observed from baseline across all symptom domains including PANSS total, positive, negative, general subscale, CGI-S (Clinical Global Impression-Severity) scores and GAF (Global Assessment of Functioning) scores. The proportion of responders was 36.8% where response was defined as 20% reduction from baseline PANSS total score. The proportion of symptom worsening at 12 weeks was 7.4% (N=15) where symptom worsening was defined as 20% increase from baseline in PANSS total score or drop-out due to insufficient response or any 2 points change on any of 4 PANSS psychotic items (delusion, conceptual disorganization, hallucinatory behavior, suspiciousness/persecution) excluding changes in which the ratings remained at nonpsychotic levels (i.e > 3). Significant improvement from baseline was also observed in the measure of parkinsonism assessed using Extrapyramidal Symptom Rating Scale (ESRS). In addition, overall, patients were satisfied with long-acting risperidone injection on a single item measure of satisfaction. When subgroup analysis was performed on the basis of previous antipsychotics before switching to long-acting risperidone, no statistically significant differences were detected between oral risperidone (N=139) and non-risperidone subgroup (N=65) on all measures of effectiveness and tolerability including baseline demographic and clinical characteristics, symptom improvements, proportion of symptom improvement or worsening and ESRS score changes.

**Conclusion :** Our study results demonstrated maintained effectiveness and tolerability of long-acting risperidone microsphere and also could confirm successful switching from not only oral risperidone but also non-risperidone to long-acting risperidone injection. (Korean J Psychopharmacol 2005;16(2):109-120)

**KEY WORDS :** Long-acting · Risperidone · Effectiveness · Safety.

## 서 론

가



1  
1  
1)  
2) 3) clozapine  
(esterification) 가  
4)  
(glycolic acid) - (lactate) 5)  
(microsphere) 6)  
가 7) 8) 30  
가 9)  
9) 2 2~3  
12 7 2 6  
가 , 25 mg  
가  
10) 1  
가  
가 , 2~4  
가 2  
2  
11-14) 3

### 대상 및 방법

12  
20  
1) 18  
2) IV  
DSM -  
3)

### 1. 효능성/안정성 평가

가 (1 ), 4 (2 ), 8  
(3 ) 12 (4 / )  
가 (PANSS),  
Clinical Global Impression(CGI), Global Assessment  
of Functioning(GAF) 가 ,  
55 가(ESRS),  
가 . 가  
가  
PANSS

CGI 가 . PANSS 가 . PANSS  
 PANSS 20% , PANSS  
 (within group comparison) paired T - test

PANSS 20% , PANSS  
 4가 (delusion, conceptual disor- (between group  
 ganization, hallucinatory behavior, suspiciousness/per- effect)  
 secution) 2 가 analysis of variance) (repeated measures  
 4 (moderate) , 가 <sup>2</sup> test

CGI 가  
 CGI 2  
 , CGI 가 4  
 2 , 3  
 가 2 가  
 1 . CGI 가

**결 과**

**1. 인구학적 특성**

1 204 ( / : 192/12)가  
 204 35.6 ± 9.9

CGI 2 가 101 , 103 ( 1).  
 , , CGI 가 2 27.2 , 8.2 ± 6.7  
 가, 1 3 가 , 2.4 가  
 2 가 4 (moderate) 192 가 ,

12 . PANSS  
 59.1 , CGI 3.3  
 (mild to moderate)

60 CGI 가 3 (mild) 4 (mo-  
 , PANSS derate)  
 " " "

" 5 가 . , , PANSS

**2. 통계분석**

가 , , CGI 가 ( 1).  
 가가  
 가 ,  
 가  
 가 가

**2. 중도 탈락 및 사유**

46  
 22.5% .  
 가 14 가 ,  
 11 . 6

LOCF(last observation carried forward) 11 ( 2), 가 1  
 . 가

32 (69.6%) 가  
 , 9 (19.6%), 3 (6.5%)  
 .

3. 리스페리돈 장기 지속형 주사제 및 기존 경구용 항정  
 신병약물의 종류와 용량  
 25 mg

**Table 1.** Baseline demographic and clinical characteristics

	Risperidone group (N=139)	Non-risperidone group (N=65)	Total group (N=204)
Age (yrs)	35.3 ± 10.2	36.3 ± 9.4	35.6 ± 9.9
Sex (M/F)	70/69	31/34	101/103
Duration of illness (yrs)	8.6 ± 7.4	7.3 ± 4.7	8.2 ± 6.7
Age at onset	26.5 ± 9.2	28.6 ± 9.8	27.2 ± 9.4
Number of hospitalization	2.1 ± 1.7	2.7 ± 2.7	2.4 ± 2.2
Diagnosis			
Schizophrenia	131 (94.2%)	61 (93.8%)	192 (94.1%)
Paranoid	92 (70.2%)	43 (70.5%)	135 (70.3%)
Undifferentiated	20 (15.3%)	7 (11.5%)	27 (14.1%)
Disorganized	5 ( 3.8%)	1 ( 1.6%)	6 ( 3.1%)
Residual	13 ( 9.9%)	10 (16.4%)	23 (12.0%)
Catatonic	1 ( 0.8%)	0 ( 0%)	1 ( 0.6%)
Schizophreniform disorder	2 ( 1.4%)	0 ( 0%)	2 ( 1.0%)
Schizoaffective disorder	3 ( 2.2%)	1 ( 1.5%)	4 ( 2.0%)
Other psychosis	3 ( 2.2%)	3 ( 4.7%)	6 ( 2.9%)
Baseline PANSS score			
Total score	58.2 ± 17.2	61.0 ± 18.2	59.1 ± 17.6
Positive subscale	13.2 ± 4.9	13.5 ± 4.7	13.3 ± 4.9
Negative subscale	13.4 ± 5.3	16.0 ± 6.1	15.6 ± 5.6
General subscale	29.6 ± 9.1	31.5 ± 9.5	30.2 ± 9.3
Baseline CGI	3.2 ± 1.0	3.4 ± 1.1	3.3 ± 1.0

PANSS : Positive and Negative Syndrome Scale, CGI : Clinical Global Impressions

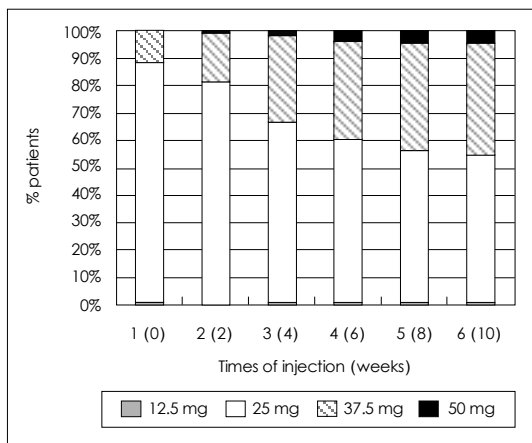
**Table 2.** Cumulative frequency and reasons for drop outs

	Baseline	4 weeks	8 weeks	12 weeks
Number of subjects	204	194	171	158
Cumulative frequency of drop outs (%)		10 (4.9%)	33 (16.2%)	46 (22.5%)
Reasons for drop outs				
Insufficient response				11 (23.9%)
Adverse event				6 (13%)
Subject non-compliant for other reasons				3 ( 6.5%)
Protocol violation				3 ( 6.5%)
Subject withdrawal consent				6 (13%)
Subject lost to follow-up				14 (30.4%)
Death				1 ( 2%)
Missing data				2 ( 4.3%)

88% 가 , 37.5 mg 22% (p<0.05), 8 (p<0.01), 12 (p<0.01)  
 , 50 mg ( 2).  
 25 mg 54% 37.5  
 mg 42% 50 mg  
 4% ( 1).  
 139  
 (68.1%) 가 , 3.7 ± 1.7 mg  
 . 39 (19.1%)  
 10.4 ± 4.4 mg ( 3).  
 , , ,  
 1

#### 4. 효능

PANSS 59.1  
 50.6 , 4

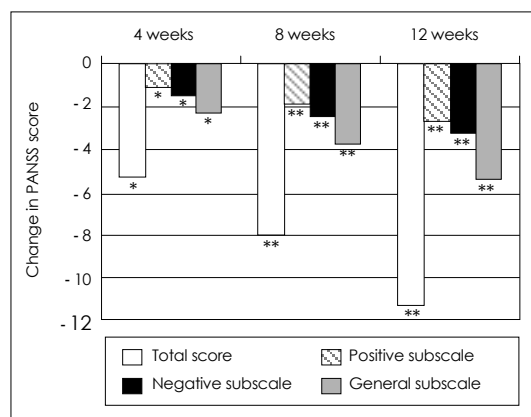


**Figure 1.** Dosage of risperidone long-acting injection.

**Table 3.** Prior oral antipsychotic medications

Prior oral antipsychotics	Number of patients (%)	Dose (mean ± s.d., mg)
Risperidone	139 (68.1)	3.7 ± 1.7
Olanzapine	39 (19.1)	10.4 ± 4.4
Quetiapine	10 ( 4.9)	370 ± 240.6
Amisulpride	5 ( 2.5)	520 ± 303.3
Haloperidol	5 ( 2.5)	17.1 ± 19.8
Trifluoperazine	2 ( 1.0%)	5 ± 0
Others	3 ( 1.5%)	
No medication	1 ( 0.5%)	

PANSS ,  
 (p<0.01. 4).  
 36.8% 가  
 가  
 PANSS 60  
 60  
 46.35%, 30.64%  
 가  
 ,  
 PANSS  
 (p<0.01, 4), 36.7%, 36.9%  
 158 ,  
 6 (3.8%) ,  
 204  
 15 (7.4%)  
 11



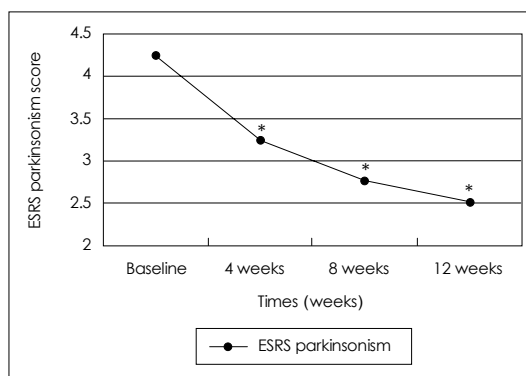
**Figure 2.** Mean change from baseline to endpoint in PANSS score. \*p<0.05 vs. baseline, \*\*p<0.01 vs. baseline.

**Table 4.** Mean changes from baseline to endpoint in PANSS score<sup>†</sup>

PANSS score	Risperidone group <sup>§</sup> (N=139)	Non-risperidone group (N=65)	Total (N=204)
Total score			
Baseline	58.2 ± 17.2	61.0 ± 18.2	59.1 ± 17.6
Endpoint	50.8 ± 19.0*	50.1 ± 15.5*	50.6 ± 17.9*
Positive subscale			
Baseline	13.2 ± 4.9	13.5 ± 4.7	13.3 ± 4.9
Endpoint	11.6 ± 5.4*	11.1 ± 4.1*	11.5 ± 5.0*
Negative subscale			
Baseline	15.4 ± 5.3	16 ± 6.1	15.6 ± 5.6
Endpoint	12.9 ± 5.3*	13.0 ± 5.1*	12.9 ± 5.2*
General subscale			
Baseline	29.6 ± 9.1	31.5 ± 9.5	30.2 ± 9.3
Endpoint	26.2 ± 9.7*	26.0 ± 7.7*	26.2 ± 9.3*

\* : p < 0.01 vs. baseline. † : paired T-test, ‡ : LOCF analysis was performed, § : Risperidone vs. Non-risperidone : statistically not significant. repeated measures ANOVA

3, 1  
139 8.0%가  
39 7.7%  
85  
4 (4.7%)  
CGI  
CGI  
3.3 2.8  
(mild to moderate)  
(very mild to mild) 3)  
CGI  
59 28.9%  
11 (5.4%)  
GAF 57.8 ± 11.6 가  
62.8 ± 12.9 67.2% 가  
(27.5%) (20.6%) (



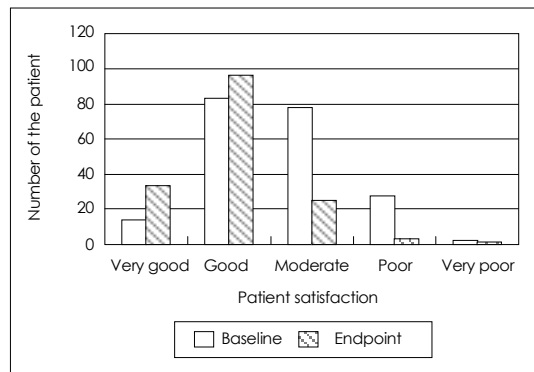
**Figure 3.** Mean change from baseline to endpoint in ESRS parkinsonism score. \* : p < 0.01 vs. baseline.

### 5. 안정성 및 환자의 만족도

가 , 가  
(

**Table 5.** Frequency of treatment-emergent adverse events (%)

Events	Total (N=204)	Risperidone (N=139)	Prior oral antipsychotics	
			Non-risperidone (N=65)	
			Olanzapine (N=39)	Non-olanzapine (N=26)
Any adverse events	137 (67.2)	96 (69.1)	26 (66.7)	15 (57.7)
Extrapyramidal symptoms	56 (27.5)	42 (30.2)	11 (28.2)	3 (11.5)
Tardive dyskinesia	3 ( 1.5)	2 ( 1.4)	0 ( 0)	1 ( 3.8)
Akathisia	25 (12.3)	16 (11.5)	6 (18.0)	3 (11.5)
Insomnia	42 (20.6)	32 (23.0)	4 (15.4)	6 (23.1)
Anxiety	25 (12.3)	20 (14.4)	2 ( 5.1)	3 (11.5)
Anticholinergic adverse event	15 ( 7.4)	11 ( 7.9)	3 ( 7.7)	1 ( 3.8)
GI trouble	13 ( 6.4)	9 ( 6.5)	3 ( 7.7)	1 ( 3.8)
Agitation	10 ( 4.9)	5 ( 3.6)	2 ( 5.1)	3 (11.5)
Sedation	1 ( 0.5)	1 ( 0.7)	0 ( 0)	0 ( 0)
Headache	2 ( 1.0)	2 ( 1.4)	0 ( 0)	0 ( 0)
Elevated hepatic enzyme	1 ( 0.5)	0 ( 0)	1 ( 2.6)	0 ( 0)



**Figure 4.** Patient satisfaction at baseline and endpoint.

5). “ ” “ ”

가 204 97 47.5% , 139 35 (25.3%), 39

“ ” “ ” 6 (15.4%)

152 129 (84.8%) ( 4). 158 43 (27.2%)

6. 병용약물 35 (32.7%), 30 4

204 77 (37.7%) (13.3%)

99 27

139 60 (27.3%) ,

(77.9%), 65 79 21 (26.6%), 32





가 4 , BPRS CGI CGI

4 가 , 3 60%

77% . Lauriello <sup>14)</sup>

PANSS 가 PANSS CGI 3 가 가 15%

20% , PANSS 4가 35% 가 , Lindenmayer

(delusion, conceptual disorganiztion, 12) 61% . 43%

2 , 가 (E-

가 4 (moderate) , SRS) 가 .

가 ,

. PANSS 가

17.9% 13.3%

PANSS 20 가 77.9% 11.2%, 37.7% 19.0%

가 .

가

LOCF 가

LOCF 가 <sup>12,13,20)</sup>

158 , 가

가

6 (3.8%) , 204

가

15 (7.4%) .

PANSS

36.8%, 9% , CGI 가 99 가 27

28.9%, 5.4% PANSS (27.2%) 가

가

PANSS CGI 20.6%, 12.3%

가

25 mg 가 88% ,  
 25 mg 가 54% 37.5  
 mg 42% . 가 가 .  
 mg 25 mg 37.5 **결 론**  
 , 37.5 mg 20  
 (N=192) (N=12)  
 , PANSS 12  
 , GAF 가 가 .  
 가 가 PANSS , ,  
 가 가 . PANSS 20%  
 가 가 . 36.8%가  
 가 2 . 12 204 22.5%  
 7.4% .  
 , 가 ,  
 9,21) 가 ,  
 가 22) .  
 가 가

중심 단어 :

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