

리스페리돈이 심혈관계에 미치는 영향

최세진* · 전진숙*[†] · 최영태**

The Cardiovascular Effect of Risperidone

Se-Jin Choi, M.D.,* Jin-Sook Cheon, M.D.,*[†] Young-Tai Choi, M.D.**

ABSTRACT

Objectives : Risperidone is a new antipsychotic drug developed to overcome the therapeutic limitation of conventional antipsychotics. It responds to negative as well as positive symptoms by blocking both dopaminergic and serotonergic receptors, causing no significant side effects such as agranulocytosis and seizure. It is, however, not known whether it induces any serious cardiovascular side effects as evoked by other conventional antipsychotic drugs. The aims of this study were to evaluate the effect of risperidone on cardiovascular function, and to discuss the factors affecting the cardiovascular function.

Methods : For 42 patients(22 males and 20 females) diagnosed as schizophrenia, schizophreniform disorder or schizoaffective disorder according to the DSM - classification, the cardiovascular functions such as heart rate, systolic and diastolic blood pressure, PR interval, QRS interval and QT interval were successively checked before and after 2 weeks and 4 weeks risperidone administration. Furthermore, variables such as body weight, Brief Psychiatric Rating Scale(BPRS), Clinical Global Impression(CGI), Extrapyramidal Symptom Rating Scale(ESRS), Anticholinergic Rating Scale(ARS), serum cholesterol level, serum triglyceride level, serum high - density - lipoprotein level, serum WBC, serum Hb, serum platelet level, prothrombin time and partial thromboplastin time were also analyzed before and after 2 weeks and 4 weeks risperidone administration.

Results :

1) Risperidone treatment resulted in a significantly decreased heart rate and increased QT interval after 4 weeks administration($p < 0.005$ respectively).

2) The scores of BPRS and CGI were significantly decreased after 2 weeks and 4 weeks risperidone administration as compared with baseline($p < 0.001$ respectively). The scores of ESRS and ASRS were significantly increased after 2 weeks and 4 weeks risperidone administration as compared with baseline($p < 0.001$ respectively).

3) There were positive correlations between heart rate after 4 weeks and total dose($P < 0.05$). Blood pressure was significantly($p < 0.05$) correlated with sex(higher in male) and significantly($p < 0.05$) positive correlated with body weight. QT interval was significantly($p < 0.05$) correlated with sex(longer in female) and smoking history(shorter in smokers).

Conclusions : Risperidone could induce significant change in heart rate and Q - T interval. Therefore, the cardiovascular safety for risperidone should be reconsidered according to the duration and dosage increase.

KEY WORDS : Risperidone · Heart rate · QT interval · Dose.

* Department of neuropsychiatry, Kosin University, School of Medicine, Pusan, Korea

** Department of Psychiatry, Busan Dong In Geriatric Hospital, Pusan, Korea

† : , 602 - 702 34
) (051) 250 - 5070/240 - 6245,) (051) 241 - 5069 E - mail) cheonjs@kosin.md

서론

19 Delay Deniker chlorpromazine (Moriarty 1984). dopamine(DA) 가 dopamine - D2 (Cohen 1994 ; Keefe Harvey 1994 ; Melzer Stahl 1976).

가 가 (Andreasen Olsen 1982 ; Crow 1980 ; Mackay 1980), (tardive dyskinesia) (compliance) (Putten 1974).

DA , 가 DA adrenergic, cholinergic, histaminergic receptor

(atypical neuroleptics) clozapine 가 1 2% (1992 ; Kaplan Sadock 1991).

Risperidone benisoxazol serotonin - S2 dopamine - D2 가 1988 risperidone

(Gelders 1990 ; Castelao 1989 ; Mesotten 1989 ; Roose 1988). risperidone 가

azine 가, 가 1 -adrenergic 가 (Cohen 1994). risperidone .

대상 및 방법

1. 연구대상

1999 6 2000 5 DSM - (American Psychiatric Association 1994) , , (schizophreniform) risperidone 42 (22 , 20) Risperidone , Risperidone , Risperidone , 1 , ,

(±) 33.83 ± 11.49 , 28.31 ± 10.75 . (±) 11.71 ± 3.74 , (±) 61.63 ± 11.98kg, 165 ± 8.03cm . 20 (48%) , 2 (5%) 가 .

가 4 (10%) . 26 (62%) , 13 (31%) , 3 (7%) .

가 1 가 14 (33%) , 28 (67%) .

2. 연구방법

risperidone 1 risperidone , 2 , 4 ,

Table 2. Comparison of changes in cardiovascular function and variables after risperidone administration

	Baseline	Risperidone administration		p-Value*	
		After 2wks	After 4wks	ANOVA	Tukey HSD
Heart rate/min	81.19 ± 11.03	77.05 ± 8.28	74.26 ± 6.70	p = 0.002	p = 0.001 (-)
Systolic BP(mmHg)	125.71 ± 12.91	122.14 ± 11.80	120.71 ± 10.22	N.S**	
Diastolic BP(mmHg)	81.43 ± 9.77	78.57 ± 9.52	77.62 ± 7.26	N.S	
PR interval(msec)	153.90 ± 25.94	159.80 ± 24.82	158.93 ± 24.82	N.S	
QRS interval(msec)	87.79 ± 19.00	90.69 ± 16.90	92.71 ± 19.04	N.S	
QT interval(msec)	357.10 ± 37.29	373.14 ± 35.17	382.14 ± 30.25	p = 0.004	p = 0.002 (-)
Body weight(kg)	61.63 ± 12.05	63.24 ± 11.73	64.61 ± 11.54	N.S	
BPRS1	54.14 ± 5.70	40.90 ± 6.80	30.81 ± 8.78	p = 0.000	p = 0.000
CGI2	5.21 ± 0.81	4.05 ± 0.96	3.17 ± 1.25	p = 0.000	(- ,
ERS3	0	1.79 ± 1.54	3.29 ± 2.18	p = 0.000	- ,
ASRS4	0	2.36 ± 1.38	4.31 ± 2.25	p = 0.000	-)
Cholesterol(mg/dl)	170.88 ± 33.48	174.48 ± 37.19	183.14 ± 28.47	N.S	
Triglyceride(mg/dl)	114.29 ± 64.76	134.19 ± 68.49	146.71 ± 70.33	N.S	
HDL5(mg/dl)	41.81 ± 14.69	41.29 ± 11.41	41.40 ± 10.82	N.S	
WBC(10e3/ul)	7.84 ± 2.87	6.21 ± 1.31	6.16 ± 1.68	p = 0.000	p = 0.001 (- , -)
Hb(g/dl)	13.06 ± 1.79	12.86 ± 1.70	12.74 ± 1.61	N.S	
Platelet(g/dl)	243.40 ± 73.11	229.29 ± 77.06	215.31 ± 59.04	N.S	
PT6(secs)	11.79 ± 1.09	11.90 ± 0.95	11.80 ± 0.86	N.S	
PTT7(secs)	34.55 ± 4.04	36.42 ± 3.54	36.69 ± 3.35	p = 0.016	P = 0.020 (-)

*One-way ANOVA with Tukey HSD, **N.S = statistically non-significant

¹Brief Psychiatric Rating Scale

²Clinical Global Impression

³Extrapyramidal Symptoms Rating Scale

⁴Anticholinergic Symptoms Rating Scale

⁵High Density Lipoprotein

⁶Prothrombin Time

⁷Partial Thromboplastin Time

cholesterol (±) 170.88 ± 33.48mg/dl, 2 174.48 ± 37.19mg/dl, 4 183.14 ± 28.47mg/dl . Triglyceride (±) 114.29 ± 64.76mg/dl, 2 134.19 ± 68.49mg/dl, 4 146.71 ± 70.33mg/dl . HDL (±) 41.81 ± 14.69mg/dl, 2 41.29 ± 11.41mg/dl, 4 41.40 ± 10.82mg/dl . WBC (±) 7.84 ± 2.87 10³/ul, 2 6.21 ± 1.30 10³/ul, 4 6.16 ± 1.68 10³/ul, 2 , (p<0.005). Hb (±) 13.06 ± 1.79g/dl, 2 12.86 ± 1.70g/dl, 4 12.74 ± 1.60g/dl . Platelet (±) 243.40 ± 73.11 10³/ul, 2 229.29 ± 77.06 10³/ul, 4 215.31 ± 59.04 10³/ul . prothrombin time (±) 11.79 ± 1.09secs, 2 11.90 ± 0.95secs, 4 11.80 ± 0.86secs, 2

partial thromboplastin time (±) 34.55 ± 4.04secs, 2 36.42 ± 3.54secs, 4 36.69 ± 3.35secs, 2 가 (p<0.05). 3. 심혈관계 기능과 여러 변인과의 상관성 (3). 4 (= 0.334, p<0.05). 2 4 가 (: 2 = - 0.339, p<0.05 ; 4 = - 0.351, p<0.05, : 2 = - 0.362, p<0.05 ; 4 = - 0.415, p<0.01), (: 2 = 0.408, p<0.01 ; 4 = 0.313, p<0.05, : 2 = 0.343, p<0.05 ; 4 = 0.305, p<0.05). QT (= 0.421, p<0.01) 4 (= 0.313, p<0.05) 2 (= 0.424, p<0.01) 4 (= 0.392, p<0.05) QT .

Table 3. Correlation between cardiovascular function and variables

	Baseline				Risperidone administration							
					After 2wks				After 4wks			
	HR ¹	Systolic BP ²	Diastolic BP	QT interval	HR	Systolic BP	Diastolic BP	QT interval	HR	Systolic BP	Diastolic BP	QT interval
Sex	-0.017	-0.128	-0.042	0.218	-0.221	-0.339*	-0.362*	0.421**	-0.095	-0.351*	-0.415**	0.313*
Body weight	-0.121	0.308*	0.237	0.063	-0.121	0.408*	0.343*	0.002	-0.112	0.313*	0.305	-0.067
Smoking history	-0.058	0.166	0.190	0.303	-0.437**	-0.193	-0.193	0.424**	-0.272	-0.216	-0.184	0.392*
Total dose	0.175	0.275	0.141	-0.103	0.160	0.120	0.040	-0.187	0.334*	0.068	-0.035	-0.178
Cholesterol 0	-0.017	0.091	0.106	0.075	-0.162	0.169	0.170	0.017	0.078	0.236	0.320*	-0.051
Cholesterol 2	0.070	0.156	0.112	0.137	-0.014	0.209	0.254	0.073	0.095	0.223	0.332*	0.046
Cholesterol 4	0.142	0.221	0.221	0.060	-0.151	0.326*	0.314*	-0.028	0.091	0.295	0.372*	-0.150
Triglyceride 0	0.083	0.036	0.043	-0.099	0.056	0.262	0.256	-0.093	0.068	0.232	0.199	-0.061
Triglyceride 2	0.113	0.097	0.082	-0.149	0.007	0.224	0.219	-0.123	0.044	0.179	0.244	-0.120
Triglyceride 4	0.073	0.127	0.094	-0.185	0.018	0.117	0.056	-0.191	0.034	0.078	0.169	-0.161
Hemoglobin 0	-0.033	0.240	0.245	0.028	0.047	0.318*	0.411**	-0.188	-0.005	0.481**	0.396*	-0.192
Hemoglobin 2	-0.111	0.267	0.258	0.056	-0.066	0.329*	0.369*	-0.300	0.048	0.508**	0.445**	-0.324*
Hemoglobin 4	-0.076	0.239	0.148	-0.018	0.080	0.280	0.303	-0.296	0.024	0.379*	0.400**	-0.287
Platelet 0	0.162	0.103	0.194	-0.027	-0.027	-0.107	-0.055	-0.103	0.213	-0.060	-0.020	-0.181
Platelet 2	0.177	0.062	0.135	-0.119	0.058	-0.010	0.082	-0.161	0.144	0.024	-0.099	-0.212
Platelet 4	0.163	0.102	0.095	-0.072	-0.038	0.014	0.111	-0.204	0.168	0.111	-0.142	-0.189

. These data represent correlation coefficients(g)

*p<0.05 **p<0.01

¹HR = heart rate

²BP = blood pressure

0 : baseline

2 : 2 weeks after risperidone administration

4 : 4 weeks after risperidone administration

고 찰

clozapine (Leysen 1988). risperidone 5-HT_{2A} ritanserine halo-peridol 200, DA D₂ haloperidol (Ereshefsky Lacombe 1993 ; Janssen 1988). Risperidone 가 . Serotonin(5-HT)₂ 가 . 가 clozapine , , , 가 (Hippus 1989 ; McKenna Bailey 1993) serotonin 가 prolactin 가 , , , (Bleich 1988). (D₁, D₂, D₃, D₄) 가 (hot flush) (Kaplan Sadock 1995). 1-adrenergic risperidone (Melzer Fatemi 1996 ; Remington 1996). (Cohen 1994 ; risperidone benzisoxazole 5-HT₂, Leysen 1992). Risperidone DA D₂, 1-adrenergic QT QRS 가 (Ken 2-adrenergic, histamine H₁ 1996 ; Richard Robert 1996). , DA D₁ muscarinic cholinergic QT 가 (Kevin 1982 ; Leysen 1988 ; Sc-hatzberg 1997). 5-HT_{2A} D₂ QRS QT 가가 Titusville(1994) D₂ 5-HT_{2A} 25 Drici (1988) risperidone ser-

tindole QT (p<0.05).
 Cohen(1994) Owen(1994) (p<0.05),
 (1994) 가 (Claus
 1992 ; Meco 1989 ; Mesotten 1989 ; Putten 1974).
 risperidone 가 (1994)
 (1966 ; 1994 ; 1998 ; Owen
 1994). BPRS, CGI

(p<0.05).
 (p<0.05),
 (p<0.05). QT
 , risperidone
 QT , risperidone
 가
 중심 단어 : QT
 참고문헌

, risperidone
 4
 Cohen
 (1994) Risperidone
 가 triglyceride 가
 , risperidone 가
 가

강대엽 · 이충순 · 최진숙 · 김형섭 · 한광수 · 황태연 · 김용희 · 이정식(1966) : 만성정신분열증 환자에 대한 리스페리돈 효과 및 안전성 비교시험. 용인정신의학보 3 : 61-77
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결론

1999 6 2000 5
 DSM -
 42 risperidone 가
 Risperidone 2
 4 ESRS ASRS 가
 1) Risperidone 4
 , QT 가 (p<
 0.005).
 2) BPRS, CGI
 2 4
 (p<0.001), ESRS, ASRS
 2 4 가 (
 p<0.001).
 3) 4 risperidone

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