

# 소아청소년 정신과 영역에서의 새로운 약물치료 ; 비정형 항정신병약물\*

## NEW DRUG THERAPY IN CHILD AND ADOLESCENT PSYCHIATRY ATYPICAL ANTIPSYCHOTICS

반 건 호\*\*†

Geon HO Bahn, M.D., Ph.D. \*\*†

요 약 :

가  
가

중심 단어 :

### 서 론

Clozapine risperidone haloperidol zine 12, 6 1). 가 가 15 risperidone 1). chlorpromazine 6, 3 가 , pimozide trifluopera-

가 가 가 가 가

\* 2002

Department of Neuropsychiatry, KyungHee University Medical School, Seoul

†Corresponding author



**Table 1.** Atypical antipsychotic medications studied in children & adolescents\*

| Generic name | Chemical class       | Dose range (mg/day) | Potency | Approximate dose equivalents (mg) | Neuropsychiatric disorder(s) studied  | Key references  |
|--------------|----------------------|---------------------|---------|-----------------------------------|---|---|
| Clozapine    | Dibenzodiazepine     | 25 - 900            | Low     | 100                               | Treatment-resistant illnesses<br>Schizophrenia<br>Bipolar disorder<br>Autistic disorder | Kumra et al., 1996<br>Kowatch et al., 1995<br>Zuddas et al., 1996   |
| Olanzapine   | Thienobenzodiazepine | 5 - 20              | Medium  | 5                                 | Bipolar disorder<br>PDD<br>Schizophrenia  | Frazier et al., 2000<br>Potenza et al., 1999<br>Kumra et al., 1998  |
| Quetiapine   | Dibenzothiazepine    | 25 - 750            | Low     | 100                               | Psychotic disorders   | McConville et al., 2000   |
| Risperidone  | Benzisoxazole        | 0.25 - 10           | High    | 2                                 | Bipolar disorder<br>Conduct disorder<br>PDD<br>Psychotic disorders<br>Tic disorders     | Frazier et al., 1999<br>Findling et al., 2000a<br>McDougle et al., 1997<br>Armenteros et al., 1997<br>Lombroso et al., 1995 |
| Ziprasidone  | Benzisothiazolyl     | 25 - 160            | Medium  | 20                                | Tic disorders   | Sallee et al., 2000a  |

\* : from Pediatric psychopharmacology (Martin et al 2003), p329

pine clozapine

가  
clozapine 1~2%  
2). 1997 clozapine 150,409  
585 19 11).  
Kumra 7) 21  
1.5~2.0%  
clozapine N -  
desmethyl - clozapine 15  
300mg  
1~2% 가 , 300~599mg  
3~4%, 600~900mg 5% 가 가  
2).  
Kay 12) clozapine 16  
troponin

## Risperidone

### 1. 일반특성

Risperidone 1993 FDA 가  
가  
가

### 2. 약동학 및 작용 기전

cytochrome P450 IID<sub>6</sub>  
9 - hydroxyrisperidone  
risperidone

가 9-hydroxyrisperidone  
3 ,  
17 . 7%  
가 . 가  
3 , 20  
. 9-hydroxyrisperidone  
21 , 30 <sup>2)</sup>  
Risperidone 5-HT<sub>2A</sub>, D<sub>2</sub>, 2-  
, H1 . -  
,  
. haloperidol D<sub>2</sub>  
, haloperidol  
5)

### 3. 적응증

14) ,  
,  
2) McDougle <sup>15)</sup> 1997  
NIMH risperi-  
done , risperidone  
,  
risperidone  
16) .  
Turgay <sup>17)</sup> ,  
48 risperidone  
risperidone 가  
, 가 . Aman <sup>18)</sup>  
risperidone (가  
)  
Fras Major <sup>19)</sup>

risperidone  
, 3mg , 2mg  
Lombroso <sup>20)</sup>  
risperidone

Bruggeman <sup>21)</sup> risperidone pimozide  
risperidone  
Perry <sup>22)</sup>  
risperidone  
가 , 가,  
McCracken <sup>23)</sup>  
, 101  
risperidone  
Olanzapine risperidone  
risperidone  
<sup>24)</sup> risperidone 5-HT<sub>1D</sub>  
15) .  
Fitzgerald <sup>25)</sup>  
risperidone

### 4. 부작용

, 가,  
<sup>26)</sup> McDougle <sup>15)</sup>  
가  
가  
McCracken <sup>23)</sup>  
,  
risperidone  
가 가  
,  
Turgay <sup>17)</sup>  
,  
Aman <sup>18)</sup>  
가  
가  
Risperidone 10%  
<sup>27)</sup>

## Olanzapine

1. 일반특성  
1997 FDA 가 .

olanzapine 가

26)

**2. 약동학 및 작용기전**

90% 21~

54 ( 30 ).

pine Olanza-  
cytochrome  
P450 가  
10 - N - glucuronide 4 ' - N - desmethyl ola-  
nzapine 가  
7%  
30% 60%  
olanzapine cytochrome  
P1A2 가 . Olanzapine  
30%  
40% 2)  
Olanzapine 5HT<sub>A</sub> : D<sub>1</sub>, D<sub>2</sub>, D<sub>4</sub> ; 1,  
M<sub>1</sub> M<sub>5</sub>, H<sub>1</sub> 5)

**3. 적응증**

2). Kumra 4)  
olanzapine clozapine

가  
Grothe (2000)  
olanzapine  
10mg 28)  
Kemner 29)  
가, 가,

olanzapine ha-  
loperidol 가 30)  
Chang Ketter<sup>31)</sup>, Khouzam El - Gabalawi<sup>32)</sup>,  
Frazier<sup>33)</sup>, olanzapine  
olanzapine Powers<sup>34)</sup>  
, Mehler<sup>35)</sup>  
olanzapine 가  
olanzapine 가  
35)  
Karam - Hage Ghaziuddin<sup>36)</sup>  
olanzapine  
olanzapine<sup>37)</sup>

**4. 부작용**

가 , 가, , ,  
26) risperidone, olanzapine,  
haloperidol 가  
olanzapine, risperidone, haloperidol  
(7.2 ± 6.3Kg, 3.9 ± 4.8Kg, 1.2 ± 3.3Kg)<sup>38)</sup>.  
가 가

**Quetiapine**

**1. 일반특성**  
1997

**2. 약동학 및 작용기전**

1.5  
CYP3A4  
sulfoxide

HT<sub>2A</sub>, -1 가 D<sub>2</sub>, D<sub>3</sub>, D<sub>4</sub>  
 Quetiapine 5-HT<sub>2</sub> 5-HT<sub>6</sub>, D<sub>1</sub> D<sub>2</sub>, H<sub>1</sub>, 1  
 2 . Quetiapine

3. 적용증

가 39) McConville  
 40) 가

4. 부작용

가 6 3)

Zotepine

1. 일반특성

1970 Thiepin . 1982  
 가 42) 가  
 43)

2. 작용기전

Zotepine zotepine D<sub>1</sub>, 5-

3. 적용증

Tanoue Oda<sup>42)</sup> 가

4. 부작용

가가 가 44)  
 가 43) 43)

Amisulpride

1. 일반특성

1986  
 45)

2. 약동학 및 작용기전

5-HT<sub>2</sub>/D<sub>2</sub>  
 mesolimbic selectivity  
 46) amisulpride sertindole, olanzapine,  
 quetiapine

3. 적용증

47)가  
 가 48) 49)

4. 부작용

가 가 가  
 가 가 가  
 45)

# Ziprasidone

## 1. 일반특성

가 50)

## 2. 약동학 및 작용기전

2~6 2  
가 5~10

Ziprasidone 5-HT<sub>1D</sub>, 5-HT<sub>2A</sub>, 5-HT<sub>2A</sub>, 5-HT<sub>2C</sub>, D<sub>2</sub>, D<sub>3</sub>, D<sub>4</sub>, 1, H<sub>1</sub>, D<sub>1</sub>, M<sub>1</sub>, ziprasidone 2 5-HT<sub>1A</sub>, ziprasidone 5)

## 3. 적응증

Sallee 28 8 ziprasidone YGTSS(Yale Global Tic Severity Scale) 가

**Table 2.** Lab tests for child & adolescent using atypical antipsychotics

| Items                   | Drugs         | Etc            |
|-------------------------|---------------|----------------|
| Weight                  | a, b, c, d    |                |
| B/P & P/R               | a, b, d, f    |                |
| EKG QT interval         | a, c, d, e, f |                |
| Serum glucose           | a, c, d       |                |
| Cholesterol(total)      | a, b, c, d    |                |
| WBC                     | a             |                |
| TFT(T4, TSH)            | d             |                |
| RBC                     | f             |                |
| Hgb                     | f             |                |
| Slit lamp ophthalmic Ex | d             | Every 6 months |
| Platelet                | a, b, c       |                |
| LFT                     | b             | Base           |
| LFT                     | a, b, c, d, f | Every 3 months |
| EEG                     | a, f          |                |

a : clozapine b : risperidone c : olanzapine d : quetiapine e : ziprasidone f : zotepine

## 4. 부작용

가 QTc  
가 QTc  
fluoroquinolone 26)

## 소아청소년 약물 치료 시 고려 사항

Table 2

51)

## References

- 1) American Medical Association(AMA)(1994) : Drug Evaluation Annual
- 2) Green WH(2001) : Child & adolescent clinical psychopharmacology. 3rd ed. Lippincott Williams & Wilkins, Philadelphia, pp89-149
- 3) Malone RP, Sheikh R, Zito JM(1999) : Novel anti-psychotic medications in the treatment of children and adolescents. Psychiatric Services 50 : 171-174
- 4) Kumra S, Jacobson LK, Lenane M, Karp BI, Frazier JA, Smith AK, Bedwell J, Lee P, Malanga CJ, Hamburger S, Rapoport JL(1998) : Childhood-onset schizophrenia : an open-label study of olanzapine in adolescents. J Am Acad Child Adolesc Psychiatry 37 : 377-385
- 5) Sadock BJ, Sadock VA(2001) : Pocket handbook of

- psychiatric drug treatment. 3rd ed. Lippincott Williams & Wilkins, Philadelphia, pp205-207
- 6) Schmidt MH, Trott GE, Blanz B, Nissen G(1990) : Clozapine medication in adolescents. In : Stefania CN, Rabavilas AD, Soldatos CR, eds. Psychiatry : a world perspective. Proceedings of the eighth World Congress of Psychiatry. Amsterdam : Excerpta Medica 1:1100-1104
  - 7) Kumra S, Frazier JA, Jacobson LK, McKenna K, Gondon CT, Lenane MC, Hamburger SD, Smith AK, Allbus KE, Alagband-Rad J, Rapoport JL(1996) : Childhood-onset schizophrenia : a double-blind clozapine-haloperidol comparison. Arch Gen Psychiatry 53 : 1090-1097
  - 8) Zuddas A, Ledda MG, Fratta A, Muglia P, and Cianchetti C(1996) Clinical effects of clozapine on autistic disorder[letter]. Am J Psychiatry 153 : 738.
  - 9) Taylor DM, McAskill R(2000) : Atypical antipsychotics and weight gain-a systemic review. Acta Psychiatr Scand 101 : 416-432
  - 10) 노명선, 구영진, 안용민, 강용구, 김용식(2002) : 비정형 항정신병 약물에 의해 유발된 당뇨병 증례. 신경정신의학 41 : 942-946
  - 11) Physician's Desk Reference(PDR)(2000) : 54th ed. Oradell NJ ; Medical economics
  - 12) Kay SE, Doery J, Sholl D(2002) : Clozapine associated pericarditis & elevated troponin I. Aust NZ J Psychiatry 36(1) : 143-144
  - 13) Findling RL, McNamara NK, Gracious BL(2000) : Pediatric uses of atypical antipsychotics. Exp. Opin. Pharmacother 1(5) : 935-945
  - 14) Snyder R, Turgay A, Aman M, Binder C, Fisman S, Carroll A, The Risperidone Conduct Study Group (2002) : Effects of Risperidone on conduct and disruptive behavior disorders in children with subaverage IQs. J Am Acad Child Adolesc Psychiatry 41 : 9 : 1026-1036
  - 15) McDougle CJ, Seahill L, McCracken JT, Aman MG, et al(2000) : Research units on pediatric psychopharmacology(RUPP) autism network : Background and rationale for an initial controlled study of risperidone. Psychopharmacology 9(1)201-224
  - 16) McDougle CJ(1999) : American Academy of Child & Adolescent Psychiatry, Annual meeting, Institute 1 : Targets of pharmacotherapy : from signs and symptoms to synapses, Chicago
  - 17) Turgay A, Binder C, Snyder R, Fisman S(2002) : Long-term safety and efficacy of risperidone for the treatment of disruptive behavior disorders in children with subaverage IQs. Pediatrics 110(3) : e34
  - 18) Aman MG, Smedt GD, Derivan A, Lyons B, Findling RL, Risperidone Disruptive Behavior Study Group(2002) : Double-blind, placebo-controlled study of risperidone for the treatment of disruptive behaviors in children with subaverage intelligence. Am J Psychiatry 159 : 1337-1346
  - 19) Fras I, Major LF(1995) : Clinical experience with risperidone(letter). J Am Acad Child Adolesc Psychiatry 34 : 833
  - 20) Lombroso PJ, Seahill L, King RA, Lynch KA, Chappell PB, BS, McDougle CJ and Leckman JF (1995) : Risperidone treatment of children and adolescents with chronic tic disorder : a preliminary report. J Am Acad Child Adolesc Psychiatry 34 : 1147-1152
  - 21) Bruggeman R, van der Linden G, Buitelaar JK, Gericke GS, Hawkridge SM, Temlett JA(2001) : Risperidone versus pimozide in tourette's disorder : A comparative double-blind parallel-group study. J Clin Psychiatry 62 : 1 : 50-56
  - 22) Perry R, Pataki C, Munoz-Silva D, Armenteros J, Silva RR(1997) : Risperidone in children and adolescents with PDD : pilot trial and follow-up. J Child Adolesc Psychopharmacology 7(3) : 167-179
  - 23) McCracken JT, McGough J, et al(Research unit on pediatric psychopharmacology autism network)(2002) : Risperidone in children with autism and serious behavioral problems. N Eng J Med 347:314-321
  - 24) Potenza MN, Holmes JP, Kanes SJ and McDougle CJ(1999) Olanzapine treatment of children, adolescents and adults with pervasive developmental disorders : an open-label pilot study. J Clin Psychopharmacol 19 : 37-44.
  - 25) Fitzgerald KD, Stewart CM, Tawile V, Rosenberg DR(1999) : Risperidone augmentation of serotonin reuptake inhibitor treatment of pediatric obsessive compulsive disorder. J Child Adolesc Psychopharmacology 9(2) : 115-123
  - 26) Findling RL, Kowatch RA, Post RM(2003) : Pediatric bipolar disorder : A handbook for clinicians. Martin Dunitz, London, pp105-117
  - 27) Took KJ, Buch BJ(1996) : Enuresis with combined risperidone and SSRI use. J Am Acad Child Adolesc Psychiatry 35(7)840-841
  - 28) Grothe DR, Calis K, Jacobson L, Kumra S, et al(2000) : Olanzapine Pharmacokinetics in Pediatric and

- Adolescent Inpatients With Childhood-Onset Schizophrenia. *J Clin Psychopharmacology* 20 : 220-225
- 29) **Kemner C, Willemsen-Swinkels SHN, De Jonge M, et al**(2002) : Open-label study of olanzapine in children with pervasive developmental disorder. *Journal of Clinical Psychopharmacology* 22 : 5 : 455-460
  - 30) **Malone RP, Cater J, Sheikh RM, Choudhury MS, Delaney MA**(2001) : Olanzapine versus haloperidol in children with autistic disorder : An open pilot study. *J Am Acad Child Adolesc Psychiatry* 40 : 8 : 887-894
  - 31) **Chang KD, Ketter TA**(2000) : Case report : Mood stabilizer augmentation with olanzapine in acutely manic children. *J Child Adolesc Psychopharmacol* 10(1) : 45-49
  - 32) **Khouzam HR, El-Babalawi F**(2000) : Case report : Treatment of bipolar I disorder in an adolescent with olanzapine. *J Child Adolesc Psychopharmacol* 10(2) : 147-151
  - 33) **Frazier JA, Biederman J, Jacobs TG, Tohen MF, et al**(2001) : A prospective open-label treatment trial of olanzapine monotherapy in children and adolescents with bipolar disorder. *J Child Adolesc Psychopharmacol* 11(3) : 239-250
  - 34) **Powers PS, Santana CA, Bannon YS**(2002) : Olanzapine in the treatment of anorexia nervosa : An open label trial. *Int J Eat Disord* 32 : 146-154
  - 35) **Mehler C, Wewetzer Ch, Schulze U, Warnke A, Theisen F, Dittmann RW**(2001) : Olanzapine in children and adolescents with chronic anorexia nervosa. A study of five cases. *European Child & Adolescent Psychiatry* 10 : 151-157
  - 36) **Karam-Hage M, Ghaziuddin N**(2000) : Olanzapine in tourette's disorder (letter). *J Am Acad Child Adolesc Psychiatry* 39 : 2 : 139
  - 37) **Lavid N, Franklin DL, Maguire GA**(1999) : Management of child and adolescent stuttering with olanzapine : Three case reports. *Ann Clin Psychiatry* 11(4) : 233-236
  - 38) **Ratzoni G, Gothelf D, Brand-Gothelf A, Reidman J, Kikinzon L, Gal G, Phillip M, Apter A, Weizman R**(2002) : Weight gain associated with olanzapine and risperidone in adolescent patients : A comparative prospective study. *J Am Acad Child Adolesc Psychiatry* 41 : 3 : 337-343
  - 39) **Findling RL**(2002) : Use of quetiapine in children and adolescents. *J Clin Psychiatry* 63 (supp 113) : 27-31
  - 40) **McConville B, Arvanitis LA, Wong J, et al**(1998) : Pharmacokinetics, tolerability, and clinical effectiveness of quetiapine fumarate in adolescents with selected psychotic disorders. Poster presented at the annual meeting of the American Psychiatric Association, Toronto, Ont, May 30-June 4
  - 41) **Martin A, Koenig K, Seahill L, et al**(1999) : Open-label quetiapine in the treatment of children and adolescents with autistic disorder. *J Child Adolesc Psychopharmacol* 9 : 99-107
  - 42) **Tanoue Y, Koa S**(1986) : Preliminary study with zotepine, a new antipsychotic drug, in severe behavioral disorders in autistic children. *Intern. Assoc. Child Adolescent Psychiatry Allied Prof(IACAPAP)*, 11th, International Congress, Paris, France, p157
  - 43) **Bazire S** : Psychotropic drug directory 2000(2000) : The professional's pocket handbook and aide memoire. Quay books, Snow Hill
  - 44) **Remschmidt H**(2001) : Schizophrenia in children and adolescents. Cambridge University Press, Cambridge
  - 45) **Leclercq Y, Azorin M, Bottai T, Dalery J et al** (2001) : Consensus on the practical use of amisulpride, an atypical antipsychotic, in the treatment of schizophrenia. *Neuropsychobiology* 44 : 41-46
  - 46) **Leucht S, Pitschel-Walz G, Engel RR, Kissling W** (2002) : Amisulpride, an usual "atypical" antipsychotic : A meta-analysis of randomized controlled trials. *Am J Psychiatry* 159 : 2 : 180-190
  - 47) **Martin A, Seahill L, Charney DS, Leckman JF** (2003) : Pediatric psychopharmacology : Principle & Practice. Oxford University Press, NY. p554
  - 48) **Pailere-Martinot ML, Leclercq Y, Martin JH, Aubin F**(1995) : Improvement of some schizophrenic deficit symptoms with low dose of amisulpride. *Am J Psychiatry* 152 : 130-133
  - 49) **Danion JM, Rein W, Fleurot O(Amisulpride Study Group)**(1999) : Improvement of schizophrenic patients with primary negative symptoms treated with amisulpride. *Am J Psychiatry* 156 : 610-616
  - 50) **Sallee FR, Kurlan R, Goetz CG, Singer H, Seahill L, Law G, Dittman VM, Chappell PB**(2000) : Ziprasidone treatment of children and adolescents with Tourette's syndrome : A pilot study. *J Am Acad Child Adolesc Psychiatry* 39 : 292-299
  - 51) **Bezchlibnyk-Butler KZ, Jeffries JJ**(2001) : Clinical Handbook of psychotropic drugs. 11th ed, Hogrefe & Huber Publishers, Seattle, pp66-67

## NEW DRUG THERAPY IN CHILD AND ADOLESCENT PSYCHIATRY ATYPICAL ANTIPSYCHOTICS

Geon Ho Bahn, M.D., PhD.

*Department of Neuropsychiatry, KyungHee University Medical School, Seoul*

Conventional antipsychotics are commonly used to treat children and adolescents suffered from schizophrenia to other neuropsychiatric conditions. Regrettably, studies for typical antipsychotics report high rates of sedation, orthostatic hypotension, and extrapyramidal side effects. Over the past few years, atypical antipsychotics have been prescribed for use in adults with psychotic symptoms. Child psychiatrists have begun using these drugs to children and adolescents hoping safe and better alternatives to the conventional antipsychotics. However, there is not enough short-term and almost no long-term data about atypical antipsychotics for pediatric patients. Therefore, the purpose of this article is to review what is known about the use of the atypical antipsychotics in young patients. To do so, an appropriate approach to the use of these drugs in child and adolescent patients may be offered.

KEY WORDS : Atypical antipsychotics · Child and adolescent.