

## 급성 조증 입원환자에 대한 항조증약물의 처방 경향\*

이소영\*\* · 정한용\*\*† · 전용호\*\*

## Trends in the Prescribing of Antimanic Agents for Acute Manic Inpatients\*

So Young Irene Lee, M.D., Ph.D.,\*\* Han-Yong Jung, M.D., Ph.D.,\*\*† Yong-Ho Jun, M.D.\*\*

## ABSTRACT

**O**bjective : This study was performed to investigate the prescribing patterns of antimanic agents in the treatment of acute bipolar disorder inpatients in Korea from 1990 through 2000. The results will serve as the basic data for the practice guideline for the pharmacotherapy of bipolar disorder patients in Korea.

**M**ethod : Retrospective chart review of bipolar disorder inpatients of Soonchunhyang Medical Center in Seoul and Chun - An was conducted for each of the year 1990, 1995, and 2000. The following data are collected ; 1) demographic data, 2) history of bipolar disorder, 3) length of hospital stay, 4) detailed drug titration records of antimanic agents and antipsychotic agents.

**R**esults : During the last decade, the frequency of lithium monotherapy was decreased obviously. Instead, more than half of the patients in 2000 were on combination therapy of lithium and anticonvulsants. Lithium - valproate combination was the preferred strategy and the use rate of carbamazepine has been decreased. In addition, most of the patients were given antipsychotic agents during the last 10 years. And recently, atypical antipsychotics were increasingly prescribed. These changes in the field of pharmacology of bipolar disorder have resulted neither in shorter hospital stays nor lower dosages of concurrent neuroleptics.

**C**onclusions : The results indicate the trends in the prescribing of antimanic agents for the treatment of bipolar disorder in Korea across the past 10 years. Mostly, the change seems to correspond to the international practice guideline. More systematic research is needed to find out the clinical benefits of the anticonvulsants in the real practice of treatment of bipolar disorder.

**KEY WORDS** : Bipolar disorder · Pharmacotherapy · Antimanic agents · Antipsychotic agents.

	서	론	가	, 1970	Baastrop <sup>2)</sup>
				lithium	
1949	John F. Cade <sup>1)</sup>	lithium			, lithium

2001

Department of Psychiatry, College of Medicine, Soonchunhyang Bucheon Hospital, Soonchunhyang University, Gyeonggi, Korea

†교신저자 : , 420 - 021 1174  
) (032) 621 - 5017, ) (032) 621 - 5018 E - mail) hanyjung@schbc.ac.kr



가 (mg/day) <sup>23)</sup> 가 72 ,  
 32.8 (SD=12.2) .  
 1 27.1 (SD=11.1) 3.2  
 (SD=4.2) ( 1).  
 1990 27 , 1995 57 , 2000 54

**3. 통계처리**  
 1990 , 1995 , 2000  
 Tukey  
 (one - way ANOVA) ,  
 (chi - square test) , ( 2). , 1990 lithium  
 가 (63.0%), lithium  
 Pearson 가 carbamazepine (25.9%)  
 SPSS 10.0 for Windows lithium 가 carbamazepine  
 p<0.05 (11.1%) . 1995 li-  
 thium 가 (71.9%), li-  
 thium 가 carbamazepine (21.1%)  
 , carbamazepine  
 가 2 (3.5%), lithium divalproex  
 가 2 (3.5%) . lithium

**결 과**

**1. 인구통계학적 특성**  
 138 가 66 가 2 (3.5%) lithium divalproex  
 가 2 (3.5%) . lithium

**Table 1.** Demographic characteristics of subjects

	Total	1990	1995	2000
Number of patients	138	27	57	54
Mean age(year)*	32.8 ± 12.2	27.0 ± 8.8	33.2 ± 13.0	35.4 ± 11.9
Male/female	66/72	16/11	24/33	26/28
Mean age of onset(year)*	27.1 ± 11.1	25.3 ± 7.7	27.2 ± 11.0	28.1 ± 11.6
Number of hospitalization*	3.2 ± 4.2	2.1 ± 2.8	3.2 ± 4.0	3.9 ± 4.9

\* : values are means ± SD

**Table 2.** Antimanic agents usage for acute manic inpatients across past 10 years

Prescribing patterns	1990(N=27)	1995(N=57)	2000(N=54)
Lithium monotherapy	17(63.0%)	41(71.9%)	19(35.2%)
Lithium+switch to carbamazepine	3(11.1%)	-	-
Lithium+carbamazepine add on	7(25.9%)	12(21.1%)	4( 7.5%)
Carbamazepine monotherapy	-	2( 3.5%)	-
Divalproex monotherapy	-	-	5( 9.3%)
Divalproex+lithium add on	-	1( 1.8%)	4( 7.4%)
Lithium+divalproex add on	-	1( 1.8%)	20(37.0%)
Lithium+lamotrigine add on	-	-	1( 1.9%)
Lithium+clonazepam add on	-	-	1( 1.9%)

2000 35.2% lithium 가 (48.3%), lithium 가 divalproex (37.0%) carbamazepine 가 (7.5%), 2000 가 2000 53.7% divalproex가 9 (16.7%) divalproex가 2000 lith- ium lamotrigine clonazepam olanzapine, clozapine 가 1 54 11 (20.8%) 가 (3). 1990 27 17 (63%), 1995 57 43 (75.4%) 가, 1990 , 1995 , 2000 2000 54 24 (44.5%) . 1990 1995 76.8% , 2000 18.9% 1990 37%, 1995 24.6%, 2000 55.6% 1995 1/4 가 1990 17.9% , 1995 23.2% 가 2000 60.4% 1990 1995 가 2~3 가 chlorpromazine 가 136 669.9 ± 514.3mg/day 가 778.2 ± 583.9mg/day, 가 566.4 ± 415.9mg/day 가

**3. 항정신병약물의 사용**

138 136 (98.5%) 가

**Table 3.** Frequency analysis of monotherapy & polypharmacy of antimanic agents vs time span

	1990(N=27)	1995(N=57)	2000(N=54)
Monotherapy	17(63.0%)	43(75.4%)	24(44.4%)
Polypharmacy	10(37.0%)	14(24.6%)	30(55.6%)

<sup>2</sup>=70.68, df=26, p=0.004

**Table 4.** Antipsychotic agents usage for acute manic inpatients across past 10 years

Augmented antipsychotics	1900		1995		2000	
	N	%	N	%	N	%
Chlorpromazine	23	85.2	42	75.0	10	18.9
Chlorpromazine + haloperidol	2	7.4	7	12.5	20	37.7
Haloperidol			6	10.7	11	20.8
Chlorpromazine + trifluoperazine	2	7.4				
Thioridazine			1	1.8		
Haloperidol + thioridazine					1	1.9
Atypical antipsychotics	Clozapine				6	11.3
	Olanzapine				3	5.7
	Risperidone				2	3.8

<sup>2</sup>=70.68, df=26, p=0.000

(p=0.016). 1990 4. 입원기간  
 , 1995 , 2000 49.1 ± 31.0 ,  
 ( 5). 1990 58.1 (SD=34.8), 1995  
 48.8 (SD=31.4), 2000 35.6 (SD=  
 19.4) ,  
 , chlorpromazine 1990 (p=0.076)( 6).  
 600.0 ± 277.1mg/day, 1995 482.7 ±  
 293.2mg/day, 2000 226.0 ± 198.1mg/  
 day (p=0.003), haloperidol ch-  
 lorpromazine 1990 rbamazepine (N=77) 46.3 ± 28.0 , lithium ca-  
 800.0 ± 0.0mg/day 가 1995 1471.4 ± , lithium divalproex  
 293.2mg/day 가 , 2000 226.0 ± (N=26) 60.2 ± 38.0  
 198.1mg/day (p= ,  
 0.017). Haloperidol 1995 , 가 (N=84)  
 1316.7 ± 544.7mg/day 가 2000 522.7 ± 45.1 ± 27.6  
 300.0mg/day (p=0.001). (N=54)가 56.1 ± 34.4  
 (p=0.04)  
 , 가 가  
 (N=82) 577.2 ± 428.8mg/day .  
 (N=54) , chlorpromazine haloperidol  
 가 821.2 ± 595.7mg/day ,  
 (p=0.006) chlorpromazine haloperidol  
 1995 가  
 가 . (p=0.005)( 6).  
 chlorpromazine 가

**Table 5.** Comparison of mean dosages of augmented antipsychotic agents

	1990	1995	2000	p-value
	Mean ± S.D.	Mean ± S.D.	Mean ± S.D.	
<b>Total</b>				
Number of patients	28	57	54	
Dosage(mg/day)	682.1 ± 378.6	689.7 ± 530.0	642.6 ± 564.4	ns*
<b>Preferred prescription</b>				
<i>Chlorpromazine</i>				
Number of patients	23	42	10	
Dosage(mg/day)	600.0 ± 277.1	482.7 ± 293.1	226.0 ± 198.1	0.003*
<i>Chlorpromazine +haloperidol</i>				
Number of patients	2	7	20	
Dosage(mg/day)	800.0 ± 0.0	1471.4 ± 537.6	732.5 ± 563.4	0.017*
<i>Haloperidol</i>				
Number of patients	-	6	11	
Dosage(mg/day)	-	1316 ± 544.7	522.7 ± 300.0	0.001**

\* : statistical significance were tested by oneway analysis of variance among 1990, 1995, and 2000 groups.

\*\* : statistical significance were tested by independent t-test between 1995 and 2000 groups.

( =0.378, p=0.01).

고 찰

2

10

DSM

zepine

1990

1995

2000

lithium

carbama-

3 1(37%) 가

1995 4 1(24.6%)

2000 7.5%

1990 , 1995 , , carbamazepine

2000

**Table 6.** Comparison of length of stay for inpatients with bipolar disorder

	1990 mean ± S.D.	1995 mean ± S.D.	2000 mean ± S.D.	p-value
<b>Total</b>				
Number of patients	27	57	54	
Length of stay(day)	58.1 ± 34.8	48.8 ± 31.4	35.6 ± 19.4	ns*
<b>Lithium</b>				
Number of patients	17	41	19	
Length of stay(day)	49.1 ± 25.3	50.4 ± 31.3	35.1 ± 19.5	-
<b>Lithium + carbamazepine</b>				
Number of patients	10	12	4	
Length of stay(day)	78.7 <sup>a</sup> ± 39.5	51.9 ± 35.5	39.2 ± 26.9	-
<b>Lithium + divalproex</b>				
Number of patients	-	2	25	
Length of stay(day)	-	94.5 <sup>b</sup> ± 62.9	49.2 <sup>b</sup> ± 27.8	-
<b>Chlorpromazine</b>				
Number of patients	23	42	10	
Length of stay(day)	54.7 ± 32.2	46.8 ± 32.1	29.7 ± 20.8	ns*
<b>Chlorpromazine + haloperidol</b>				
Number of patients	2	7	20	
Length of stay(day)	61.0 ± 16.9	87.4 ± 34.8	44.8 ± 23.9	0.005*
<b>Haloperidol</b>				
Number of patients	-	6	11	
Length of stay(day)	-	43.5 ± 24.6	41.2 ± 28.4	ns**

<sup>a</sup> : significantly different by oneway analysis of variance within 1990 group (p=0.025).

<sup>b</sup> : not significantly different by oneway analysis of variance within 1995 and 2000 group.

\* : statistical significance were tested by oneway analysis of variance among 1990, 1995, and 2000 groups.

\*\* : statistical significance were tested by independent t-test between 1995 and 2000 groups.

1990 (3.6%)  
 1995 divalproex가 2000 (53.7%).  
 1989 1994 1995 2000  
 5  
 3 1 (35.2%)  
 3 2  
 lithium  
 (87%)  
 10  
 therapeutic index가  
 divalproex  
 lithium  
 carbamazepine  
 divalproex  
 가  
 26)  
 1949 lithium  
 가 1)  
 1971 lithium  
 26)  
 Moncrieff<sup>15)</sup>  
 carbamazepine lithium  
 가  
 valproex  
 1995 5  
 1995  
 divalproex 가가  
 , 2000 divalproex가  
 가 16.7% , lithium  
 57 2 (3.6%)  
 가 divalproex 가 37.0% 가  
 5 2000 가  
 가 divalproex  
 lithium 가 diva-  
 lproex가  
 1995  
 2000 . Fenn <sup>25)</sup> 1989  
 1994 가  
 , lithium 1989  
 84% 1994 43% di-  
 valproex lithium 1989  
 , 1994 25% 가 . 10  
 carbamazepine lithium carbamazepine  
 24% 18% Fenn  
 lithium <sup>25)</sup>

carbamazepine 1999 90.7%가

2002 31)

가 lithium divalproex Janicak 27)

divalproex가 가

가 lithium 가 가

carbamazepine Post 28)

lithium hen 34)

32)33) , Zarate To-

lithium 1990 100%

1995 96.7% 2000

84.4%

2000 divalproex가 21) 가

가 가

5 4 lithium 가 가

lithium

50 1990 1995 가 chlo-

first - line therapy rpromazine 가

Moncrieff 15) 가 haloperidol 1995 23.2%

2000 60.4% 가

10 가

가

가

가 가

가

가

가 35)36) 1996 North

(98.5%)가 Carolina 61 29)

1 75%가

10 haloperidol 가

1975

Shopsin 37) haloperidol ch-

lorpromazine 가

, Chou 29) 1990 3

, 92% 가

, Tohen 30) 1981



38) 가 , 2002 300.0mg/day, 732.5 ± 563.4mg/day), 가

olanzapine .

2000 5 1 가 , 39)

가 10

가 , chlorpromazine 가

. Chlorpromazine 가 ,

가 600~700mg/day ,

가 .

가 , Tohen 36)

. , ,

. Baldessarini 23) haloperidol .

가 chlorpromazine 가 ch-

lorpromazine 가 3.45 , , ,

가

가 가 1995 haloperidol 가 , , ,

haloperidol chlorpromazine 가 ,

chlorpromazine 가

(1316 ± 544.7mg/day, 1471.4 ±

537.6mg/day).

가

가

가

haloperidol , 2000

lorpromazine haloperidol ch-

zine 가 1995 chlorproma-

(522.7 ±

중심 단어 :

---

참고문헌

---

1. Cade JF. Lithium salts in the treatment of psychotic excitement. Med J Aust 1949;2:349-352.

2. Baastrup PC, Poulsen JC, Schou M, Thomsen K, Amdisen A. Prophylactic lithium: double blind discontinuation in manic-depressive and recurrent-depressive disorders. Lancet 1970;15:2:326-330.

3. Schou M. Lithium prophylaxis in manic-depressive psy-

- choses. *Nervenarzt* 1971;42:1-10.
4. Schou M. Prophylactic lithium maintenance treatment in recurrent endogenous affective disorders. In: *Lithium. Its role in psychiatric research and treatment*. Ed by Gershon S, Shopsin B, New York, Plenum Press; 1973. p.269-293.
  5. Chou, JC. Recent advances in treatment of acute mania. *J Clin Psychopharmacol* 1991;11:3-21.
  6. Schou M. Phases in the development of lithium treatment in psychiatry. In: *The neurosciences: paths of discovery II*. Ed by Samson F, Adelman G, Boston, MA, Birkhauser; 1992. p.149-166.
  7. Lenox RH, Manji HK. Lithium. In: *Textbook of psychopharmacology*. Ed by Schatsberg AF and Nemeroff CB, Washington DS, American Psychiatric Press;1998. p.399-400.
  8. Cookson J. Lithium: balancing risks and benefits. *Br J Psychiatry* 1997;171:120-124.
  9. Takezaki H, Hanaoka M. The use of carbamazepine (Tegretol) in the control of manic-depressive psychosis and other manic, depressive states. *Clinical Psychiatry* 1971; 13:173-182.
  10. Keck PE, McElroy SL. Antiepileptic drugs. In: *Textbook of psychopharmacology*. Ed by Schatsberg AF and Nemeroff CB, Washington DS, American Psychiatric Press;1998. p.437.
  11. Lambert PA, Cavaz G, Borselli S, Carbel S. Action neuropsychotrope d'un nouvel anti-épileptique: le Depamide. *Ann Med Psychol* 1966;1:707-710.
  12. Dunn RT, Frye MS, Kimbrell TA, Denicoff KD, Leverich GS, Post RM. The efficacy and use of anticonvulsants in mood disorders. *Clin Neuropharmacol* 1998;21: 215-235.
  13. Goodman FK, Jamison KR. Biochemical and pharmacological studies. In: *Manic-depressive illness*. Ed by Goodwin FK Jamison KR, New York, Oxford University Press;1990. p.416-502.
  14. Goodwin GM. Lithium revisited. A reply. *Br J Psychiatry* 1995;167:573-574.
  15. Moncrieff J. Lithium revisited. A re-examination of the placebo-controlled trials of lithium prophylaxis in manic-depressive disorder. *Br J Psychiatry* 1995;167:569-574.
  16. Moncrieff J. Lithium: evidence reconsidered. *Br J Psychiatry* 1997;171:113-119.
  17. Moncrieff J. Forty years of lithium treatment. *Arch Gen Psychiatry* 1998;55:92-93.
  18. Lambert PA, Venaud G. Comparative study of valproamide versus lithium as prophylactic treatment in affective disorders. *Nervure* 1994;17:1-9.
  19. Bowden CL. Predictors of response to divalproex and lithium. *J Clin Psychiatry* (suppl 3) 1994;56:25-30.
  20. Denicoff KD, Smith-Jackson EE, Disney ER, Ali SO, Leverich GS, Post RM. Comparative prophylactic efficacy of lithium, carbamazepine, and the combination in bipolar disorder. *J Clin Psychiatry* 1997;154:1456-1458.
  21. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders 3rd rev ed*, Washington, DC, American Psychiatric Press;1987.
  22. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders 4th ed*, Washington, DC, American Psychiatric Press;1994.
  23. Baldessarini RJ, Katz B, Cotton P. Dissimilar dosing with high-potency and low-potency neuroleptics. *Am J Psychiatry* 1984;141:748-752.
  24. Mukherjee S. Mechanisms of the Antimanic Effect of Electroconvulsive Therapy. *Convuls Ther* 1989;5:227-243.
  25. Fenn HH, Robinson D, Luby V, Dangel C, Buxton E, Beattie M, et al. Trends in pharma-cotherapy of Schizoaffective and bipolar affective disorders: a 5-year naturalistic study. *Am J Psychiatry* 1996;153:711-713.
  26. Lennkh C, Simhandl C. Current aspects of valproate in bipolar disorder. *Int Clin Psychopharmacol* 2000;15:1-11.
  27. Janicak PG, Javaid JI, Sharma RP, Leach A, Dowd S, Davis JM. A two-phase, double-blind randomized study of three haloperidol plasma levels for acute psychosis with reassignment of initial non-responders. *Acta Psychiatr Scand* 1997;95:343-350.
  28. Post RM. Comparative pharmacology of bipolar disorder and schizophrenia. *Schizophr Res* 1999;39:153-158.
  29. Chou JC, Zito JM, Vitrai J, Craig TJ, Allingham BH, Czobor P. Neuroleptics in acute mania: a pharmacoepidemiologic study. *Ann Pharmacother* 1996;30:1396-1398.
  30. Tohen M, Zhang F, Taylor CC, Burns P, Zarate C, Sanger T, et al. A meta-analysis of the use of typical antipsychotic agents in bipolar disorder. *J Affect Disord* 2001;65:85-93.
  31. American Psychiatric Association. *Practice Guidelines for the Treatment of Psychiatric disorders. Compendium 2002*, Washington, DC, American Psychiatric Press;2002.
  32. Levine J, Chengappa KN, Brar JS, Gershon S, Yablonsky E, Stapf D, et al. Psychotropic drug prescription patterns among patients with bipolar I disorder. *Bipolar Disord* 2000;2:120-130.
  33. Blanco C, Laje G, Olfson M, Marcus SC, Pincus HA. Trends in the treatment of bipolar disorder by outpatient psychiatrists. *Am J Psychiatry* 2002;159:1005-1010.
  34. Zarate CA Jr, Tohen M. Antipsychotic drug treatment in first-episode mania: a 6-month longitudinal study. *J Clin Psychiatry* 2000;61:33-38.
  35. Zarate CA Jr, Tohen M, Baldessarini RJ. Clozapine in severe mood disorders. *J Clin Psychiatry* 1995;56:411-417.
  36. Tohen M, Zarate CA Jr. Antipsychotic agents and bipolar disorder. *J Clin Psychiatry* (Suppl 1) 1998;59:38-48.
  37. Shopsin B, Gershon S, Thompson H, Collins P. Psychoactive drugs in mania. A controlled comparison of lithium carbonate, chlorpromazine, and haloperidol. *Arch*

- Gen Psychiatry 1975;32:34-42.
38. Tohen M, Jacobs TG, Grundy SL, McElroy SL, Banov MC, Janicak PG, et al. Efficacy of olanzapine in acute bipolar mania: a double-blind, placebo-controlled study. The Olanzapine HGGW Study Group. Arch Gen Psychiatry 2000;57:841-849.
39. Rifkin A, Doddi S, Karajgi B, Borenstein M, Munne R. Dosage of haloperidol for mania. Br J Psychiatry 1994; 165:113-116.