Bulletin of the *Transilvania* University of Braşov
Series VI: Medical Sciences • Vol. 4 (53) No. 1 - 2011

PATTERNS OF ANTIPSYCHOTIC USE MODEL IN TREATMENT OF BIPOLAR I DISORDER – A 12 MONTHS OBSERVATIONAL STUDY

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Abstract: *Although bipolar disorder is one of the most disabilitating of all psychiatric illness in terms of risk for suicide, need for hospitalization, and suffering, the available pharmacologic agents for its treatment, until relatively recently, have been quite limited. Although some estimates suggest that the lifetime prevalence of bipolar disorder in the world wide is between 1% and 1.5%, this rate would be higher if patients with bipolar spectrum disorders beyond bipolar I and II disorder were included. The public health importance of this disease is heightened by the high rate of suicidality and the high economic toll it can take, including lost work days and cost of care, as well as poor financial decision-making characteristics of the manic phase of the illness. We tried to evaluate the current practice in treatment of acute manic episode in Bipolar I Disorder.*

Key words: *antipsychotics, bipolar disorder.*

1. Introduction

Bipolar disorders are prevalent, major psychiatric illnesses with high rates of morbidity, comorbidity, disability, and mortality, even early in the course of the illness [1–3].

Over recent decades, the proportion of persons from the general population exposed to psychotropic drugs has dramatically increased in developed countries [4]. Although the efficiency of the antipsychotic treatment has been scientifically documented in many clinical research studies, there are still insufficient data regarding the real use of antipsychotics. in the current practice among the hospitalized patients with bipolar disorders.

The first-generation antipsychotics such as haloperidol have clear efficacy in the treatment of acute mania and their long-term use in bipolar disorder is no longer limited, despite concerns about their side effects [5].

The recent studies showed that atypical antipsychotics have been used increasingly in the management of psychiatric disorders, particularly for acute mania.

These agents have been thought to be generally better tolerated and to have lower rates of extrapyramidal symptoms (EPS) than the first generation, "typical" antipsychotics.

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2. Method

The study was a 12-months non-interventional and observational study, conducted in 2 psychiatric departments for acute patients in Psychiatry and Neurology Hospital Brasov, between January 2010 and December 2010. Patients with age above 18 years were considered for entry into the study if they were eligible according to criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) as having Bipolar I Disorder in acute manic episode.

Investigators independent of current doctors were instructed to record all the data about pharmacotherapy that had been prescribed in the current practice at day of discharge. We first determined overall numbers and proportions of patients prescribed the major classes of drugs. Statistics were used to test for differences in the distribution of categorical variables across the time period. T tests were used to examine the differences among continuous variables. Stepwise logistic regressions were conducted to examine patient demographic and clinical factors associated with medication regimens.

3. Results

The study gathered 79 patients (45 female and 34 male) diagnosed with Bipolar I Disorder in severe manic episode. The prescribed psychotropics used in treatment of patients with Bipolar I Disorder are presented in Table 1.

93% (73 patients) were treated with antipsychotics which represent in increasing percentage in strength accord with literature. The use of anticonvulsants is above 80%, and these trends may be related to the ease of prescription of valproic acid, its tolerability, and the increased awareness among psychiatrists and patients regarding the efficacy of valproic acid.

Classes of psychotropics used in treatment of manic episode Table 1

Characteristics	WOMEN		MEN	
	N	%	N	%
Atypical antipsychotics	23	52	18	57
Conventional antipsychotics	18	40	14	44
Benzodiazepines	37	83	26	82
Mood stabilizers	36	80	28	88
Average age (years)	46,6		49,67	
Average onset age (years)	35,71		36,85	
Average hospitalization (days)	26,7		25,88	

For demographic statistics, we calculated the mean age, the percentage of women, and the distribution of groups according to their home base (urban or rural). We calculated the percentages of patients receiving mood stabilizers or antipsychotics, mood stabilizers alone, antipsychotics alone, or both antipsychotics and mood stabilizers. For patients receiving antipsychotics, we calculated the percentages receiving first-generation and second-generation antipsychotics. For patients receiving mood stabilizers, we calculated the percentages receiving pharmacotherapy with older anticonvulsants, and with newer anticonvulsants. We assessed also variations in pharmacotherapy by age, gender, and education. We calculated the percentage of patients receiving either mood stabilizers or antipsychotics for each of these groups.

In the class of atypical antipsychotics, the most frequently used in treatment of women with Bipolar I Disorder were quetiapine 30%, olanzapine 22% and clozapine 5%. In the men cases, the proportion of patients treated atypical was 32% for olanzapine, 16% for quetiapine and 9% for clozapine. We observed the fact that clozapine was used more frequent in the patients with low average of age and age of onset both in men and women statistically significant ($p<0,05$).

Type of antipsychotics Table 2

Characteristics		Atypical antipsychotics			Conventionals
		olanzapine	quetiapine	clozapine	haloperidol
W O M E N	N	9,00	12,00	2,00	18,00
	%	22,00	30,00	5,00	43,00
	Average age (years)	43,44	49,00	39,50	48,55
	Average age at onset (years)	32,00	35,50	25,50	35,90
	Average hospitalization (days)	29,55	24,83	28,50	28,75
M E N	N	10,00	5,00	3,00	14,00
	%	32,00	16,00	9,00	43,00
	Average age (years)	47,90	55,00	45,60	50,43
	Average age at onset (years)	35,70	41,20	30,00	40,81
	Average hospitalization (days)	24,10	21,40	27,60	24,50

There were no differences between men and women regarding the average of hospitalization (25,88 days vs. 26,7).

An important number of clinical trials have demonstrated that quetiapine is effective in the treatment of acute mania. quetiapine (up to 800 mg/day), demonstrated significant improvement as early as day 4 [6].

One of the interesting findings was that patients with Bipolar I Disorder treated with haloperidol had the highest age of onset in women group (35,9 years).

There were no differences between women and men regarding conventional neuroleptics treatment, the percentage was quite similar (43%). The average of onset of the illness was higher in men group treated with atypical antipsychotics comparative with women group, statistically significant ($p<0,05$).

It is important to notice that conventional neuroleptics were still a used in high proportion despite their side-effects.

Although clozapine represent the last option in treatment of severe manic episode, it is used often in cases with the age of onset below 30 years of age and surprisingly in the treatment of young women (average years of onset 25,5).

4. Conclusions

This study examined the prescription patterns in a sample of patients treated for Bipolar I Disorder hospitalized for an acute manic episode. The percentage of patients receiving pharmacotherapy with antipsychotics increased over time.

There was no significant change in the overall proportion of patients who were prescribed antipsychotics. However, over the years, there was a decrease in the use of conventional antipsychotics and a corresponding increase in the use of the newer antipsychotics, probably related to their more benign side effect profile and the mood-stabilizing properties of some of these medications.

Despite that fact, conventional neuroleptics are still used in a significant proportion in treatment of manic episode (above 40%). Benzodiazepines were prescribed in almost 80% of the cases and were often prescribed in combination with a mood stabilizer.

An important difference between our findings and other published data on pharmacy patterns for bipolar disorder in privately insured populations is the greater use of antipsychotics compared with mood stabilizers in our sample. Furthermore, we found that use of antipsychotic monotherapy in treatment of manic episode is very rare in our study.

Consistent with prior studies, use of combined regimens was common. This may reflect the complexity of managing bipolar disorder. There are data that suggest that combinations of mood stabilizers [7], or a mood stabilizer in conjunction with an antipsychotic [8-10], may have higher efficacy than either medication alone. However, the extent and variety of combinations documented in this study suggest that there is a substantial discrepancy between evidence-based treatments and routine clinical practice in the treatment of bipolar disorder. Identification of patient subgroups that may benefit from these combined regimens is an important area for future research.

References

1. Goodwin, F.K., Jamison, K.R.: *Manic-Depressive Illness*. New York, Oxford University Press, 2000.
2. Tohen, M., Zarate, C.A Jr., Hennen, J., et al.: *McLean-Harvard First-Episode Mania Study: prediction of recovery and first recurrence*. In: American Journal of Psychiatry 160 (2003):2099–2107.
3. Tondo, L., Isacsson, G., Baldessarini, R.J.: *Suicide in bipolar disorder: risk and prevention*. In: CNS Drugs 17 (2003) : 491–511.
4. Kessler, R.C., Chiu, W.T., Demler, O., et a.l: *Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey replication*. In: Archives of General Psychiatry 62 (2005): 617–627.
5. Pincus, H.A., Tanielian, T.L., Marcus, S.C. et al.: *Prescribing trends in psychotropic medications: primary care, psychiatry, and other medical specialties.* In: JAMA 1998; 279:526–531.
6. Thas, M.E., Macfadden, W., Weisler, R.H. et al.: *Efficacy of quetiapine monotherapy in bipolar I and II depression: a double-blind, placebo-controlled study (the BOLDER II study*). In: J Clin Psychopharmacol 2006; 26:600–609.
7. Miklowitz, D.J., George, E.L., Richards, J.A., Simoneau, T.L., Suddath, R.L.: *A randomized study of family-focused psychoeducation and pharmacotherapy in the outpatient management of bipolar disorder*. In: Arch Gen Psychiatry 2003; 60:904–912.
8. Geddes, J.R., Goodwin, G.M., Rendell, J. et al.: *Lithium plus valproate combination therapy versus monotherapy for relapse prevention in bipolar I disorder (BALANCE): a randomised open-label trial*. In: Lancet 2010; 375:385–395.
9. Derry, S., Moore, R.A.: *Atypical antipsychotics in bipolar disorder: systematic review of randomised trials*. In: BMC Psychiatry 2007; 7:40.
10. Bowden, C.L., Calabrese, J.R., Mcelroy, S.L. et al.: *A randomized, placebo-controlled 12-month trial of divalproex and lithium in treatment of outpatients with bipolar I disorder. Divalproex Maintenance Study Group*. In: Arch Gen Psychiatry 2000; 57:481–489.