

ORIGINAL ARTICLE

OUTPATIENT DRUG PRESCRIBING PATTERN FOR BIPOLAR
DISORDER PATIENTS IN SOUTHERN THAILAND

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Abstract

Objective: To examine the psychotropic prescribing pattern among Thai bipolar disorder patients in southern Thailand and to compare results with other studies in developed countries and the study conducted in Bangkok, central Thailand. **Method:** All clinical outpatients records of bipolar patients who attended the psychiatric clinic of Songklanagarind Hospital were systematically reviewed. **Results:** There were 298 patients during the study period from January to March 2003. Nearly half of the patients (48.6%) were prescribed mood stabilizers, with lithium (35.2%) and valproate (13.4%) being the two most common drugs. The other half (48.6%) were prescribed antidepressants of which nortriptyline and the generic form of fluoxetine were prescribed in nearly equal numbers. Antipsychotics were also prescribed in about half of the patients (43.3%). For those who received antipsychotics, 93.0% received FGAs; only 6 patients (4.7%) received an SGA. **Conclusion:** This study shows rather similar prescribing patterns as compared to those of reports from developed countries. The exception was our clinicians' prescribing of more FGAs, which was a similar finding to that of the study from Bangkok. Further study has been recommended to find out whether prescribing patterns will change in the future. *ASEAN Journal of Psychiatry, Vol.10, No.2, July – Dec 2009: XX XX*

Key words: Prescribing pattern, bipolar disorder, Thailand

Introduction

Many drugs or drug groups have been prescribed in the treatment of bipolar disorder such as lithium, anticonvulsants (valproate, carbamazepine, lamotrigine) and recently the second generation antipsychotics (SGAs) [1]. The expanding varieties of drug treatment for this illness have confused some clinicians and also caused the increase use of medication. [2] Many studies have found that most bipolar

patients receive polypharmacy more than monotherapy [3-5]. Although numerous treatment guidelines have been published in the hope of solving these problems [6-9], changing the prescribing patterns of clinicians remains challenging.

Prescribing psychotropic medication is unlike prescribing other drugs because there are many factors involved and variations of prescribing patterns have been observed [10]. It was found that

bipolar African Americans, even when demographically similar to white patients, were more likely to receive maintenance treatment via the first generation antipsychotics (SGAs) despite the risk for neuroleptic –induced tardive dyskinesia [11]. There have been other studies on drug prescribing for bipolar patients in developed countries [3-5, 12] however, only one study concerning this topic in Thailand has ever been published and that study was conducted in Bangkok [13]. Therefore the objective of this report was to examine the prescribing of medications in the treatment of bipolar disorder at the outpatient clinic of Songklanagarind Hospital which is the only university hospital in southern Thailand ,and to compare our results with those from the study conducted in Bangkok [13] and others in developed countries [3-5, 12].

Methods

All clinical outpatient records of bipolar patients aged over 15 who attended the psychiatric clinic of Songklanagarind Hospital between 1 January 2003 and 31 March 2003 were examined. All patients were diagnosed by using the ICD-10 criteria. Relevant patient information such as gender, age , ethnicity and data concerning psychotropic prescribing patterns such as type of medication, route of administration, dose and frequency were collected. Data on illness factors such as phase of treatment, duration of illness and compliance to medication were not collected as the primary focus of this

research was not to study these aspects but to audit the psychotropic prescribing patterns in our hospital.

Data were entered into Excel spreadsheets and analyzed using SPSS version 11.0. Categorical data were described in number and percentage, where as continuous data were presented as mean \pm standard deviation (SD) and median (range). The chi-square (χ^2) test was used for the analysis of discrete data. In order to minimize the likelihood of type I error (given the number of comparisons performed), the alpha level required to demonstrate significance was set at 0.01. Post hoc analyses were conducted using Tukey's HSD test. This study was approved by the Ethics Committee, Faculty of Medicine, Prince of Songkla University.

Results

In total, 1751 patients attended the outpatient psychiatric clinic during the study period and 1750 of them had meaningful data for analysis. Of the 1750 cases, only 17.0% (n = 298) were diagnosed with bipolar disorder (BD). The proportion of females in the sample was 61.1% (n = 182). Patients within the age range of 25-54 comprised 70.2 % of the total sample. Regarding the diagnostic type of BD, unspecified type was predominant (47.9%). Table 1 shows characteristics of the studied population.

Table 1 Characteristics of bipolar disorder patients

Characteristics		N	%
Sex	Female	182	61.1
	Male	116	38.9
Age (year)	15-24	39	13.1
	25-34	59	19.8
	35-44	72	24.2
	45-54	78	26.2
	55-64	34	11.4
	> 64	16	5.3
Ethnicity	Thai	266	89.3
	Muslim	28	9.4
	Chinese	4	1.3
Type of diagnosis	manic	37	12.4
	depressive	114	38.3
	mixed	4	1.4
	unspecified	143	47.9

Regarding psychotropic prescribing patterns, results were found as follows:

I. Mood stabilizer prescribing

Of the 298 patients with a diagnosis of BD, 35.2% (n=105) were prescribed lithium. The proportion of patients on lithium differed significantly according to specific BD diagnosis ($\chi^2=78.56$, $p<.001$), with higher rates of prescribing among the manic (54.1%) and unspecified groups (55.2%).

Overall, the mean daily dose of lithium was 866.67mg (SD=297.32; range = 300-2400). The mean dose did not differ according to specific BD diagnosis ($F(2,101)=0.46$, $p=0.63$).

Analysis indicated that 17.8% (n=53) of patients with BD who were prescribed lithium also received antipsychotics. The majority of patients were prescribed lithium in conjunction with an oral FGA (98.1%), one patient was prescribed

lithium with an FGA and depot combination (1.9%). No patients were prescribed lithium in conjunction with SGA or depot monotherapy.

Forty patients with BD (13.4%) were also prescribed sodium valproate, with a mean daily dose of 727.50mg (SD=279.18; range=200-1500). The proportion of patients on valproate differed significantly according to specific BD diagnosis ($\chi^2=24.98$, $p<.001$). Patients with an unspecified type of BD were more likely to be prescribed sodium valproate compared with the other types. Of the 105 patients with BD on lithium, 4 (3.8%) were also prescribed sodium valproate. The mean daily dose of sodium valproate did not differ between the types of BD diagnoses ($F(2,34)=0.32$, $p=.73$).

II. Antipsychotic prescribing

Of the overall 1750 outpatient cases, 38.2% (n=668) were prescribed antipsychotics during the study period.

When considering the whole patient population the mean CPZe (chlopromazine equivalent) dose per day was 183.63mg (SD=182.74).

Mean antipsychotic doses according to diagnosis are presented in Table 2. As

expected, the three highest mean CPZe doses were recorded for patients with schizophrenia, schizoaffective disorder and manic episode of bipolar disorder (BD – manic type) respectively.

Table 2 Total mean dose of antipsychotics by diagnosis

Dose (CPZe mg/day)		
Primary Diagnosis	Mean (SD)	N
Schizophrenia	254.66 (190.72)	286
Schizoaffective Disorder	253.87 (181.12)	41
Functional Psychosis	154.68 (175.05)	39
Organic/Drug Psychosis	128.51 (93.93)	21
BD-manic type	247.00 (249.41)	25
BD-depressive type	74.24 (70.76)	28
BD-mixed type	80.30 (26.63)	3
BD-unspecified type	118.09 (120.74)	73
Major Depression	51.75 (45.04)	61

Mean CPZe(SD) = 183.63 (182.74) mg/day

Of the 298 bipolar patients, 43.3% (n=129) were recorded as receiving an antipsychotic medication during the study period. Depression and mixed BD type patients all received oral monotherapy of antipsychotics. However, 93.2% (n=68) and 76% (n=19) of unspecified-BD and manic type respectively received oral antipsychotics. Since so few patients (n=3) were diagnosed with mixed-BD, they were excluded from any analysis comparing route of administration and doses across diagnoses.

Almost all bipolar patients who received antipsychotics were prescribed FGAs

alone (93.0%;n=120). Only 6 patients received SGAs alone (4.6%), 2 patients received a depot preparation (1.6%), and one patient received FGA in conjunction with a depot (0.8%). There were significant differences in the proportion of patients receiving an oral alone, depot alone or combination therapy according to the specific type of bipolar diagnosis ($\chi^2=18.62$, $p<.01$). Unspecified type patients were more likely to receive an oral monotherapy, and patients with manic type were more likely to receive two or more oral antipsychotics.

Table 3 Doses of antipsychotics for bipolar patients (combined groups)

Antipsychotics	Mean Dose (SD)		CPZe (SD)		N
	(mg/day)	range	(mg/day)	range	
Orals FGAs					
Chlorpromazine	114.58 (86.27)	25-300	114.58 (86.27)	25-300	30
Haloperidol	3.95 (5.71)	0.25-20	197.50 (285.36)	12.5-1000	15
Perphenazine	9.85 (8.69)	2-40	123.11 (108.73)	25-500	53
Pimozide	1.92 (1.81)	0.75-4	126.50 (119.36)	49.5-264	3
Thioridazine	79.52 (67.97)	10-300	79.52 (67.97)	10-300	19
Trifluoperazine	30.0 (-)	-	600 (-)	-	1
Oral SGAs					
Risperidone	1.00 (0.55)	0.5-2.0	90.91 (49.79)	45-182	6
Depot					
Zuclopenthixol IM	4.89 (2.77)	1.8-7.1	102.50 (58.26)	38-150	3*

* one patient received FGA in conjunction with a depot

As Table 3 shows, few bipolar patients were prescribed SGA or depot preparations. There was considerable variation in the mean CPZe doses of conventional oral antipsychotics, although the low frequency of pimozide and trifluoperazine prescribing made it difficult for reliable comparisons to be made. Patients taking haloperidol were more likely to have a higher mean daily CPZe dose compared with chlorpromazine, perphenazine or thioridazine, although this trend barely approached significance ($F(3,100)=2.09$, $p=.10$).

Specific type of BD diagnoses were considered in relation to mean CPZe doses (mania, depression and unspecified). Analysis indicated there were significant differences in mean total CPZe doses according to diagnosis ($F(2,123)=10.05$,

$p<.001$). Post hoc analyses revealed that patients with manic type had a significantly higher mean daily CPZe dose ($x=247.00$) compared to those with depressive type ($x=74.24$; $p<.001$) or unspecified type ($x=118.09$; $p<.001$).

III. Antidepressant prescribing

Almost half of bipolar patients (48.6% ; $n=145$) were prescribed an antidepressant. The proportions of patients receiving a tricyclic antidepressant (TCA) or a selective serotonin reuptake inhibitor (SSRI) are shown in Table 4. Only a small number of patients were prescribed mianserin ($n=8$) or mirtazapine ($n=1$) but these were not included in the table as dosing frequencies for these drugs were not available.

Table 4 Mean doses of antidepressants for bipolar patients with BD

Antidepressant	Mean Dose (SD)		N
	(mg/day)	range	
TCA's			
Amitriptyline	52.31 (35.86)	20-150	13
Clomipramine	50.00 (-)	-	1
Imipramine	70.83 (40.05)	25-125	6
Nortriptyline	45.92 (26.60)	10-100	57
SSRI's			
Fluoxetine	25.16 (10.88)	4-60	55
Fluvoxamine	83.33 (57.74)	50-150	3
Sertraline	50.00 (-)	-	1

The proportion of patients receiving antidepressants differed significantly according to specific type of BD diagnosis ($\chi^2=179.21$, $p<.001$), the rates not unexpectedly being highest among those with depression (73.7%; $n=107$) and lowest among those with mixed or manic type (0.7%; $n=1$). The majority of patients taking an antidepressant were prescribed the SSRI fluoxetine in generic form (37.9% of all antidepressant prescribing) or the tricyclic antidepressant nortriptyline (39.3% of all antidepressant prescribing). As few patients with manic or mixed type received an antidepressant, comparisons of mean doses according to specific type of BD diagnosis were not performed.

Only a small proportion of bipolar patients were prescribed an antidepressant in conjunction with a mood stabilizer (15.7%). The most common mood stabilizer taken in conjunction with an antidepressant was lithium (66.6%).

IV. Benzodiazepine prescribing

About one-third (34.2% ; $n =93$) of the patients were prescribed benzodiazepine. The prescribing rates differed significantly according to specific type of BD diagnosis ($\chi^2=33.03$, $p<.001$), with depressive type patients being more likely to be prescribed benzodiazepines compared with manic and

unspecified type patients. The most commonly prescribed benzodiazepines were lorazepam (41.9%; $n=39$) and clorazepate (34.4%; $n=32$).

V. Antiparkinson drug prescribing

Finally, 46 (15.4%) patients with BD received antiparkinson medications, usually in conjunction with FGAs ($n=39$). Very few patients were prescribed antiparkinson drugs in conjunction with a depot only ($n=2$) or an FGA and depot combination ($n=1$).

Discussion

The data revealed that almost half (48.6%) of bipolar patients treated in our university hospital received mood stabilizers including lithium (35.2%) and valproate (13.4%). These data were similar to Levine's [3], Ghaemi's [4], Frangou's [14] and Sukanich's [13] who also found that lithium and valproate were two of the most commonly prescribed medications for this disorder. In this study, lithium was the most commonly used mood stabilizer, similar to Bahk's study in Korea [12]. The lithium - valproate ratio in this study (2:6:1) differed from Sukanich's study in Bangkok (0.9:1) [13]. Doctors in our hospital seemed to prescribe lithium as a first line agent more than doctors in

Bangkok who prescribed both lithium and valproate as first line drugs. It should be noted that carbamazepine was not prescribed as a mood stabilizer in our patients; a finding similar to the Bangkok study where carbamazepine and topiramate were prescribed in only 16 of 280 cases (5.7%). This was in contrast to Bahk's study in Korea where carbamazepine in combination with lithium were the second commonly used [12].

Although this study cannot predict a declining trend of lithium use in our hospital, another more recent study of ours [15], which found that 10 of 73 patients (13.7%) had abnormal thyroid function after receiving lithium, may influence the prescribing rate of lithium in the following years.

In regard to the dosage of mood stabilizers, when compared with results of a study in Korea [12], it was found that Thai patients received a lower dosage of lithium (866.67 ± 297.32 vs 1060 ± 207 mg/day) and also of valproate (727.52 ± 279.18 vs 1056 ± 258 mg/day). One possible explanation may be patient symptom severity, as this study collected data from outpatients while Bahk's study reported data collected from inpatient wards [12].

A result from our study, differ from United States [4-5] and United Kingdom [14] reports but is similar to a study in Bangkok [13], is the more frequent use of older and cheaper medications like FGAs and TCAs. It is not yet known whether the use of such medications is due to the Thai clinicians' sensitivity to the financial status of patients. Since the Thai government introduced the 30 baht (approximately 0.75 USD in 2003) health care scheme, under which Thai people pay only 30 Thai baht per visit to a state hospital for any medical health care received, the cost of medications is a significant consideration at all government health care centers. For example, the price of the original

risperidone 2 mg in our hospital is 74 times higher than that of the generic haloperidol 5 mg [10,16].

However, the number of patients receiving SGAs in this study was relatively low (6 cases, 2.0%) when compared with the study in Bangkok (31.7%) [13] or reports from Baldessarini (11%) [5], Ghaemi (27.2%) [14] and Bahk (61.3%) [12].

Regarding antidepressants, nearly half (45.3%) of our patients were prescribed antidepressants of which nortriptyline and the generic form of fluoxetine were chosen by their doctors in nearly equal numbers. This finding was rather similar to Baldessarini's report [5] which found that the most commonly prescribed drug class were antidepressant (50%). Blanco [17] also reported that antidepressants were prescribed alone in about one – fifth of bipolar cases in US. Although most of our cases who received antidepressants suffered from the depressive type of BD, the frequent use of antidepressants does alarm worries about the risk of polarity switching and long term patient outcomes. Sukanich et.al [13] also warned Thai clinicians to pay more attention and be cautious with the use of TCAs in bipolar patients.

This study has some limitations that should be considered. The first thing is diagnosis, of which the unspecified BD was the most prevalent. This might be chiefly attributed to the heavy workload of our psychiatrists, who due to time constraints simply categorize patients as BD only without further detailed interviewing to find out the appropriate subtype. In this study all the BD only cases were classified as unspecified subtype. Second, we did not collect data on the illness factors such as phase of drug treatment, drug compliance, duration of illness, or severity of symptoms which might be important given the fact that the dosage of medications might be different

