Remission Rate of Atypical Antipsychotic Treatment of Bipolar Depression: Experience at Srinagarind Hospital, Northeast Thailand

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Objective: *To determine the remission rate when using atypical antipsychotic treatment for bipolar depression at Srinagarind Hospital, Khon Kaen, Thailand.*

Material and Method: *The authors reviewed the patient records for 18 persons, both in- and out-patients, with DSM-IV-TR bipolar depression, treated with atypical antipsychotic(s), at the Department of Psychiatry, Srinagarind Hospital, between May 2005 and April 2008. The remission rate using atypical antipsychotic treatment was assessed using survival analysis while the patterns of prescribing atypical antipsychotics were delineated using percentages.*

Results: *Of the 18 patients, 15 fulfilled the remission criteria. The mean time to remission was 10.3 weeks (SD 8.4). The incidence-density of the remission rate for bipolar depression treated with atypical antipsychotics was 8.1 per 100 person-weeks (SD 2.4, 95% CI 4.5-13.4). One patient achieved remission using only atypical antipsychotic monotherapy while 17 received a combination of atypical antipsychotics plus one or more of the following: antidepressants, anticonvulsants, anxiolytics and/or lithium. The present study revealed that remission was 1.4 times higher among females than males and 13 times higher among married than singles.*

Conclusion: *The incidence-density of the remission rate using atypical antipsychotics for treatment of bipolar depression was 8.1 per 100 person-weeks. Almost all of the patients were treated with a combination of atypical antipsychotics plus other groups of medications. Higher remission was associated with females and married persons.*

Keywords: *Bipolar depression, Atypical antipsychotics, Remission rate*

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Bipolar depression is a major depression experienced among patients who have had a previous manic, hypomanic, or mixed episode(1). By closely observing a number of bipolar I disordered patients for about 13 years, it was found that the patients spent 47.3% of the time with some sort of mental disorder, of which over two-thirds (67.4%) was depression, one-fifth (18.8%) mania or hypomania and one-tenth (12.5%) in a cycling or mixed episode(2). Bipolar I disorder patients suffered from depression three times more often than from mania or hypomania(3). It was determined that special treatment and close monitoring were needed during the depressive state(4). Thus far, the treatment effectiveness for bipolar depression remains limited(5). Currently, bipolar depression is treated with mood stabilizers, antidepressants(6,7) and atypical antipsychotics(8,9); however, publications on the results of treatment for bipolar depression are scarce. The authors, therefore, undertook such research on patients seen at Srinagarind Hospital. The authors tried to include other perspectives of the statistically relevant treatment results, *i.e.,* the incidence-density of the remission rate for the use of atypical antipsychotics for the treatment of bipolar depression.

The objectives of the present study were to determine (a) the remission rate of bipolar depression treated with atypical antipsychotics (b) the pattern of atypical antipsychotics prescriptions for the treatment of bipolar depression and (c) the factors that might affect the remission rate of bipolar depression.

Material and Method

The authors conducted a retrospective historical study on data between May 1, 2005 and April

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30, 2008 from both psychiatric in- and out-patient records of bipolar and depressive patients seen at Srinagarind Hospital. The Khon Kaen University Ethics Committee for Human Research reviewed and approved the present protocol.

The inclusion criteria were (a) the record had to meet the diagnostic criteria of the DSM-IV-TR for bipolar depression or major depressive disorder - the latter was checked for any chance of having had a previous history of bipolar disorder (b) the main treatment had to be atypical antipsychotics until remission was diagnosable (c) the criteria for remission required that no significant symptoms or signs of major depression, mania, hypomania or mixed episode occurred for 2 months consecutively any time after the index episode. The exclusion criteria were (a) the index episode was not truly a major depression (907 cases) (b) the symptoms were unclear and there was no definite diagnosis (130 cases) (c) the records could not be found for whatever reason (46 cases) or (d) the treatment did not include atypical antipsychotics during the period of bipolar depression (33 cases).

Finally, the records of 18 patients with true bipolar depression were reviewed.

Both SPSS 16 and STATA 8 software were used to do the descriptive statistical analysis of the data. The primary statistical procedure was Kaplan-Meier survival analysis. Odds ratio with 95% confidence interval (95% CI) was used to present the factors associated to remission.

Results

The sample comprised 13 (72.2%) females and five (27.8%) males, averaging 47.7 years of age (SD 12.9). Most were married (77.8%) and held at least a bachelor degree. They had a wide diversity of occupations, although the majority was government employees (Table 1).

The diagnoses were (a) bipolar I disorder - the most recent episode being moderate depression (14 patients; 77.8%) and (b) bipolar I disorder - the most recent episode being severe depression with psychotic features (4 patients; 22.2%). The use of atypical antipsychotics is presented in Table 2. Quetiapine was the principal antipsychotic used to treat bipolar depression at Srinagarind Hospital. One patient who received atypical antipsychotic as a monotherapy, while the remainder (17 patients) received combination treatment including atypical antipsychotic plus antidepressants (13/17 patients), anticonvulsants (9/17), anxiolytics (9/17) or lithium (4/17) (Table 3).

Table 1. Demographic characteristic 18 patients

Demographic characteristics	Number (%)
Sex	
Male	5 (27.8)
Female	13 (72.2)
Age	
21-40	5 (27.8)
41-60	10 (55.6)
older than 60	3 (16.6)
Marital status	
Single	4 (22.2)
Married	14(77.8)
Education	
Below Bachelor degree	5 (27.8)
Bachelor degree	11 (61.1)
Master degree	1 (5.6)
Other	1 (5.6)
Occupation	
Businessman	1 (5.6)
Farmer	1 (5.6)
Housewife	5 (27.8)
Wage earner	1 (5.6)
Government employee	8 (44.4)
Unemployed	2 (11.1)

At the end of the present study, 15 (83.33%) of the patients achieved remission. The mean time to remission was 10.3 weeks (SD 8.4). The treatment of bipolar depression with atypical antipsychotics had a remission rate of 8.1 per 100 person-weeks (SD 2.4, 95% CI 4.5-13.4) (Fig. 1). The probability of remission was (a) 1.4 times higher for females than males (b) 13 times for married than singles (Table 4).

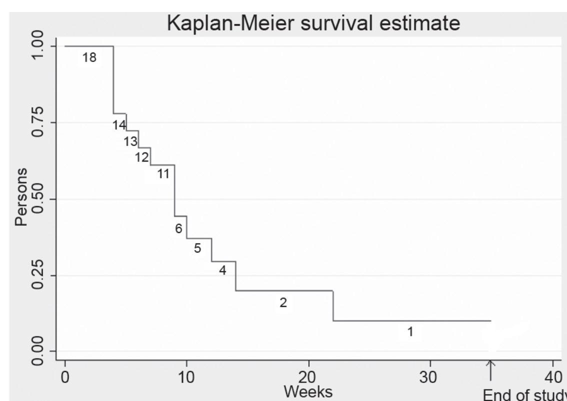

Fig. 1 The number of patients and the time to remission (weeks)

Table. 2 Subtypes of bipolar depression and prescription patterns of atypical antipsychotics

Subtypes	Atypical antipsychotics: number (%)			
	Aripiprazole	Olanzapine	Quetiapine	Risperidone
Bipolar I disorder, most recent depressive episode				
Moderate	3 (16.7)	3 (16.7)	5 (27.8)	3 (16.7)
Severe with psychotic Features	0	1 (5.6)	1 (5.6)	2 (11.1)
Total	3 (16.7)	4 (22.2)	6 (33.3)	5 (27.8)

Table 3. Combination of atypical antipsychotics with other medications

Atypical antipsychotics	Combination drugs: number (%)			
	Antidepressants	Anticonvulsants	Anxiolytics	Lithium
Aripiprazole	2 (15.4)	0	2 (22.2)	0
Olanzapine	2 (15.4)	3 (33.3)	1 (11.1)	2 (50.0)
Quetiapine	4 (30.8)	4 (44.4)	3 (33.3)	1 (25.0)
Risperidone	5 (38.5)	2 (22.2)	3 (33.3)	1 (25.0)

Table 4. Demographic and clinical characteristics in relation to remission of bipolar depression

Demographic and clinical characteristics	Remission (non-remission)	p-value Chi-square test (2 sided) (Fisher's exact test)	Odds ratio (95% CI)
Sex		1.000	1.375 (0.096-19.643)
Female	11 (2)		
Male	4 (1)		
Marital status		0.108	13.000 (0.771-219.107)
Married	13 (1)		
Single	2 (2)		
Education		0.515	0.750 (0.541-1.040)
Bachelor degree and higher	9 (3)		
Below bachelor degree	6 (0)		
Occupation		1.000	0.750 (0.055-10.233)
Employment	9 (2)		
Unemployment	6 (1)		
Family history of mental illness		1.000	0.824 (0.661-1.026)
No	14 (3)		
Yes	1 (0)		
Psychosocial stressor		1.000	0.812 (0.642-1.028)
No	13 (3)		
Yes	2 (0)		
Alcohol drinking		1.000	0.824 (0.661-1.026)
No	14 (3)		
Yes	1 (0)		
Psychotics features during bipolar depression		1.000	0.812 (0.642-1.028)
No	13 (3)		
Yes	2 (0)		
Suicidal ideation		1.000	0.786 (0.598-1.033)
No	11 (3)		
Yes	4 (0)		

Discussion

This is one of a very few studies on the treatment of bipolar depression in Thailand. Despite being a retrospective study, the high remission rate of the present study strongly suggests that atypical antipsychotics-besides being mood stabilizers[10]-were effective in treating bipolar depression. Indications for their use in the present study included (a) difficult cases (b) having psychotic features and (c) multiple drug treatment. Although quetiapine was approved as a monotherapy for bipolar depression[11], only one patient in the present study was treated with this atypical antipsychotic monotherapy. Most of the combinations with atypical antipsychotics were with: antidepressants (76.5%), anticonvulsants (52.9%), anxiolytics (52.9%) and/or lithium (23.5%). The rationale for prescribing a combination of medications included: severity, insomnia, loss of appetite, anxiety, and psychotic features. The current study accords with other studies, which indicated that quetiapine either alone or in combination with other medication is effective for bipolar depression[9]. The low rate of use of quetiapine alone in treatment of bipolar depression at Srinagarind Hospital may reflect the clear indication for multiple medications or perhaps continued education is needed for staff psychiatrists.

The respective remission rate of bipolar depression among patients treated with quetiapine, olanzapine and/or the combination of olanzapine and fluoxetine (OFC) was 52.9%, 32.8% and 48.8%[4,12]. Most of the patients in the current study experienced remission. The incidence-density of the remission rate in Srinagarind Hospital for bipolar depression treated with atypical antipsychotics was 8.1 per 100 person-weeks.

As in other studies, olanzapine, OFC and quetiapine had good outcomes for the treatment of bipolar depression compared with the placebo[8,9,12,13] but withdrawals due to adverse events were found[8]. However, by comparison, the current study found no patients with adverse events after use of these atypical antipsychotic drugs. The present study confirmed that atypical antipsychotic monotherapy could benefit patients with bipolar depression although most required combination treatment. Other than atypical antipsychotics to treat bipolar depression, the most common combination used at Srinagarind Hospital was atypical antipsychotic + antidepressant. The strategy of using combination therapy might explain the higher remission rate of the present study.

The higher chance of remission among females and married persons agrees with other studies[14,15]. Many female patients in the present study were married, were government employees and had a higher level of education, all of which were factors that favored remission[14-16]. By contrast, many factors in the present study - *i.e.,* employed status, high education level, absence of psychosocial stressors, absence of psychotic features during the index episode, absence of suicidal ideation-did not have any statistically significant effect on remission, perhaps because of the small number of cases studied.

Most psychosocial interventions studied have proven beneficial as adjuncts to pharmacotherapy with no substantial differences in efficacy between the treatment[17,18]. In addition, every patient in the present study had concomitant psychotherapy and/or psycho-education. This factor might have influenced the higher gross rate of remission.

This was a retrospective study with a small sample size, all the patients included were from Srinagarind Hospital; and most were university graduates and government employees so the results of the study might not represent the remission rate for the treatment of bipolar depression with atypical antipsychotics in the general population.

Conclusion

The incidence-density of the remission rate using atypical antipsychotics to treat bipolar depression was 8.1 per 100 person-weeks. Being married or female was associated with a higher remission rate. Atypical antipsychotic monotherapy could lead bipolar depression patients to remission, however most of the patients in the presented study were given a combination of atypical antipsychotic and some other drug group(s), usually an atypical antipsychotic plus anti-depressant. A prospective study with a larger, more diverse sample is needed to compare outcomes among the various subgroups.

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Potential conflicts of interest

None.

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อัตราการสงบของ bipolar depression จากการรักษาโดยยาต้านโรคจิตกลุ่มใหม่ในโรงพยาบาลศรีนครินทร์ภาคตะวันออกเฉียงเหนือ ประเทศไทย

กุศลาภรณ์ วงษ์นิยม, พูนศรี รังษีขจี

วัตถุประสงค์: *เพื่อศึกษาอัตราการสงบของ bipolar depression จากการรักษาโดยยาต้านโรคจิตกลุ่มใหม่ในโรงพยาบาลศรีนครินทร์ จังหวัดขอนแก่น ประเทศไทย*

วัสดุและวิธีการ: *เก็บข้อมูลย้อนหลังจากเวชระเบียนผู้ป่วยในและผู้ป่วยนอกที่ได้รับการวินิจฉัยว่าเป็น bipolar depression ตามเกณฑ์ DSM-IV-TR ที่มารับการรักษาที่หน่วยจิตเวช โรงพยาบาลศรีนครินทร์ จังหวัดขอนแก่น ระหว่างเดือนพฤษภาคม พ.ศ. 2548 ถึง เดือนเมษายน พ.ศ. 2551 จำนวน 18 คน วิเคราะห์อัตราการสงบของโรคจากการรักษาด้วยยาต้านโรคจิตกลุ่มใหม่โดยใช้ survival analysis ศึกษารูปแบบการใช้ยาต้านโรคจิตกลุ่มใหม่ในการรักษา bipolar depression ด้วยค่าร้อยละ*

ผลการศึกษา: *ผู้ป่วยทั้งหมด 18 คน เข้าสู่ภาวะสงบของโรคตามเกณฑ์ที่กำหนด 15 คน ระยะเวลาเฉลี่ยที่โรคเข้าสู่ภาวะสงบ 10.3 สัปดาห์ (SD 8.4) อัตราการสงบของ bipolar depression จากยาต้านโรคจิตกลุ่มใหม่ ร้อยละ 8.1 คนต่อสัปดาห์ (SD 2.4, 95% CI 4.5-13.4) มีผู้ป่วยเพียง 1 คน ที่ใช้ยาต้านโรคจิตกลุ่มใหม่เพียงตัวเดียว ผู้ป่วย 17 คน มีการใช้ยาร่วมกันระหว่างยาต้านโรคจิตกลุ่มใหม่กับยากลุ่มอื่นอย่างน้อย 1 ชนิด ได้แก่ ยาต้านเศร้า ยากันชัก ยาคลายกังวล และ/หรือ ลิเทียม ผู้ป่วยที่เป็นเพศหญิงมีอัตราการสงบของโรคมากกว่าเพศชาย 1.4 เท่า และผู้ที่สมรสมีอัตราการสงบของโรคมากกว่าผู้ที่เป็นโสด 13 เท่า*

สรุป: *อัตราการสงบของ bipolar depression จากการรักษาโดยยาต้านโรคจิตกลุ่มใหม่ คือ ร้อยละ 8.1 คนต่อสัปดาห์ รูปแบบการรักษาส่วนใหญ่เป็นการใช้ยาต้านโรคจิตกลุ่มใหม่ร่วมกับยากลุ่มอื่น ปัจจัยที่มีผลต่อการสงบของโรคคือเพศหญิงและสถานภาพสมรส*