Psychiatria Danubina, 2011; Vol. 23, No. 2, pp 189–193 *Brief report*

ADHERENCE TO TURKISH PSYCHIATRIC ASSOCIATION GUIDELINE FOR BIPOLAR DEPRESSION TREATMENT IN A SPECIALIZED MOOD DISORDERS OUTPATIENT UNIT

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SUMMARY

Background: *Bipolar patients spend up to one third of their lives in depression however, acute treatment guidelines mainly focused on the manic phase of illness. With recent attention to the importance of evidence-based medicine in psychiatry, a number of treatment guidelines have emerged to aid clinicians in clinical decision making. Here, we aim to measure concordance with the Turkish Psychiatric Association Treatment Guideline for Bipolar Disorders (TPATGBD) for the depressive phase of illness.*

Subjects and Methods: *Bipolar patients attending the Rasit Tahsin Mood Disorders Outpatient Unit of Istanbul Bakırköy Research and Training Hospital for Psychiatry, Neurolgy & Neurosurgery, were assessed using standardized forms based on a nation-wide mood disorders follow-up program. Concordance of implementations with the TPATGBD were evaluated step by step for each level of depression severity.*

Results: *Concordance rates with the first step recommendations of the guideline were 29.4%, 27.4% and 87.5% for mild-moderate, moderate-severe (without psychosis) and severe depression (with psychosis), respectively. Concordance rates with the second step recommendations of the guideline were lower for bipolar depressions without psychosis. Overall, adherence to the guideline did not impact on time to remission (p=0.19).*

Conclusions: *Despite considerable efforts to develop and disseminate evidence-based guidelines, they are not widely followed by clinicians and important opportunities clearly exist to educate clinicians about the feasibility and utility of clinical guidelines for bipolar disorder. Systematic studies in the future are required to clarify our understanding of clinicians' attitudes to the use of guidelines and to explain the discrepancy between guidelines and clinical practice.*

Key words: *treatment guidelines - bipolar depression - adherence*

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INTRODUCTION

Bipolar disorder is a serious mood disorder characterized by episodes of depression and episodes of mania or hypomania. It affects up to 3.5% of the population (Buckley 2008, Hirschfeld et al. 2003). Most patients with bipolar disorder experience depression as their first episode (Angst et al. 2000) and many will spend up to one third of their lives with significant depressive symptoms (Kupka et al. 2007). Treatment guidelines for bipolar disorder are mainly focused on the manic phase of the illness (Oral and Vahip 2004) but in recent years the increased availability of new treatment options for bipolar depression has necessitated the development of clinical guidelines and therapeutic algorithms for this phase of the illness (Divac et al. 2009, Yatham et al. 2006, Hirschfeld 2005). The development of these guidelines and algorithms has also been driven by increased cost-awareness and the increasing pressure to improve cost-efficiency (Divac et al. 2009). In 2003, the Turkish Psychiatric Association (TPA) published local Treatment Guidelines for Bipolar Disorders (BDTG) to enhance evidence-based care and improve outcomes (Vahip & Yazıcı 2003).

In this paper we aim to measure adherence to the Turkish Psychiatric Association Guidelines for Bipolar Depression Treatment within a specialized mood disorders outpatient unit.

SUBJECTS AND METHODS

Subjects

Bipolar patients attending the Rasit Tahsin Mood Disorders Outpatient Unit (RTMDU) of Istanbul Bakırköy Research and Training Hospital for Psychiatry, Neurology & Neurosurgery, were screened for the study. Available data from 263 depressive episodes in 142 patients between Februrary 2003-January 2008 were assessed.

Method

All patients were assessed using standardized forms based on a nation-wide mood disorders follow-up program, SKIP-TURK (Tırpan et al. 2004). The treatments prescribed by clinicians for "mild/moderate bipolar depression", "moderate/severe bipolar depression (without psychosis)" and "severe bipolar

depression with psychotic features" were recorded. Inpatient data were excluded from these analysis as standardised data was not consistently available for these epsiodes. Concordance of prescribed treatments with the BDTG guideline was evaluated in a stepwise fashion for each level of depression severity.

Biometrics and statistics

Statistical analyses were performed using Statistical Package for Social Sciences (SPSS) 17 for Windows. Descriptive statistics are presented and, where appropriate, dimensional data (non-parametric) were compared using the mann-Whitney U test and categorical data were compared using the Chi-squared test.

Ethics

All patients signed written informed consents for follow-up and the study was approved by Instutional Board Review.

RESULTS

Clinical characteristics of the sample

Over two thirds of patients were female (69%, n=98) and most were diagnosed as having bipolar disorder, type I (92.3%, n=131). The mean age was 39.7 years and mean duration of bipolar illness was 15.9 years. The first ever episode of illness was depression for approximately half of the patients (52.3%, n=55) and almost ten percent of patients had a history of rapid cycling bipolar disorder (9.9%, n=14). The proportion of 263 depressive episodes in terms of severity was 77.6% (n=204) for mild/moderate depression, 19.4% (n=51) for moderate/severe depression without psychosis and 3% (n=8) for severe depression with psychotic features.

Evaluation of adherence to BDTG guideline for the treatment of bipolar depression

MILD /MODERATE BIPOLAR DEPRESSIVE EPISODES

More than half of mild or moderate depressive episodes (59.8%) remitted after the first step interventions, while the remission rates were 21.5% after second step interventions and 18.6% after third step interventions

Adherence to the first step recommendations:

Clinicians followed the first step recommendations of the BDTG guidelines in only one third of mild/moderate depressive episodes (29.4%). We found that clinicians more often added lamotrigine (LTG) (16.2%) to the current medication regimen instead of following the guideline's first step recommendations (optimizing mood stabilizer levels (10.6%) or adding an antidepressant (14.8%)).

Adherence to second step recommendations:

More than half of the mild/moderate episodes (55%, n=60) remitted after following the first step recommandations. Clinicians added a new antidepressant (AD) agent for 25.6% of the remaining depressive episodes and overall the adherence rate was only 17% (n=14) for the second step recommendations (add an AD or try a different AD)

Adherence to third step recommendations: 42.8% of the mild/moderate episodes remitted after following the first and second step recommendations of the guideline (6/14). The most common treatments for the third step were adding an AD (21.1%), increasing AD dosage (15.8%) or adding a second generation antipsychotic (13.2%).

Overall, only a small number of mild/moderate bipolar depressive episodes (15.7%, n=6) were treated in full adherence (all three steps) with the guidelines.

MODERATE/SEVERE BIPOLAR DEPRESSIVE EPISODES (WITHOUT PSYCHOSIS)

Remission rates were 50.9% (n=26), 23.5% (n=12) and 25.6% (n=13) for the first, second and third step interventions, respectively.

Adherence to the first step recommendations: The most common treatment for moderate/severe bipolar depressive episodes were adding an AD (29.4%, n=15) or adding lamotrigine (13.7%, n=7). ECT was performed for just one moderate/severe depressive episode and this patient was hospitalized. Adherence rates with the guidelines was only 27.4% (n=14) for the first-step recommendations (adding an AD and waiting for 3-4 weeks or applying ECT).

Adherence to second step recommendations: Half of the depressive episodes remitted following the first-step recommendations of the guidelines. Only two of the depressive episodes were treated according to the second step recommendations of the guidelines (8%). Clinicians commonly preferred adding an AD (28%), increasing the AD dosage (16%), adding a second generation antipsychotic or lamotrigine (24%).

Adherence to third step recommendations: Two of the episodes remitted after following the first and second step recommendations of the guideline. We found that clinicians prescribed AD (15.4%) or lamotrigine (15.4%) for the remainder of these depressive episodes (n=13).

SEVERE BIPOLAR DEPRESSIVE EPISODES (WITH PSYCHOTIC FEATURES)

Nearly all of the patients (7/8) with severe bipolar depressive episodes and psychotic features were taking lithium. The adherence rate with the guidelines was 87.5% (7/8) and 42.8% of these episodes remitted after the application of first-step recommendations (lithium+AD combination, lithium+AD+antipsychotic combination or ECT). We found that clinicians followed the second-step recommendations of the guidelines (lithium+antipsychotic+different AD or ECT) for all

episodes (n=4) and that these episodes remitted. Only one depressive episode did not remit after second step interventations without adherence to guideline and this patient was hospitalized for this episode.

Overall, adherence to the guideline did not impact on time to remission (p=0.19, Table 3).

Table 1. Recommendations of TPA guideline for bipolar depression

Mild-Moderate	Moderate-Severe (without psychosis)	Severe (with psychosis)	Mild-Moderate
First Step	Li optimization	Li+AD	Li+AD
Recommendation	Li+AD	ECT	Li+AD+SGA
			ECT
Second Step	Li+ different AD	Li+different AD	Li+different AD+SGA
Recommendation		ECT	ECT
Third Step	Li+AD combination	Li+AD combination	Li+AD combination +SGA
Recommendation	Li+LTG	Li+LTG	Li+LTG
	MS+SGA	MS+SGA	MS+SGA
			ECT

Li:Lithium, AD:Antidepressant, SGA:Second Generation Antipsychotic, ECT: Electroconvulsive Therapy, LTG:Lamotrigine

Table 2. Rates of adherence to guideline for the treatmnet of bipolar depression

Severity of episode	1st step		2nd step		3rd step	
	(%)*	n	(%)*	n	(%)	n
Mild/Moderate	29.4	60	17.0	14	15.7	6
Moderate/Severe (without psychosis)	27.4	14	8.0	7	-	-
Severe (with psychosis)	87.5	7	100	4	-	-

*Percentages reflect the proportion of the adherence rates within the each level of depression such as mild/moderate, moderate/severe without psychosis and severe with psychosis

Table 3. Comparison of time to remission

Adherence to guideline	n	Mean (week)	Standard Deviation	p
Yes	55	8.65	10.96	0.190
No	169	6.62	5.60	0.190

DISCUSSION

To date there are very few studies which have assessed adherence to national treatment guidelines for bipolar disorder in clinical practice. Recently, Divac et al. (2009) conducted a survey at the Institute of Psychiatry, Clinical Centre of Serbia and about 65% of psychiatrists who responded stated that they adhered to the national or relevant international therapeutic guidelines (although obviously it would be interesting to see if this was actually the case in practice). In a small survey of clinicans in the United States Perlis et al (Perlis 2007) found that among 312 respondents 64.1% reported making routine use of treatment guidelines during clinical decisions,19.6% were using American Psychiatric Association treatment guidelines while 33.0% reported using all published guidelines. These concordance rates are higher than our results in which we have found that only one third of clinicians followed TPA BDTG for depressive episodes without psychosis. The concordance rate with the guidelines for severe depression with psychosis in our study was much higher than rates of other episodes (although the number of severe psychotic depressive episodes was small (n=8)). We might therefore conclude that clinicians tend to follow recommendations of guidelines only for severe situations or alternatively relatively frequent second generation antipsychotic prescription might explain this high concordance rate for severe depression with psychosis.

In the last few years, several studies have suggested that some of the second generation antipsychotics are effective for the treatment of bipolar depression (Cruz et al. 2009) and quetiapine has recently been approved bythe FDA for this purpose (Thase et al. 2006, Calabrese et al. 2005). Second generation antipsychotics were recommended as first-line treatment choice in psychotic depression of TPA guidelines as it was published in 2003. The TPA are currently updating these guidelines and presumably quetiapine may be one of their first-line recommendations.

The most common first-step implementation of clinicians for bipolar depression treatment without considering concordance with guidelines was adding an AD (21.3%). Although antidepressants were usually prescribed for bipolar depressive episodes, the effectiveness of them has been largely inferred from studies of unipolar depression. Calabrase and his colleagues (2004), reported that antidepressant monotherapy continues to be the most common

treatment for bipolar I depression, despite little or no evidence proving its efficacy. In early studies antidepressants have been shown to have some positive effects but, recent large-scale studies have found that antidepressants have only little (if any) benefit for the treatment of bipolar disorder (Keck 2007). In the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) Sachs et al (2007), reported that adjunctive antidepressant treatment for bipolar depression neither improved depressive symptoms nor increased the risk of affective switch into mania. In contrast to this, AD agents, particularly SSRIs, are still recommended for the first line treatment with a mood stabilizer within the TPA and other international guidelines (Yatham et al. 2006, Hirschfeld 2005).

The Agency for Health Care Policy and Research Depression Guideline Panel emphasised that guidelines should be geared to: (i) optimize symptom reduction in a majority of patients, (ii) assist physicians to make more informed decisions (AHCPR 1993a, AHCPR 1993b). Grimshaw and Russell (1993) concluded that when guidelines are systematically implemented, most have significant, positive clinical effects, although the magnitude of their effects can vary. The assumption overall is that use of guidelines will improve clinical outcomes and/or cost efficiency, and that greater adherence to guidelines should potentiate that effect. However, in our study we found that adherence to the guideline for treatment of bipolar depression did not have any impact on time to remission (p=0,19). It is interesting to note that Dennehy et al. (2005) reported that increased adherence to Texas Medical Algorithm recommendations was associated with larger decreases in overall psychiatric symptoms and depressive symptoms over time, but did not impact either immediate or long-term reductions in manic symptoms.

A number of factors may affect clinician adherence to treatment guidelines. Shaneyfelt et al. (1999) indicated that the reasons physicians do not follow guidelines fell into different categories, including: lack of awareness, lack of agreement, lack of belief that outcomes will be affected by use of guidelines, and lack of familiarity. Many interventions have been proposed to enhance adherence to treatment guidelines, including education, continuous quality improvement, feedback methods, opinion leaders, reminders, incentives and penalties, and computerized systems. While different versions of these interventions have been effective in some studies, none are unequivocally superior, and many involve complex interventions and/or substantial cost (Dennehy et al. 2004). Computerized assessments may represent an improvement over other assessment methods, and preliminary findings using this approach indicate that this system of guideline adherence monitoring is feasible **(**Dennehy et al. 2004**)**. In our study clinicians were not formally trained to follow guidelines, but they were all interested in this study and also very experienced in the management of mood disorders. We can speculate that most of them were also aware of the TPA guideline recommendations.

There are some limitations of this study. First, patients were selected from a homogeneus data pool and data were evaluated retrospectively, even though we used a semistructured form (SKIPTURK) for the clinical interwiews. Second, we did not consider the type of bipolar disorders so the results may not reflect the whole bipolar spectrum. Third, we did not evaluate clinicians' attitudes to prescription, their basic knowledge and their level of awareness of guidelines.

CONCLUSION

Overall, these results suggest that, despite considerable efforts to develop and disseminate evidence-based guidelines, they are not widely followed by clinicians and important opportunities clearly exist to educate clinicians about the feasibility and utility of clinical guidelines for bipolar disorder. It is still unclear why such a discrepancy between practice and guidelines persists. Systematic studies in the future are required to clarify our understanding clinicians' attitudes to the use of guidelines, as well as the feasibility and cost-effectiveness of implementing guidelines.

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