Bipolar Disorders 2008: 10: 617–624

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BIPOLAR DISORDERS

Original Article

Quality of life and its association with insight, adverse effects of medication and use of atypical antipsychotics in patients with bipolar disorder and schizophrenia in remission

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Yen C-F, Cheng C-P, Huang C-F, Yen J-Y, Ko C-H, Chen C-S. Quality of life and its association with insight, adverse effects of medication and use of atypical antipsychotics in patients with bipolar disorder and schizophrenia in remission.
Bipolar Disord 2008: 10: 617–624. © 2008 The Authors Journal compilation © 2008 Blackwell Munksgaard

Objective: The present study aimed: (i) to compare the level of quality of life (QOL) among subjects with bipolar disorder (BD) and schizophrenia who were in remission and healthy control subjects and (ii) to examine the association of QOL with insight, adverse effects of medication and use of atypical antipsychotics among subjects with BD and schizophrenia who were in remission by controlling other confounding factors.

Methods: The QOL on the four domains of the World Health Organization Questionnaire on Quality of Life: Short Form – Taiwan version (WHOQOL-BREF) were compared between 96 subjects with BD in remission, 96 subjects with schizophrenia in remission and 106 healthy control subjects. The association between the four QOL domains and subjects' insight, adverse effects of medication and use of atypical antipsychotics were examined using multiple regression analyses in the subjects with BD and schizophrenia in remission.

Results: The results demonstrated that the subjects with BD in remission had similarly poor levels of QOL in all four domains as those subjects with schizophrenia in remission, and both subjects with BD and schizophrenia had poorer QOL than those in the control group. For both subjects with BD and schizophrenia in remission, insight was negatively associated with QOL on the physical domain, and adverse effects of medication were negatively associated with QOL on the physical and environment domains. Use of atypical antipsychotics was not associated with QOL, but subjects with BD receiving olanzapine perceived better psychological QOL than those receiving risperidone and better psychological and social relationship QOL than those receiving no atypical antipsychotic.

Conclusions: The results of the present study indicate that subjects with BD are dissatisfied with their QOL, even when they are in a remitted state. Clinicians must consider the negative influences of insight and adverse effects of medication on QOL of patients with BD and schizophrenia in remission.

Key words: adverse effects of medication – antipsychotic – bipolar disorder – insight – schizophrenia

Received 27 January 2007, revised and accepted for publication 27 July 2007

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The authors of this paper do not have any commercial or financial involvements that might pose a conflict of interest in connection with this manuscript.

The quality of life (QOL) of patients with mental disorders is emphasized in a consumer-oriented and holistic view of health care (1). Bipolar disor-

der (BD) and schizophrenia have long courses, a high tendency to relapse, and adverse impacts on multiple dimensions of functioning. Assessments of the impact of BD and schizophrenia on QOL are important in deciding how aggressively the disorders should be treated and for how long, measuring outcomes, assessing the health needs of patients, and allocating resources (2). QOL has been investigated in a number of studies of patients with schizophrenia (3); meanwhile, there is growing interest in QOL research in populations with BD (4).

Both patients with BD and with schizophrenia reported poorer QOL than those without mental disorder or in the general population (5, 6). However, contradictory findings have been reported regarding the difference in the level of QOL between patients with mood disorders and with schizophrenia (7, 8). One possible explanation for the controversy is that previous studies on this issue did not consider the confounding effect of psychopathology, which influences the perceived QOL in patients with BD (9, 10) and schizophrenia (11). Further research on patients in remission may provide more information for the difference in the level of QOL between patients with BD and with schizophrenia.

Insight has been considered as a predictor of clinical outcomes for mental illnesses (12, 13). However, while some studies reported no association between insight and QOL among patients with psychosis (8, 14–16), others found that different dimensions of insight were associated with domain-specific QOL in different directions (17, 18). Meanwhile, very few studies have examined the association between QOL and insight among patients with schizoaffective or mood disorders (8, 9, 19). Gazalle et al. (9) suggested that the mismatch between objective and subjective measures during acute mania may be associated with a lack of insight into their own illness. It is therefore desirable to evaluate the association between QOL and insight by a standard multi-dimensional measure in remitted patients with schizophrenia or BD.

Adverse effects of medication are common in treating patients with BD (20) and schizophrenia (21, 22). Subjective QOL is negatively influenced by the side effects of treatment in schizophrenic patients (8, 11, 23, 24). However, little is known about the impact of the adverse effects of pharmacotherapy for BD on QOL.

Atypical antipsychotic agents have been found to be effective not only for the treatment of schizophrenia, but also for the treatment of BD (25). While several studies have examined the association between QOL and use of atypical antipsychotics in patients with schizophrenia, the results are still controversial (26–31). Compared with the studies on schizophrenia, relatively few studies have addressed the impact of treatment with atypical antipsychotics on QOL in patients with BD (32, 33). Further studies are urgently needed before any firm conclusions can be reached.

Previous studies have found that duration of illness (14), educational level (5), sex (5), age (23), perceived social support (8) and medical adherence (34) are associated with QOL of patients with mental illnesses. These factors must be considered when examining the correlates of QOL in patients with BD and schizophrenia. The present study aimed: (i) to compare the level of QOL of subjects with remitted BD, with remitted schizophrenia and healthy control subjects; and (ii) to examine the association of QOL with insight, adverse effects of medication and use of atypical antipsychotics among subjects with BD and with schizophrenia in remission by controlling for other confounding factors.

Methods

Participants

The estimated sample size of this study was calculated based on our two major study hypotheses. Power was set at 80% and alpha was set at 0.05. With the expected SD and correlation coefficients from our pilot data, a sample of at least 94 was necessary for each group to test our hypotheses. From September 2002 to August 2004, 96 subjects with BD type I (BDI) and 96 subjects with schizophrenia who were in remitted state were enrolled from two university hospital psychiatric outpatient units. Two psychiatrists assessed all patients systematically to confirm the diagnoses of BDI and schizophrenia based on the diagnostic schemes of DSM-IV (35). The exclusion criteria were comorbid mental retardation, obvious head injury or substance use disorder. Psychopathology of subjects with schizophrenia was determined by using the 30-item Mandarin-Chinese version (36) of the Positive and Negative Syndrome Scale (PANSS) (37). Psychopathology of subjects with BDI was determined by using items 1–10 on the Young Mania Rating Scale (YMRS) (38) and the 24-item Hamilton Rating Scale for Depression (HAM-D) (39), except for the insight item. A current state of remission was defined by total PANSS score of ≤ 60, YMRS score of ≤ 6 and a HAM-D score of ≤ 6 (13, 40, 41).

We also enrolled 106 healthy control subjects using local advertisements. A psychiatrist interviewed all subjects responding to the advertisement using the diagnostic interviews to confirm that control subjects had no schizophrenia, BD, depressive disorders, or substance use disorder. Those subjects who had mental retardation or obvious head injury were also ruled out.

Measures

World Health Organization Questionnaire on Quality of Life: Short Form – Taiwan version. The World Health Organization Questionnaire on Quality of Life: Short Form (WHOQOL-BREF) was developed by the WHO to evaluate health-related QOL and make cross-cultural comparisons (42). The WHOQOL-Taiwan group has adapted the WHOQOL-BREF for use in Taiwan (43). The WHOQOL-BREF-Taiwan version contains 28 five-point items that assess general (2 items) and 4 specific domains of QOL, including 7 items in physical health, 6 in psychological, 4 in social relationships, and 9 in environmental domains, with well-established validity and reliability (43). The transformed scores of the four QOL domains were in the range of 0–100. Higher scores on the WHOQOL-BREF-Taiwan version indicate a higher perceived QOL.

Schedule of Assessment of Insight – Expanded version. The Schedule of Assessment of Insight – Expanded version (SAI-E) (44) measures multiple dimensions of insight, including compliance with treatment, recognition of illness, relabeling of psychotic phenomena, and awareness of changes in mental functioning and psychosocial consequences of the illness. The full score of the SAI-E is 24, with higher SAI-E scores indicating greater insight.

Questionnaire on Adverse Effects of Medication for Bipolar Disorder and Schizophrenia. We developed the self-administrated Questionnaire on Adverse Effects of Medication for Bipolar Disorder and Schizophrenia (QAEM-BS), containing 26 items, to evaluate the patients' perceived adverse effects induced by the mood stabilizers, antipsychotics, antidepressants or benzodiazepine (21, 22) used for treating BD and schizophrenia in the preceding two weeks. The positive items were summed up to represent the total severity of adverse effects of medication. The one-week test–retest reliability (r) of the QAEM-BS in the present study was 0.88 ($p < 0.001$). A psychiatrist assessed the severity of perceived adverse effects in 22 participants based on the QAEM-BS, and the intraclass correlation coefficient (ICC) between participants' self-reports and the psychiatrist's assessment were statistically significant (ICC = 0.724, $p < 0.005$).

Social Support Scale. The self-administrated Social Support Scale (SSS), containing 15 four-point items, was modified by Wang (45) from the Inventory of Socially Supportive Behavior developed by Barrera and Sandler (46). The higher the SSS scores, the higher the level of subjects' perceived social support.

Medication Adherence Behavior Scale. We used the four-point, seven-item Medication Adherence Behavior Scale (MABS) to evaluate subjects' medication-taking behaviors during the previous month, including incomplete implementation of prescriptions, taking medication at incorrect intervals or in incorrect doses, and premature termination of therapy (47). The higher the MABS score, the higher the subject's medication adherence.

Data regarding subjects' clinical and demographic characteristics and the kind of antipsychotics used for treatment were also recorded.

Procedure and statistical analysis

The protocol was approved by the Institutional Review Board of Kaohsiung Medical University. All subjects provided their written informed consent. Two psychiatrists performed the semi-structured interviews to determine insight, psychopathology and medical adherence for the subjects with BD or schizophrenia. A research assistant explained the methods of completing the self-administered questionnaires to each subject to help them complete the questionnaires by themselves and collected the data regarding QOL, adverse effects of medication and social support. The socio-demographic characteristics of all subjects, as well as duration of illness of subjects with BD and schizophrenia and previous mood episodes of subjects with BD, were also collected.

Levels of QOL on four domains of the WHOQOL-BREF between the groups of subjects were compared by the analysis of covariance (ANCOVA). We used two models of multiple regression analysis to examine the association between QOL and correlated factors. In the first model, the association between QOL and insight, adverse effects of medication and use of atypical antipsychotics were examined using the multiple regression analyses by controlling for other confounding factors in the subjects with BD and schizophrenia. In the second model, the factors

interacting between diagnoses and other factors were further included into the multiple regression analyses to examine the differences in the effects of correlated factors on QOL between BD and schizophrenia. An alpha value of 0.05 was used to indicate significance for all statistical tests.

We also compared the level of QOL among the subjects with BD and schizophrenia receiving olanzapine, risperidone, clozapine and no atypical antipsychotic, respectively. Because the number of subjects in each group was small, we used the Mann–Whitney *U*-tests to compare them.

Results

In subjects with BD, the mean of the present scores on the YMRS was 0.7 (SD = 1.7; range = 0–6) and on the HAM-D 0.8 (SD = 1.9; range = 0–6). In subjects with schizophrenia, the mean of the present scores on the PANSS was 49.6 (SD = 7.7; range = 32–60). These means of scores indicated that all subjects with BD or schizophrenia were in a state of remission.

The socio-demographic data, social support, duration of illness, previous mood episodes, insight, adverse effects of medication and medical adherence in groups of subjects with BD and with schizophrenia and healthy control subjects are shown in Table 1. Among subjects with BD who received atypical antipsychotics (n = 27), risperidone (n = 14; 51.9%) and olanzapine (n = 11; 40.7%) were the most common. Among the subjects with schizophrenia who received atypical antipsychotics (n = 71), risperidone (n = 41; 57.7%), olanzapine (n = 16; 22.5%) and clozapine (n = 8; 11.3%) were the most common.

Before comparing the QOL among the three groups, we examined the differences in age and proportion of gender among them. Subjects with BD were older than those with schizophrenia and control subjects ($F = 19.677$, $p < 0.001$) and no difference in the proportion of gender was found ($\chi^2 = 0.431$, $p > 0.05$). The levels of QOL on four domains of the WHOQOL-BREF among the three groups of subjects were compared by using ANCOVA, controlling for age (Table 2). The results indicated that both subjects with BD and schizophrenia had poorer QOL on the physical, psychological, social relationship and environment domains than those in the control group after controlling for the effects of age. However, no difference in the QOL on any domain was found between subjects with BD and schizophrenia.

The association of QOL with insight, adverse effects of medication and use of atypical antipsychotics by using multiple regression analyses to control for other factors in subjects with BD and schizophrenia are shown in Table 3. The results indicated that those who had a higher level of insight and perceived more severe adverse effects of medication had poorer QOL on the physical domain; meanwhile, those who perceived more severe adverse effects of medication had poorer QOL on the environment domain. However, neither insight, perceived adverse effects of medication, nor use of atypical antipsychotic was associated with QOL on the psychological or social relationship domain. To examine whether the effects of correlated factors on QOL were different between subjects with BD and schizophrenia, we further included the factors interacting between diagnoses and correlated factors into the multiple

Table 1. Socio-demographic data, social support, duration of illness, previous mood episodes, insight, medical adherence, adverse effects of medication and use of atypical antipsychotics

	Bipolar (n = 96)		Schizophrenia (n = 96)		Control (n = 106)	
	Mean (SD)	n (%)	Mean (SD)	n (%)	Mean (SD)	n (%)
Socio-demographic characteristics						
Age (years)	40.8 (12.7)		32.5 (8.1)		33.8 (8.1)	
Education (years)	11.8 (3.4)		11.9 (1.9)		12.0 (1.1)	
Gender: female		46 (47.9)		50 (52.1)		55 (51.9)
Social support on the SSS	28.6 (9.5)		26.1 (10.3)		29.2 (8.9)	
Duration of illness (months)	149.0[a] (126.6)		104.5[b] (70.6)		–	
Previous mood episodes	5.1 (4.8)					
Insight on the SAI-E	14.0 (7.4)		11.6 (7.3)		–	
Medical adherence on the QAEM-BS	21.6 (5.6)		22.8 (6.1)			
Adverse effects of medication on the QAEM-BS	5.9 (4.5)		6.9 (5.3)		–	
Treated by atypical antipsychotics		27 (28.1)		71 (74.0)		

SSS = Social Support Scale; SAI-E = Schedule of Assessment of Insight-Expanded version; QAEM-BS = Questionnaire on Adverse Effects of Medication for Bipolar Disorders and Schizophrenia.
[a]Median duration of illness = 126 months.
[b]Median duration of illness = 89 months.

Table 2. Quality of life of subjects in the bipolar, schizophrenia and control groups determined by ANCOVA, adjusting for age

	Bipolar mean (SD)[a]	Schizophrenia mean (SD)[a]	Control mean (SD)[a]	*F*	*Post hoc*
Physical	56.9 (1.5)	55.3 (1.5)	70.8 (1.4)	24.221[c]	Control > bipolar Control > schizophrenia
Psychological	48.6 (1.5)	49.1 (1.4)	54.5 (1.3)	5.620[b]	Control > bipolar Control > schizophrenia
Social relationship	53.3 (1.6)	50.4 (1.6)	62.2 (1.5)	16.2462[c]	Control > bipolar Control > schizophrenia
Environment	48.4 (1.2)	46.0 (1.2)	51.9 (1.1)	6.374[b]	Control > bipolar Control > schizophrenia

[a]Estimated marginal means.
[b]$p < 0.01$.
[c]$p < 0.001$.

Table 3. Variables associated with quality of life in multiple linear regression analyses

	Physical		Psychological		Social relationship		Environment	
	β	*t*	β	*t*	β	*t*	β	*t*
Insight on the SAI-E	−0.170	−2.255[a]	0.059	0.745	−0.132	−1.742	0.039	0.522
Adverse effects of medication on the QAEM-BS	−0.341	−5.160[b]	−0.123	−1.780	−0.116	−1.743	−0.294	−4.476[b]
Treated by atypical antipsychotics	−0.002	−0.030	0.087	1.121	0.059	0.793	0.046	0.628
Diagnosis (1: schizophrenia)	−0.023	−0.284	0.061	0.716	−0.062	−0.763	−0.060	−0.750
Duration of illness	−0.011	−0.130	0.117	1.293	−0.037	−0.426	0.061	0.702
Medical adherence on the QAEM-BS	−0.022	−0.291	−0.034	−0.430	0.016	0.214	0.079	1.048
Age	0.056	0.587	0.112	1.130	0.247	2.591[a]	0.081	0.860
Gender (1: female)	−0.010	−0.154	−0.027	−0.397	0.115	1.761	0.072	1.115
Education	−0.072	−1.017	0.036	0.488	0.005	0.067	0.008	0.109
Social support on the SSS	0.261	3.890[b]	0.352	5.035[b]	0.350	5.207[b]	0.305	4.591[b]
R^2	0.253		0.185		0.248		0.264	
F-value	6.121[b]		4.114[b]		5.961[b]		6.507[b]	

[a]$p < 0.05$.
[b]$p < 0.001$.
SAI-E = Schedule of Assessment of Insight-Expanded version; QAEM-BS = Questionnaire on Adverse Effects of Medication for Bipolar Disorders and Schizophrenia; SSS = Social Support Scale.

regression analyses. The results indicated that the change of R^2 was not significant in the physical ($\Delta R^2 = 0.005$, $F = 0.157$, $p = 0.996$), psychological ($\Delta R^2 = 0.017$, $F = 0.468$, $p = 0.878$), social relationship ($\Delta R^2 = 0.050$, $F = 1.534$, $p = 0.148$) or environment ($\Delta R^2 = 0.047$, $F = 1.468$, $p = 0.172$) domain of QOL, which indicated that the effects of insight and adverse effects of medication on QOL existed in both subjects with BD and schizophrenia.

The results of the Mann–Whitney *U*-test found that the subjects with BD receiving olanzapine had higher scores on the psychological QOL domain than those receiving risperidone ($Z = -2.943$, $p < 0.01$) and those receiving no atypical antipsychotic ($Z = -2.635$, $p < 0.01$), as well as having higher scores on the social relationship QOL domain than those receiving no atypical antipsychotic ($Z = -2.132$, $p < 0.05$). Because the subjects with BD receiving olanzapine were not different from the other two groups in demographic and clinical characteristics, social support and insight, and perceived more severe adverse effect of medication than those receiving no atypical antipsychotic ($Z = -2.495$, $p < 0.05$), these differences in QOL could not be accounted for by other factors. On the other hand, no difference in any domain of QOL was found among the subjects with schizophrenia receiving olanzapine, risperidone, clozapine or no atypical antipsychotic.

Discussion

This is the first study comparing the QOL among subjects with BD and schizophrenia who are in a remitted state. The study design could reduce the

confounding effect of psychopathology. We found that subjects with BD in remission had similarly poor QOL compared with subjects with schizophrenia in remission. This result is in line with the study of Depp et al. (48), and further supports the idea that subjects with BD are dissatisfied with their QOL, even when they are in remitted state. We also found that subjects with BD and schizophrenia in remission have poorer QOL than the control subjects. Compared with the general population, subjects with BD and schizophrenia may have additional needs, fewer personal and environmental resources, and a serious needs dilemma due to stigma, which may make them less satisfied with their QOL (3).

The present study found that those subjects with BD and schizophrenia who had a higher level of insight had poorer QOL on the physical domain. The stigma elicited by the psychiatric diagnosis may partially account for the association (49). Individuals who have been given a psychiatric diagnosis tend to be viewed as dangerous, unpredictable, inexplicable, and unlikely to improve (50), and by accepting the diagnosis, patients accept the negative attitudes and stigma associated with the diagnosis (17). Public stigma toward psychiatric patients is prevalent everywhere, including medical services (51). To avoid encountering prejudice from others, individuals with psychiatric diagnoses may choose not to seek medical services even though they may have physical discomfort (52). Delay in looking for assistance from medical services may aggravate their physical problems. However, the reason why insight was negatively associated with QOL only on the physical domain and not with other QOL domains in the present study needs to be examined in further studies.

This is the first study to examine the association between QOL and adverse effects of medication in patients with BD. We found that, as in patients with schizophrenia, adverse effects of medication were associated with poor QOL in specific domains in patients with BD. Although the severity of psychopathology is negatively correlated with QOL (10, 53), and improving the level of psychopathology using medication appears to be important in improving QOL, intolerable adverse effects of medication may compromise patients' QOL, which may further compromise their medical adherence. Poor medical adherence results in recurrence of psychopathology, which adversely influences the patients' QOL in a vicious cycle. Adverse effects of medication may also affect patients' cognition and emotion and increase the risk of somatization (18), which may further make patients dissatisfied with their QOL. The findings of this study indicate that clinicians must help patients with BD or schizophrenia identify and manage the adverse effects of therapy. Frequent discussions with patients may encourage them to continue treatment and to accept the balance of benefits and adverse effects of treatment.

The present study examined QOL of subjects with BD and schizophrenia under naturalistic treatment conditions, and found that the subjects with BD and schizophrenia receiving atypical antipsychotics do not have superior QOL compared with those receiving no atypical antipsychotic. This result is in line with the naturalistic treatment study of Kilian and Angermeyer (54) and the antipsychotic-changing study of Jones et al. (27). By further comparing QOL among subjects receiving different kinds of atypical antipsychotics, we found that subjects with BD receiving olanzapine perceived better psychological QOL than those receiving risperidone, and better psychological and social relationship QOL than those receiving no atypical antipsychotic. Previous studies also found that olanzapine has a unique effect in improving QOL of subjects with BD (29, 55, 56). However, the numbers of subjects with BD receiving olanzapine and risperidone in the present study were relatively small.

The results obtained in the present study need to be interpreted in light of several study limitations. First, no information from family members, friends or professionals was used to confirm participants' self-evaluation of the level of QOL, insight and adverse effects of medication. Second, the study examined QOL of subjects under naturalistic treatment conditions, and did not trace previously prescribed medication. Some subjects may have received atypical antipsychotics after no response to conventional antipsychotics or mood stabilizers, which might limit the possibility of concluding that there is an association between QOL and atypical antipsychotics.

Acknowledgements

This study was supported by grant NSC 91-2413-H-037-005 and NSC 92-2413-H-037-010 awarded by the National Science Council, Taiwan (ROC).

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