



ELSEVIER

Available online at www.sciencedirect.com

Psychiatry Research xx (2007) xxx–xxx

PSYCHIATRY
RESEARCH

www.elsevier.com/locate/psychres

Manic symptoms and quality of life in bipolar disorder

Fernando Kratz Gazalle ^{a,b}, Pedro Curi Hallal ^c, Ana Cristina Andreazza ^b,
 Benício Noronha Frey ^b, Márcia Kauer-Sant'Anna ^b, Fernanda Weyne ^b,
 Sabrina Corrêa da Costa ^b, Aida Santin ^b, Flávio Kapczinski ^{a,b,*}

^a *Psychiatric Research Unit, Post-Graduate Psychiatry Program, Federal University of Rio Grande do Sul, Porto Alegre, RS, Brazil*

^b *Bipolar Disorders Program, University Hospital, Federal University of Rio Grande do Sul, Porto Alegre, RS, Brazil*

^c *Federal University of Pelotas, Pelotas, RS, Brazil*

Received 10 October 2005; received in revised form 4 May 2006; accepted 26 July 2006

Abstract

This study evaluates the influence of manic symptoms on quality of life in a sample of adult bipolar disorder (BD) patients. This was a cross-sectional study including 125 BD outpatients from a university-based program. All patients were diagnosed using the Structured Clinical Interview for DSM-IV for BD. Manic symptoms and quality of life were assessed using the Young Mania Rating Scale (YMRS) and the World Health Organization Quality of Life Instrument–Short Version (WHOQOL–BREF), respectively. In the unadjusted analysis using linear regression, the score of manic symptoms was inversely associated with scores of quality of life within the social domain of the WHOQOL. In the adjusted analysis, the score of manic symptoms was inversely associated with the social, physical, and psychological domains of the WHOQOL. In a separate analysis at the YMRS items, items 4 (irritability) and 5 (sleep) were associated with lower quality of life.

© 2006 Elsevier Ireland Ltd. All rights reserved.

Keywords: Bipolar disorder; Quality of life; Manic symptoms; Depressed mood

1. Introduction

Bipolar disorder (BD) is estimated to affect 6% of the population (Judd and Akiskal, 2003), and is characterized by recurrent major depressive and manic or hypomanic episodes. According to the World Health Organization (WHO), BD is considered the sixth leading cause of disability amongst all medical and

psychiatric conditions (Murray and Lopez, 1997). Studies have demonstrated that the annual costs of BD to the society range from 1.8 to 45 billion US dollars; indirect costs due to work absence are the most important ones (Wyatt and Henter, 1995; Das Gupta and Guest, 2002; Hakkaart-van Roijen et al., 2004). In addition, Morselli et al. recently published an update of the GAMIAN-Europe/BEAM survey, and demonstrated that less than half of the total BD sample ($n=968$) had an active job (Morselli et al., 2004). The authors also concluded that the negative impact of BD on patients was evident in all countries (Morselli et al., 2004). Although the functional impairment of bipolar patients is usually attributed to depressive and manic episodes,

* Corresponding author. Laboratório de Psiquiatria Experimental, Centro de Pesquisas, Hospital de Clínicas de Porto Alegre, Ramiro Barcelos 2350, Zip code 90035-000, Porto Alegre, RS, Brazil. Tel.: +55 51 32227309; fax: +55 51 32228047.

E-mail address: kapcz@terra.com.br (F. Kapczinski).

high rates of unemployment have been described even in clinically remitted patients (Strakowski et al., 1998; Zarate et al., 2000).

It seems that quality of life, as determined by illness intrusiveness, is compromised in subjects with BD even during periods of euthymia. BD is at least as intrusive as several other chronic medical conditions (Robb et al., 1997). Subjects with type II BD report greater impairment in all domains compared with type I. In fact, long-term cohort studies have shown that both type-I and type-II BD patients experience clinical symptoms over approximately half of their lives (Judd and Akiskal, 2003).

The concept of quality of life is not limited to lack of disease. It encompasses the individual's mental, physical, social, functional and spiritual perception of well-being (Guyatt et al., 1993). The measurement of quality of life has had many different purposes in clinical research, and it has been considered a helpful measure of both functional (Yatham et al., 2004) and symptomatic (Thunedborg et al., 1995) recovery or impairment in mental care settings. Although several studies have assessed quality of life in unipolar depressive disorder, less attention has been given to BD (Namjoshi and Buesching, 2001; Dean et al., 2004). It was previously shown that euthymic and depressed outpatients with BD are able to provide reliable self-reports on their quality of life, a finding that encourages new studies within this group (Leidy et al., 1998).

A recent review found that the vast majority of the studies were performed with small sample sizes, illustrating the difficulty of including a large number of BD patients in quality of life studies (Namjoshi and Buesching, 2001). Another review on quality of life and BD stated that there is a need for more assessment of quality of life in (hypo) manic patients (Michalak et al., 2005).

In a large sample ($n=1157$) of outpatients in a primary care setting, Das et al. recently found that patients who screened positive for BD had lower mental and physical quality of life scores than those who screened negative (Das et al., 2005). Interestingly, some studies have demonstrated lower levels of quality of life in bipolar depression in comparison with unipolar depression (Yatham et al., 2004). Levels of depressive symptoms (Russo et al., 1997; Vojta et al., 2001; Yatham et al., 2004; Sierra et al., 2005), female gender (Robb et al., 1998), and time undiagnosed (Gazalle et al., 2005), have been put forward as predictors of worse quality of life in BD samples.

The association between socio-demographic characteristics and quality of life was found for gender, age,

education, employment status and living arrangement. Differences in quality of life were found between groups with different clinical characteristics, such as diagnosis, hospitalization during the last 12 months and age at first hospitalization. Using socio-demographic and clinical variables in addition to psychosocial variables appears to be promising for understanding quality of life in psychotic patients (Caron et al., 2005). Another study, including schizophrenia spectrum disorder patients, found that subjects with a comorbid depressive syndrome had greater awareness of their mental illness, its social consequences and treatment efficacy, but poorer overall quality of life (Sim et al., 2004).

The aim of the present study was to evaluate the effect of a score of manic symptoms on quality of life in a sample of adult BD outpatients. Both unadjusted and adjusted analyses are presented. The effect of distinct manic symptoms on quality of life was also tested.

2. Methods

This study was a cross-sectional survey of 125 outpatients with BD, 18 years or older, consecutively assessed from September 2003 to November 2004. All patients were recruited from the Bipolar Disorders Program of the Hospital of the Federal University of Rio Grande do Sul, Porto Alegre, Brazil.

All patients met the Diagnostic and Statistical Manual of Mental Disorders, Fourth edition (DSM-IV) (American Psychiatric Association, 2000) criteria for type I, type II, or not otherwise specified BD. Diagnostic interviews were carried out by trained psychiatrists using the Structured Clinical Interview (SCID) for DSM-IV (First et al., 1996).

Patients were referred to the program by general practitioners and community-based psychiatrists. About 90% of the sample had type-I BD; the remainder of the sample consisted of type-II BD and not otherwise specified BD. About 80% of the patients had previously been hospitalized due to an acute episode. All patients were diagnosed and treated before their inclusion in the program.

The outcome variable was quality of life. The cross-culturally validated version of the World Health Organization's Quality of Life Instrument–Short Version (WHOQOL–BREF) (The Whoqol Group, 1998) was used. The WHOQOL–BREF is a self-administered, multidimensional scale used to assess physical, psychological, social and environmental aspects of quality of life. Each of these domains is treated as a separate

Table 1
Description of the sample in terms of demographic variables, item 1 (depressed mood) of the Hamilton Depressive Rating Scale (HDRS) and each item of the Young Mania Rating Scale (YMRS)

Variable	Bipolar patients (N=125)
Sex	
Men (%)	26.4
Women (%)	73.6
Age (years)	
Mean (S.D.)	42.1 (11.7)
<40 (%)	41.6
40–59 (%)	52.8
≥60 (%)	5.6
HDRS – Item 1	
0 (%)	37.1
1 (%)	25.8
2 (%)	19.4
3 (%)	16.1
4 (%)	1.6
YMRS	
Mean (S.D.)	4.16 (4.62)
Item 1	0.32 (0.66)
Item 2	0.37 (0.80)
Item 3	0.18 (0.60)
Item 4	0.57 (0.98)
Item 5	1.23 (1.25)
Item 6	0.47 (1.17)
Item 7	0.29 (0.58)
Item 8	0.33 (0.95)
Item 9	0.09 (0.36)
Item 10	0.16 (0.56)
Item 11	0.20 (0.60)

numeric variable. The higher the score, the higher the quality of life. Previous studies have used this instrument for assessing quality of life in BD patients (Brieger et al., 2004; Chand et al., 2004).

Table 2
Crude and adjusted linear regression coefficients of quality of life (WHOQOL) according to the Young Mania Rating Scale (YMRS)

WHOQOL domains	Crude analysis		Adjusted analysis ^a	
	Coefficient (95% CI)	P value ^b	Coefficient (95% CI)	P value ^b
Physical	0	0.067	0	0.030
	−0.17 (−1.5; 0.52)		−0.19 (−1.56; 0.08)	
Psychological	0	0.168	0	0.046
	−0.13 (−1.40; 0.24)		−0.16 (−1.45; −0.15)	
Social	0	0.032	0	0.033
	−0.20 (−1.85; 0.09)		−0.19 (−1.86; −0.08)	
Environmental	0	0.168	0	0.143
	−0.13 (−1.07; 0.19)		−0.13 (−1.04; 0.153)	

^a Adjusted for sex, age, family income and item 1 of the Hamilton Depression Rating Scale.

^b Wald test.

Demographic and socioeconomic data were collected using a standardized and structured questionnaire. Manic symptoms were assessed using the Young Mania Rating Scale (YMRS) (Young et al., 1978) while depressive symptoms were evaluated using the Hamilton Depression Rating Scale (HDRS) (Hamilton, 1960).

Analyses were carried out in SPSS 10.0. Unadjusted and adjusted analyses were performed for each domain of quality of life separately using linear regression models. The outcome variable in each model was the domain of quality of life, treated as a numeric variable. The numerical YMRS was included as an independent variable. In the adjusted analyses, the effect of the total score of the YMRS on quality of life was controlled for sex, age, family income and depressive mood as assessed by the HDRS. Pearson correlation coefficients were calculated between each item of the YMRS and the WHOQOL domains.

The Ethics Committee of the Hospital de Clínicas de Porto Alegre gave ethical clearance. Written informed consent was collected before the interview from all patients.

3. Results

A total of 125 patients were included in the present analysis. Out of these, 90% were BD type I. Table 1 shows that almost three in every four (73.6%) were women, and the mean age was 42.1 years. It also describes the sample in terms of the results of the HDRS. In terms of the YMRS, the mean score was 4.16 (S.D.=4.62). Items 4 and 6 presented the highest mean scores.

Table 3

Association between each item of the Young Mania Rating Scale (YMRS) and the domains of quality of life (WHOQOL)

YMRS	WHOQOL domains							
	Physical		Psychological		Social		Environmental	
	<i>R</i>	<i>P</i> *	<i>R</i>	<i>P</i> *	<i>R</i>	<i>P</i> *	<i>R</i>	<i>P</i> *
Elevated mood	0.129	0.160	0.174	0.057	0.071	0.440	0.209	0.022
Increased motor activity-energy	0.030	0.746	−0.019	0.838	−0.257	0.005	−0.111	0.228
Sexual interest	−0.151	0.101	−0.138	0.134	0.001	0.990	−0.034	0.713
Sleep	−0.274	0.002	−0.186	0.042	−0.188	0.039	−0.262	0.004
Irritability	−0.329	0.001	−0.328	0.001	−0.208	0.022	−0.225	0.014
Speech	0.056	0.542	−0.005	0.955	−0.102	0.269	−0.009	0.926
Language–thought disorder	0.041	0.660	0.077	0.403	−0.033	0.719	0.038	0.679
Content	−0.118	0.200	−0.031	0.736	−0.029	0.755	−0.037	0.692
Disruptive–aggressive behavior	0.013	0.885	0.044	0.637	−0.102	0.269	−0.017	0.856
Appearance	−0.199	0.029	−0.137	0.135	−0.113	0.218	−0.062	0.499
Insight	0.043	0.642	0.077	0.403	−0.054	0.558	−0.001	0.988

R=Pearson's correlation coefficient. *P**=significant results are displayed in italic.

The mean values and standard deviations of the four domains of the WHOQOL for the whole sample were as follows: physical (mean=50.7, S.D.=20.3), psychological (mean=48.8, S.D.=20.7), social (mean=51.0, S.D.=22.8) and environmental (mean=53.0, S.D.=16.0). The distribution of all four domains was tested using the Kolmogorov–Smirnov test, and all distributions were normal.

Table 2 presents the unadjusted and adjusted analyses of the association between each domain of quality of life and the total score of manic symptoms by the YMRS. In the unadjusted analysis, patients with higher scores of manic symptoms presented significantly lower values of the social domain of quality of life. The same trend was observed for YMRS scores and the physical domain of the WHOQOL, but the association was of borderline significance ($P=0.07$). The environmental and the psychological domains of quality of life were not significantly associated with the YMRS score in the unadjusted analysis. After adjustment for confounding, higher YMRS scores were found to be significantly associated with lower scores of quality of life within the social, physical and psychological domains. The environmental domain of quality of life was not significantly associated with scores of the YMRS scale.

In Table 3, the correlation between each item of the YMRS and quality of life domains is presented. Items 4 (sleep) and 5 (irritability) were inversely associated with all domains of quality of life. Furthermore, item 10 (appearance) was inversely associated with the physical domain, item 2 (increased motor activity-energy) was inversely associated with the social domain, and item 1 (elevated mood) was positively associated with the environmental domain.

4. Discussion

In a cross-sectional study including 125 BD outpatients, a score of manic symptoms was inversely associated with the physical, psychological and social domains of quality of life. Although the sample size was adequate to detect significant associations, the hypothesis presented here should be confirmed in larger datasets. Particularly, the association between each item of the YMRS and quality of life may have suffered from lack of power. In addition, cross-sectional studies are possibly affected by the reverse causality bias, and establishing the temporal relationship between the outcome and the exposure is a challenge in studies with this design. Data regarding the effects of chronic exposure to manic symptoms on quality of life should be confirmed in by prospective studies. It should also be considered that measurement of quality of life is challenging, and may lead to some degree of misclassification. However, a previous study suggested that BD patients provide reliable self-reports of quality of life.

Previous studies have shown that levels of depressive symptoms (Russo et al., 1997; Vojta et al., 2001; Yatham et al., 2004; Sierra et al., 2005) and number of years undiagnosed (Gazalle et al., 2005) have been associated with poorer QOL in BD patients. We now show that manic symptoms are also related to poorer QOL in BD patients. This effect was clearer when confounding variables such as demographic factors and depressed mood were controlled for. Thus, independently of gender, age, income and scores of depressed mood, patients with higher scores of manic symptoms showed poorer QOL in all domains of quality of life, except the environmental one.

Quality of life was shown to be higher in patients in remission in comparison with those in acute episodes of mood disorders (Namjoshi and Buesching, 2001). Improvements in quality of life should be one of the main goals in the treatment of BD. A recent study (Yatham et al., 2004) showed that bipolar depressive patients have worse psychological quality of life than unipolar depressives. This finding highlights the importance of recognizing the history of previous manic symptoms in patients in a major depressive episode (Ghaemi et al., 1999; Das et al., 2005). The deleterious consequences of a delayed diagnosis of BD have been recently documented (Gazalle et al., 2005).

Irritability was associated with three of the four domains assessed using the WHOQOL instrument (Table 3). It should be mentioned that irritability is an important symptom of unipolar depression as well. However, depressed mood was controlled in our analysis, which makes it unlikely that the depressive syndrome would explain the results reported in the present study.

Vojta et al. demonstrated that manic/hypomanic patients had lower mental, but not physical quality of life than euthymic BD patients (Vojta et al., 2001). In a long-term study of unipolar patients, Dunner et al. found that those who switched to mania/hypomania during the follow-up had higher “interpersonal sensitivity” than the “true unipolars” (Dunner, 2003). Also, the presence of manic symptoms may be associated with increased impulsivity and suicidal tendencies observed in BD (Mitchell et al., 2001; Angst et al., 2002).

Understanding why BD patients present lower QOL scores as compared to unipolar patients is a major challenge (Yatham et al., 2004). The present study suggests that, apart from depressive mood, manic symptoms are an important component of the lower QOL reported among patients with BD.

Acknowledgements

This work was supported by grants from CNPq–Brazil, CAPES–Brazil, FINEP (HCPA)–Brazil.

The authors thank Professor Marcelo P. A. Fleck for his thoughtful comments on the use of the WHOQOL instrument.

References

American Psychiatric Association, 2000. Diagnostic and Statistical Manual of Mental Disorders, 4th edition. American Psychiatric Press, Washington, DC. Text revision.

- Angst, F., Stassen, H.H., Clayton, P.J., Angst, J., 2002. Mortality of patients with mood disorders: follow-up over 34–38 years. *Journal of Affective Disorders* 68, 167–181.
- Brieger, P., Rottig, S., Marneros, 2004. Quality of life in bipolar depressive and bipolar affective patients. *Psychiatrische Praxis* 31, 304–309.
- Caron, J., Mercier, C., Diaz, P., Martin, A., 2005. Socio-demographic and clinical predictors of quality of life in patients with schizophrenia or schizo-affective disorder. *Psychiatry Research* 15 (137), 203–213.
- Chand, P.K., Matoo, S.K., Sharan, P., 2004. Quality of life and its correlates in patients with bipolar disorder stabilized on lithium prophylaxis. *Psychiatry and Clinical Neurosciences* 58 (3), 311–318.
- Das, A.K., Olfson, M., Gameroff, M.J., Pilowsky, D.J., Blanco, C., Feder, A., Gross, R., Neria, Y., Lantigua, R., Shea, S., Weissman, M.M., 2005. Screening for bipolar disorder in a primary care practice. *Journal of the American Medical Association* 293, 956–963.
- Das Gupta, R., Guest, J.F., 2002. Annual cost of bipolar disorder to UK society. *British Journal of Psychiatry* 180, 227–233.
- Dean, B.B., Gerner, D., Gerner, R.H., 2004. A systematic review evaluating health-related quality of life, work impairment, and healthcare costs and utilization in bipolar disorder. *Current Medical Research and Opinion* 20, 139–154.
- Dunner, D.L., 2003. Clinical consequences of under-recognized bipolar spectrum disorder. *Bipolar Disorders* 5, 456–463.
- First, M.B., Spitzer, R.L., Gibbon, M., Williams, J.B., 1996. *User's Guide to Structured Clinical Interview for DSM-IV (SCID-I)*. Biometrics Research, New York.
- Gazalle, F.K., Andreatza, A.C., Cereser, K.M., Hallal, P.C., Santin, A., Kapczynski, F., 2005. Clinical impact of late diagnosis of bipolar disorder. *Journal of Affective Disorders* 86, 313–316.
- Ghaemi, S.N., Sachs, G.S., Chiou, A.M., Pandurangi, A.K., Goodwin, F.K., 1999. Is bipolar disorder still underdiagnosed? Are antidepressants overutilized? *Journal of Affective Disorders* 52, 135–144.
- Guyatt, G.H., Feeny, D.H., Patrick, D.L., 1993. Measuring health-related quality of life. *Annals of Internal Medicine* 118, 622–629.
- Hakkaart-van Roijen, L., Hoeijenbos, M.B., Regeer, E.J., ten Have, M., Nolen, W.A., Veraart, C.P., Rutten, F.F., 2004. The societal costs and quality of life of patients suffering from bipolar disorder in the Netherlands. *Acta Psychiatrica Scandinavica* 110, 383–392.
- Hamilton, M., 1960. A rating scale for depression. *Journal of Neurology, Neurosurgery and Psychiatry* 23, 56–62.
- Judd, L.L., Akiskal, H.S., 2003. The prevalence and disability of bipolar spectrum disorders in the US population: re-analysis of the ECA database taking into account subthreshold cases. *Journal of Affective Disorders* 73 (1–2), 123–131.
- Leidy, N.K., Palmer, C., Murray, M., Robb, J., Ravicki, D.A., 1998. Health-related quality of life assessment in euthymic and depressed patients with bipolar disorder. Psychometric performance of four self-report measures. *Journal of Affective Disorders* 48, 207–214.
- Michalak, E.E., Yatham, L.N., Lam, L.W., 2005. Quality of life in bipolar disorder: a review of the literature. *Health and Quality of Life Outcomes* 1, 3–72.
- Mitchell, P.B., Wilhelm, K., Parker, G., Austin, M.P., Rutgers, P., Malhi, G.S., 2001. The clinical features of bipolar depression: a comparison with matched major depressive disorder patients. *Journal of Clinical Psychiatry* 62, 212–216 (quiz 217).

- Morselli, P.L., Elgie, R., Cesana, B.M., 2004. GAMIAN-Europe/BEAM analysis of unemployment, family history, treatment satisfaction and impact of the bipolar disorder on life style. *Bipolar Disorders* 6, 487–497.
- Murray, C.J., Lopez, A.D., 1997. Global mortality, disability, and the contribution of risk factors: global burden of disease study. *Lancet* 349, 1436–1442.
- Namjoshi, M.A., Buesching, D.P., 2001. A review of the health-related quality of life literature in bipolar disorder. *Quality of Life Research* 10, 105–115.
- Robb, J.C., Cooke, R.G., Devins, G.M., Young, L.T., Joffe, R.T., 1997. Quality of life and lifestyle disruption in euthymic bipolar disorder. *Journal of Psychiatric Research* 31, 509–517.
- Robb, J.C., Young, L.T., Cooke, R.G., Joffe, R.T., 1998. Gender differences in patients with bipolar disorder influence outcome in the medical outcomes survey (SF-20) subscale scores. *Journal of Affective Disorders* 49, 189–193.
- Russo, J., Roy-Byrne, P., Reeder, D., Alexander, M., Dwyer-O'Connor, E., Dagadakis, C., Ries, R., Patrick, D., 1997. Longitudinal assessment of quality of life in acute psychiatric inpatients: reliability and validity. *Journal of Nervous and Mental Disorder* 185, 166–175.
- Sierra, P., Livianos, L., Rojo, L., 2005. Quality of life for patients with bipolar disorder: relationship with clinical and demographic variables. *Bipolar Disorders* 7, 159–165.
- Sim, K., Mahendram, R., Siris, S.G., Heckers, S., Chong, S.A., 2004. Subjective quality of life in first episode schizophrenia spectrum disorders with comorbid depression. *Psychiatry Research* 15, 141–147.
- Strakowski, S.M., Sax, K.W., McElroy, S.L., Keck Jr., P.E., Hawkins, J.M., West, S.A., 1998. Course of psychiatric and substance abuse syndromes co-occurring with bipolar disorder after a first psychiatric hospitalization. *Journal of Clinical Psychiatry* 59, 465–471.
- The WHOQOL Group, 1998. Development of the World Health Organization WHOQOL-BREF. *Quality of life assessment. Psychological Medicine* 28, 551–558.
- Thunedborg, K., Black, C.H., Bech, P., 1995. Beyond the Hamilton depression scores in long-term treatment of manic-melancholic patients: prediction of recurrence of depression by quality of life measurements. *Psychotherapy and Psychosomatics* 64, 131–140.
- Vojta, C., Kinosian, B., Glick, H., Altshuler, L., Bauer, M.S., 2001. Self-reported quality of life across mood states in bipolar disorder. *Comprehensive Psychiatry* 42, 190–195.
- Wyatt, R.J., Henter, I., 1995. An economic evaluation of manic-depressive illness. *Social Psychiatry and Psychiatric Epidemiology* 30, 213–219.
- Yatham, L.N., Lecrubier, Y., Fieve, R.R., Davis, K.H., Harris, S.D., Krishnan, A.A., 2004. Quality of life in patients with bipolar I depression: data from 920 patients. *Bipolar Disorders* 6, 379–385.
- Young, R.C., Biggs, J.T., Ziegler, V.E., Meyer, D.A., 1978. A rating scale for mania: reliability, validity and sensitivity. *British Journal of Psychiatry* 133, 429–435.
- Zarate Jr., C.A., Tohen, M., Land, M., Cavanagh, S., 2000. Functional impairment and cognition in bipolar disorder. *Psychiatry Quarterly* 71, 309–329.