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Transtorno afetivo bipolar: perfil farmacoterapêutico e adesão ao medicamento

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Bipolar affective disorder: pharmacotherapeutic profile and adherence to medication

TRANSTORNO AFETIVO BIPOLAR: PERFIL FARMACOTERAPÊUTICO E ADESÃO AO MEDICAMENTO

TRANSTORNO AFECTIVO BIPOLAR: PERFIL FÁRMACO-TERAPÉUTICO Y ADHESIÓN A LA MEDICACIÓN

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ABSTRACT

This cross-sectional and descriptive study aimed to verify the adherence of patients with Bipolar Affective Disorder (BAD) to medication and to identify possible causes of adherence and non-adherence to medication according to the pharmacotherapeutic profile. The study was carried out in a mental health service in a city in the interior of the state of São Paulo. Participants included 101 patients with BAD. Structured interviews and the Morisky-Green test were used for data collection, and the Statistical Package for Social Science was employed for data analysis. Most subjects (63%) did not adhere to medication. Although there were no significant differences between the adherent and non-adherent groups for the researched variables, the use of polypharmacotherapy and complex treatment regimens was observed in treatment for BAD. In practice, implementing strategies to improve the adherence of patients to medication treatment remains a challenge.

DESCRIPTORS

Bipolar disorder
Medication adherence
Outpatients
Nursing care

RESUMO

Este estudo teve como objetivos verificar a adesão de portadores de transtorno afetivo bipolar (TAB) à terapêutica medicamentosa e identificar possíveis causas de adesão e não adesão ao medicamento de acordo com o perfil farmacoterapêutico. Trata-se de estudo transversal, descritivo, realizado em Núcleo de Saúde Mental de um município do interior paulista. Participaram do estudo 101 pacientes com TAB. Para coleta dos dados, utilizou-se a entrevista estruturada e o teste de Morisky-Green e, para a análise dos mesmos, o programa Statistical Package for the Social Science. Os resultados mostraram que a maioria (63%) dos sujeitos investigados não adere ao medicamento. Apesar de não ter ocorrido diferenças significativas entre o grupo de aderentes e não aderentes, para as variáveis investigadas, foi possível verificar a utilização de polifarmacoterapia e regimes terapêuticos complexos no tratamento do TAB. Permanece como desafio a implementação de estratégias que possam melhorar, na prática, a adesão de pacientes ao tratamento medicamentoso.

DESCRIPTORIOS

Transtorno bipolar
Adesão à medicação
Pacientes ambulatoriais
Cuidados de enfermagem

RESUMEN

Se objetivó verificar la adhesión de afectados por transtorno afectivo bipolar (TAB) a la terapéutica medicamentosa e identificar posibles causas de adhesión y no adhesión, de acuerdo al perfil fármaco-terapéutico. Estudio transversal, descriptivo, realizado en Núcleo de Salud Mental de municipio del interior paulista. Participaron 101 pacientes con TAB. Datos recolectados mediante entrevista estructurada y test de Morisky-Green, analizados con software Statistical Package for the Social Science. Los resultados demostraron que la mayoría (63%) de los sujetos investigados no adhiere a la medicación. A pesar de no haberse determinado diferencias significativas entre el grupo de adherentes y no adherentes para las variables investigadas, fue posible verificar la utilización de polifarmacoterapia y regímenes terapéuticos complejos en el tratamiento del TAB. Permanece como desafío la implementación de estrategias que puedan mejorar en la práctica la adhesión del paciente al tratamiento medicamentoso.

DESCRIPTORIOS

Trastorno bipolar
Cumplimiento de la medicación
Pacientes ambulatorios
Atención de enfermería

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INTRODUCTION

Bipolar affective disorder (BAD) is a multifactorial and chronic illness, associated with important negative effects on patients' quality of life⁽¹⁾. It is characterized by important mood swings between the extremes of euphoria (mania) and depression⁽²⁾. Manic episodes strongly tend to recur.

Although research on the diagnosis, epidemiology, neurobiology and treatment of BAD has increased in recent years, patients in the broad bipolar spectrum are still sub-diagnosed and treated inadequately⁽³⁾. Among the costs of this disorder, the financial, psychological and social costs for patients as well as society stand out⁽⁴⁾.

It is a fact that BAD contains a strong biological component and, thus, its main treatment form involves mood stabilizers⁽⁵⁾. Patients are chronic and adherence to drugs therapy is fundamental to increase the chance of a better prognosis.

Studies on adherence in chronic illnesses, however, demonstrate that patients stop or do not even start taking the drugs because they consider their effects unsatisfactory or have experienced their collateral effects⁽⁶⁻⁷⁾.

Non-adherence to the medication substantially limits treatment efficacy and can cause greater relapse, mental health emergency service and hospitalization rates⁽⁸⁾. It is highlighted that non-adherence to medication therapy is characterized by the divergence between the medical prescription and the patient's behavior. This phenomenon is subject to different factors' influences, which directly affect the patients because they determine their behavior towards the recommendations related to their disease treatment. Among these factors, those related to the therapeutics can be mentioned.

Due to the complexity involves in the adherence phenomenon, health professionals should equally take into account all related factors⁽⁶⁾.

In a literature review⁽⁹⁾ in MEDLINE (1966-2004), using the descriptors *adhesion* or *adherence* or *compliance* and *treatment* and *bipolar*, 16 titles were identified, with outcomes related to treatment adherence in BAD, none of which was developed in Brazil. Thus, the need for research is highlighted, as well as monitoring and assessment of patients' prescribed medication use.

The above context also appoints the need to enhance, in health services, actions that contribute to prevent problems in BAD patients deriving from inadequate medication use. Knowing the factors involved in medication treatment monitoring will permit testing interventions that improve adherence and, perhaps, control of the disorder and consequent re-hospitalizations.

This study aimed to verify BAD patients' adherence to prescribed medication treatment, through the application of the Morisky-Green Test (MGT)⁽¹⁰⁾ and to identify possible causes of medication adherence and non-adherence, according to the variables related to the drugs therapy profile.

METHOD

This cross-sectional and descriptive research was developed at a Mental Health Center (MHC) affiliated with the Unified Health System, located in an interior city in São Paulo State. Approval was obtained from the Institutional Review Board (Protocol No. 0206/CEP-CSE-FMRP-USP). Participants signed the informed consent term in compliance with National Health Council Resolution (CNS 196/96). All 101 patients participated who had a medical appointment scheduled at the MHC within one year after the start of the data collection participated and complied with the following inclusion criteria: diagnosed with BAD, established by a physician responsible for the outpatient diagnosis; prescribed medication for continuous use; age of 18 years or older and able to communicate verbally in Portuguese.

For data collection, the structured interview technique was used. With a view to guaranteeing that all patients received standardized questions, a script was used with the subjects' identification data (gender, age, education, among others) and identification data of their drugs treatment profile (number of medication types used, total number of pills taken per day, number of times per day the medication is taken, among others). Adherence levels were determined through the application of the Morisky-Green test⁽¹⁰⁾. This test permits identifying the patient's adherence level and distinguish whether non-adherence

is due to intentional (questions: *when you feel good, do you sometimes not take your medication?* and *when you feel bad taking the medication, do you sometimes not take it?*), or non-intentional behavior (questions: *do you sometimes forget to take your medication?* and *are you sometimes careless with the time you take your medication?*). Previous studies have demonstrated the utility of this instrument and established its validity⁽¹⁰⁻¹²⁾.

The interviews were held with the patients at the MHC. When the patient could not attend the institution for the interview, it was held at the patient's home, on a pre-established date and time.

The quantitative approach was used for data analysis. After applying the instrument, data were typed in a structured database in the format of an Excel worksheet. After typing and printing the first simple frequency list, coding errors or typos were verified and corrected. Then, the data were transported for analysis in Statistical Package for the Social Sciences (SPSS), version 11.5. Also, statisti-

It is a fact that bipolar affective disorder (BAD) contains a strong biological component and, thus, its main treatment form involves mood stabilizers. Patients are chronic and adherence to drugs therapy is fundamental to increase the chance of a better prognosis.

cal associations between the dependent and independent variables were investigated, using the chi-square test (χ^2). The association hypothesis was accepted when $p < 0.05$.

RESULTS

Study subject characteristics

In the study period, 101 patients diagnosed with BAD had a medical appointment scheduled at the place of study. All of them accepted to participate in the study. Table 1 displays the study participants' characteristics.

Table 1 shows that the most (70.3%) of the interviewed patients were female, with a higher frequency in the age range from 41 to 50 years (31.8%). Also, higher percentages of patients were married (44.6%) and retired (23.8%). Nevertheless, the high percentages of single (30.7%) and separated/divorced patients (11.9%) stand out, all of whom divorced after the appearance of the BAD. As for diagnosis time, most of the patients (68.4%) had been diagnosed for up to ten years, and a large percentage (26.7%) for more than 15 years. Concerning occupation, only 14.8% of the interviewees had a fixed job contract and 23.8% had retired due to the disorder.

Adherence to the medication treatment

Through the application of the Morisky-Green⁽¹⁰⁾ test, it was identified that, out of 101 interviewed BAD patients, the majority (63%) does not adhere to the medication treatment.

Table 2 presents the subjects' distribution regarding medication adherence and the number of medication types, total pills taken per day and number of times per day they take the medication.

Table 1 – Distribution of study subjects according to socio-demographic characteristics and diagnosis time

VARIABLE	N	%
Gender		
Female	71	70.3
Male	30	29.7
Total	101	100
AGE		
20–30 years	15	14.8
31–40 years	18	17.8
41–50 years	32	31.8
51–60 years	22	21.8
61–70 years	14	13.8
Total	101	100
MARITAL STATUS		
Married	45	44.6
Single	31	30.7
Widowed	06	5.9
Separated/divorced	12	11.9
Fixed partner	06	5.9
Others	01	1.0
Total	101	100
DIAGNOSIS TIME'		
0–05 years	40	39.7
06–10 years	29	28.7
11–15 years	10	9.9
16–20 years	07	6.9
21 years or more	10	9.9
Does not know	05	4.9
Total	101	100
OCCUPATION		
Retired	24	23.8
Unemployed	11	10.9
Worker on a fixed contract	15	14.8
Autonomous worker	12	11.9
Housewife	21	20.8
Others	18	17.8
Total	101	100

Table 2 – Distribution of study subjects according to medication adherence and drugs therapy profile variables

Drugs-related variables		Adherence			PR(95%CI) [#]	*p
		Yes n (%)	No n (%)	Total n (%)		
Total number of pills taken per day	1 to 5	24 (34.3)	46 (65.7)	70 (100)	0.81(0.48-1.38)	0.462
	6 to 10	13 (41.9)	18 (58.1)	31 (100)		
	Total	37 (36.6)	64 (63.4)	101 (100)		
Number of times per day medication is taken	1	04 (44.4)	05 (55.6)	09 (100)	1.47(0.62-3.47)	0.505
	2	20 (40.8)	29 (59.2)	49 (100)		
	3**	13 (30.2)	30 (69.8)	43 (100)	1.35 (076-2.37)	
	Total	37 (36.6)	64 (63.4)	101 (100)		
Number of medication types used	1	08 (38.1)	13 (61.9)	21 (100)	1.05(0.56-1.94)	0.876
	2 or +	29 (36.3)	51 (63.8)	80 (100)		
	Total	37 (36.6)	64 (63.4)	101 (100)		

PR=prevalence rate (95%CI); #=confidence interval; +p-test chi-square; **3 times per day – reference category

Table 2 reveals that no significant association existed between medication adherence and the variables: total number of pills taken per day, number of times per day medication is taken and number of medication types used. Some data related to these variables are clinically relevant and should be presented in further detail though, as follows.

Figure 1 displays the study subjects' distribution according to the number of medication types used.

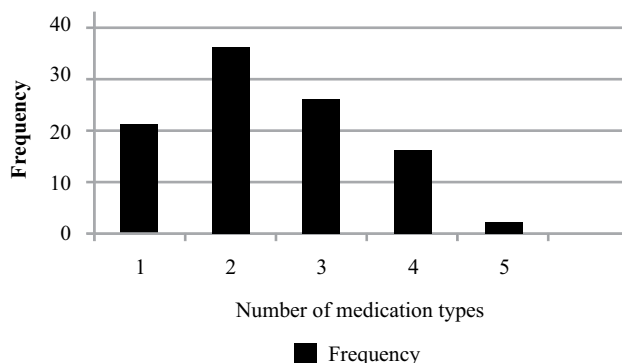


Figure 1 – Distribution of study subjects according to total number of medication types taken per day

Figure 1 shows that, to most of the study participants (61.4%), 2 or 3 medication types were prescribed, with two drugs as the highest frequency for 36 patients. It should be highlighted that the prescriptions, provided by the physicians at the place of study, only contained psychotropic drugs, so that only these drugs were considered in the present study. Thus, it is highlighted that 4 types of drugs (psychotropic drugs) were prescribed to 16 participants for home use.

Figure 2 shows the subjects' distribution according to the total number of pills taken per day.

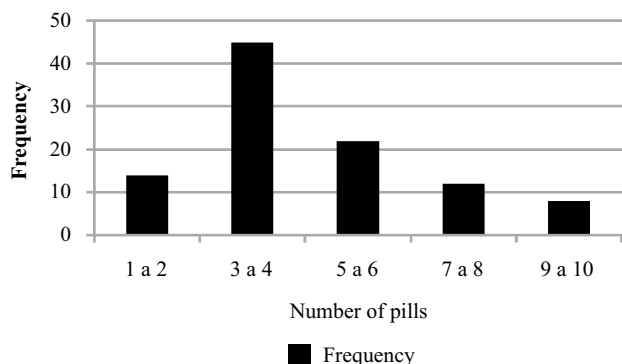


Figure 2 – Distribution of study subjects according to total number of pills taken per day

It is observed in Figure 2 that most patients (44.5%) take between 3 and 4 pills per day. It is highlighted that almost half of the interviewed subjects (41.6%) take 5 or more pills per day.

Figure 3 shows the study subjects' distribution according to the number of times per day they take the prescribed drugs.

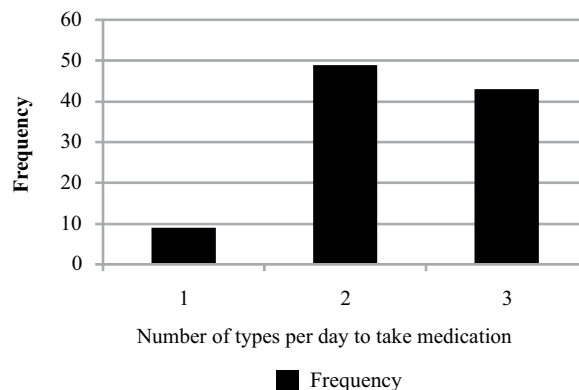


Figure 3 – Study subjects' distribution according to the number of times per day they take medication

Figure 3 reveals that most (48.5%) of the participants take their medication twice a day.

DISCUSSION

Concerning the study subjects' characteristics, it was identified that most of them were female. Literature appoints that no significant gender differences are observed in bipolar disorder⁽¹³⁾. What can explain the large number of women attended at this health service, however, is the fact that men with bipolar affective disorder seek medical care significantly less than women⁽¹³⁾.

As for the high percentage of single (30.7%) and separated/divorced (11.9%) patients, a study reveals that the divorce rate among people with BAD is approximately two to three times higher in comparison with individuals without the disease⁽¹⁴⁾. About 50% of all partners reported that they would not have married or had children with the patients if they knew they had a mood disorder⁽²⁾.

With regard to the diagnosis time, most patients (68.4%) have been diagnosed for up to ten years and many (26.7%) for more than 15 years. Identifying the start age of the bipolar affective disorder represents a clinical challenge. It is essential, especially at the start of treatment, to establish a high-quality therapeutic alliance with the patients, as this aspect will facilitate their introduction to, acceptance of and adherence to preventive treatment⁽¹⁵⁾.

In this study, only 14.8% of the interviewed people had a formal job. In the specific case of bipolar affective disorder, a study⁽¹⁶⁾ demonstrated that, despite the high unemployment rate among people with this diagnosis,

they strongly want to keep their job and display high academic performance levels, comparing themselves with people with other affective disorder types. This study⁽¹⁶⁾ reveal that, when they do not have symptoms of the disorder, BAD patients are capable of keeping up a good performance at work. Medication side effects and crisis episodes during work represent the main negative influences on its maintenance. Therefore, employers need to be sufficiently flexible and sensitive to changes in these people's needs, offering different support levels at different times⁽¹⁶⁾.

In this context, health professionals are responsible for working in articulation with the community, involving non-governmental organizations, social solidarity institutions, among others, so as to encourage and help patients in their socio-professional reintegration. They should also orient patients about signs appointing the start of a crisis in the disorder and to recognized, at work, the change processes that can precipitate the appearance of symptoms, preventing relapses.

As for medication treatment adherence, it is highlighted that most interviewed BAD patients (63%) do not adhere. Non-adherence rates can increase the reoccurrence of mania and crisis experiences. These constitute one of the causes associated with rehospitalization and suicide⁽¹⁷⁾.

In this respect, a bibliographic study on people's adherence/non-adherence to health treatment showed that conceptions on the issue in research revealed a limited perspective on the patients' role in their treatment process, considering them submissive to professionals and health services, as opposed to active subjects in their process of living with the disorder and treatment. The same study revealed that patients receive the greatest burden of responsibility for treatment adherence/non-adherence, while professionals and health services need to be co-responsible in this process⁽¹⁸⁾. Hence, the recurring idea is that patients should follow and comply with health professionals' recommendations and that their behavior should coincide with medical indications. When they fail to observe these indications, they are considered non-adherent to treatment⁽¹⁸⁾.

In view of the complexity of the medication treatment adherence process, mental health professionals need profound knowledge on different therapeutic modes, as the approach of this problem, through an exclusively biological or psychological view, may not attend to patients' actual demands.

To effectively act on problems related to non-adherence to treatment, health professionals need to know the reasons that make patients not adhere to the treatment, as well as their conceptions about the prescribed medication. In this respect, a study⁽¹⁹⁾ appoints that, to promote patients' health-related behavioral changes, such as treatment adherence, health professionals need to evoke patients' good motivations.

Concerning the drugs therapy profile of the patients under analysis, it was verified that, for most of them, two

to three types of medication were prescribed. It should be highlighted that four psychotropic drugs were prescribed to 16 of them for use at home.

As different phases characterized BAD, some agents may be effective in one phase of the disorder only. Polypharmacy is frequently used to treat persistent subsyndromic symptoms after monotherapy has failed⁽²⁰⁾.

Thus, monotherapy is an exception instead of a rule in BAD cases, which is one of the main difficulties for patients' treatment adherence⁽²¹⁾. It is also known that the simultaneous prescription of various drugs as a therapeutic strategy and the growing number of these agents in the market can contribute to enhance the beneficial effects of therapy, but can also result in unwanted effects and medication interactions. Concerning psychotropic drugs, especially antipsychotics, some of their collateral effects are painful and even disabling, which can constitute a bottleneck for patients' adherence⁽²²⁾.

In this study, almost half of the interviewees take five or more pills per day. The number of drugs taken per day can interfere in adherence due to the greater probability of side effects, besides intake difficulties. For each pill taken, the risk of non-adherence increases by 12%⁽²³⁾.

In this respect, in another study⁽²⁴⁾, it was identified that there are BAD patients who, in the belief that they are taking a lot of medication, tend to question the actual need for the prescribed doses, as well as their ability to support these doses. Friends and relatives' opinions reinforce this belief, who stimulate non-adherence to the medication. This study also found that, in view of these situations, BAD patients feel the need to be submitted to a strict and individual assessment by the health team concerning the established medication therapy, so as to feel safer. Nurses play a fundamental role in the welcoming and orientation of these clients.

It is very important for the health team to prioritize drugs that interfere as little as possible in the patient's life habits and facilitate the automation of medication intake in a personalized way, associating them with daily activities like breakfast, reading the newspaper, television programs etc., with a view to avoiding forgetting, especially in complex therapies that involve various medication types and a large number of daily doses.

CONCLUSION

These research results point towards a patient sample with low medication adherence levels. Although no significant differences were found between the group of adherent and non-adherent patients concerning the research variables, it could be verified that, in BAD, monotherapy is really an exception instead of a rule and that patients are submitted to complex therapeutic regimens, involving the intake of various pills per day. It should be highlighted that, in this study, only psychotropic drugs were considered, underesti-

mating this complexity in patients with comorbidities who use other medication classes for treating these problems.

Putting in practice strategies that can improve the adherence of BAD patients to medication treatment in prac-

tice remains a challenge. Educative approaches that consider patients as the center of the care process, allowing them to expose their treatment-related doubts, anxieties, difficulties, opinions and experiences can represent an important measure to minimize non-adherence.

REFERENCES

1. Sajatovic M, Jenkins JH, Safavi R, West JA, Cassidy KA, Meyer WJ, et al. Personal and societal construction of illness among individuals with rapid-cycling bipolar disorder: a life-trajectory perspective. *Am J Geriatr Psychiatry*. 2008;16(9):718-26.
2. Sadock BJ, Sadock VA. *Compêndio de psiquiatria: ciência do comportamento e psiquiatria clínica*. 9a ed. Porto Alegre: Art-Med; 2007.
3. Marchi R. *Escala clínica para prever a adesão ao tratamento: transtorno bipolar do humor [tese doutorado]*. Campinas: Pontifícia Universidade Católica de Campinas; 2008.
4. Lam D, McCrone P, Wright K, Kerr N. Cost-effectiveness of relapse-prevention cognitive therapy for bipolar disorder: 30-month study. *Br J Psychiatry*. 2005;186:500-6.
5. Lotufo Neto F. *Terapia comportamental cognitiva para pessoas com transtorno bipolar*. *Rev Bras Psiquiatr*. 2004;26 Suppl 3:44-6.
6. Gimenes HT, Zanetti ML, Haas VJ. Fatores relacionados à adesão do paciente diabético à terapêutica medicamentosa. *Rev Latino Am Enferm*. 2009;17(1):46-51.
7. Tschoner A, Fleischhacker WW, Ebenbichler CF. Experimental antipsychotics and metabolic adverse effects-findings from clinical trials. *Curr Opin Investig Drugs*. 2009;10(10):1041-8.
8. Lew KH, Chang EY, Rajagopalan K, Knoth RL. The effect of medication adherence on health care utilization in bipolar disorder. *Manag Care Interface*. 2006;19(9):41-6.
9. Santin A, Cereser K, Rosa A. Adesão ao tratamento no transtorno bipolar. *Rev Psiquiatr Clin*. 2005;32 Supl 1:105-9.
10. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care*. 1986;24(1):67-74.
11. Svarstad BL, Chewing BA, Sleath BL, Claesson C. The Brief Medication Questionnaire: a tool for screening patient adherence and barriers to adherence. *Patient Educ Couns*. 1999;37(2):113-24.
12. Strelec MAAM, Pierin AMG, Mion Júnior D. A influência do conhecimento sobre a doença e a atitude frente à tomada dos remédios no controle da hipertensão arterial. *Arq Bras Cardiol*. 2003;81(4):343-54.
13. Dias RS, Kerr-Corrêa F, Torresan RC, Santos CH. Transtorno bipolar do humor e gênero. *Rev Psiquiatr Clín*. 2006;33(2):80-91.
14. Moreno RA, Moreno DH, Soares MBM, Ratzke R. Anticonvulsants and antipsychotics in the treatment of Bipolar Disorder. *Rev Bras Psiquiatr*. 2004;26 Supl 3:37-43.
15. Maurel M, Kaladjian A, Fakra E, Besnier N, Adida M, Azorin JM. Treatment of a first manic episode. *Encephale*. 2010;36 Suppl 1:S23-6.
16. Jones MM. The experience of bipolar disorder at work. *Int J Psychosoc Rehabil*. 2005;10(1):61-70.
17. Pompili M, Serafini G, Del Casale A, Rigucci S, Innamorati M, Girardi P, et al. Improving adherence in mood disorders: the struggle against relapse, recurrence and suicide risk. *Expert Rev Neurother*. 2009;9(7):985-1004.
18. Reiners AAO, Azevedo RCS, Vieira MA, Arruda ALG. *Produção bibliográfica sobre adesão/não-adesão de pessoas ao tratamento de saúde*. *Ciênc Saúde Coletiva*. 2008;13 Supl 2: 2299-306.
19. Rollnick S, Miller WR, Butler CC. *Entrevista motivacional no cuidado da saúde: ajudando pacientes a mudar o comportamento*. Porto Alegre: Artmed; 2009.
20. Machado-Vieira R, Soares JC. Transtornos de humor refratários a tratamento. *Rev Bras Psiquiatr*. 2007;29 Supl 2:S48-54.
21. Gazalle F, Hallal PC, Tramontina J, Rosa AR, Andreazza AC, Zanatto V, et al. Polypharmacy and suicide attempts in bipolar disorder. *Rev Bras Psiquiatr*. 2007;29(1):35-8.
22. Miasso AI, Cassiani SHB, Pedrão LJ. Transtorno afetivo bipolar e terapêutica medicamentosa: identificando barreiras. *Rev Latino Am Enferm*. 2008;16(4):739-45.
23. Colombrini MRC, Lopes MHBM, Figueiredo RM. Adesão à terapia antiretroviral para HIV/Aids. *Rev Esc Enferm USP*. 2006;40(4):576-81.
24. Miasso AI. *Entre a cruz e a espada: o significado da terapêutica medicamentosa para a pessoa com transtorno afetivo bipolar, em sua perspectiva e na de seu familiar [tese doutorado]*. Ribeirão Preto: Escola de Enfermagem de Ribeirão Preto, Universidade de São Paulo; 2006.

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