Original Article

Bipolar disorder and medication: adherence, patients' knowledge and serum monitoring of lithium carbonate[1]

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Objectives: this study featured patients with affective bipolar disorder who were making use of lithium and received care at an outpatient care center located in a country town in the state of Sao Paulo in 2009; it assessed the adherence and knowledge of these patients in relation to the medication prescribed to them and verified the proportion of blood tests performed per year in the service, for each individual, to measure lithium levels in the blood. Method: descriptive study with quantitative approach, involving 36 participants. Structured interviews and review of medical records were used for data collection and descriptive statistics for data analysis. Results: difficulties in reporting the dosage of the medication prescribed and a high rate of non-adherence were identified among the participants. None of the participants in the study was submitted to two tests a year to measure lithium levels in the blood, which is the minimum proportion of tests recommended by the literature for maintenance treatment using lithium carbonate. Conclusion: this study highlights the critical factors for the promotion of patients' safety in monitoring lithium drug therapy.

Descriptors: Bipolar Disorder; Lithium Carbonate; Monitoring, Physiologic; Medication Adherence; Treatment Refusal.

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Introduction

Bipolar disorder (BD) is serious, chronic and recurrent and it is present in about 1% to 2% of the population. For the bipolar spectrum, the estimative is higher, at about 5%, as the criteria adopted are less strict and conservative[1]. BD has a serious impact on patients' lives and it can cause functional damage, self-care difficulties, socially unacceptable behavior and interpersonal relationship issues[2].

A continuous pharmacological treatment is needed to control this disorder. Thus, adherence to medication is essential for people with BD to respond satisfactorily to the treatment[3-4]. Several factors, however, contribute to the poor adherence to medication, being the lack of knowledge about the medications an important factor[5-6]. Therefore, the level of patients' knowledge should be identified in planning nursing actions aimed at optimizing the treatment[7].

Adherence to drug therapy is a subject of interest for the literature, since it is a factor that can be potentially modified in order to improve patients' prognosis[3,8].

It can be highlighted that the BD treatment has a broad range of therapeutic resources but the "gold standard" medication for the treatment of this disorder is lithium carbonate[3,5,9-10]. Although effective, this substance requires specific care as it has a narrow therapeutic range, high risk of intoxication[9-12] and slow onset of action, is subject to serum variation levels due to pharmacological interactions, and presents elimination and dosage-plasma level variations among people[7]. The serum monitoring of lithium carbonate levels is important for treatment effectiveness and patients' safety[9-12]. Therefore, it is necessary to investigate whether this is being regularly carried out at psychological healthcare services.

The whole context shows that adherence to treatment[3-4,8], knowledge about the drug therapy[6-8] and serum monitoring of lithium carbonate levels[9,10-12] are essential for the safety of patients who make use of this medication. These aspects are strictly related to the nursing practice, which plays a unique role in patients' education with the purpose of promoting adherence to medications and reducing the harm that may be caused by their inadequate use. Based on this, this study brings relevant contributions to nursing care in relation to people with affective bipolar disorder, in particular to those people undergoing lithium therapy.

Objective

This study is aimed at: identifying and characterizing patients with affective bipolar disorder using lithium carbonate and who were assisted at an outpatient care center located in a country town in the state of Sao Paulo, Brazil, in 2009; assessing the adherence and knowledge (name, dosage and frequency of use) of these patients in relation to the prescribed medications and verifying the proportion of blood tests performed in the service per year for each individual to measure lithium levels in the blood.

Method

This is a retrospective, cross sectional and descriptive study with a quantitative approach. It was carried out at a public health outpatient care center located in a country town in the state of Sao Paulo, Brazil. The project was undertaken upon approval by the Research Ethics Committee (Registration number 0206/CEP-CSE-FMRP-USP) and all participants signed Informed Consent Forms.

All the eligible patients were those who had had medical appointment scheduled at the place of study during the period between 1 January and 31 December 2009 and who fulfilled the following inclusion criteria: to have been diagnosed with affective bipolar disorder (established by the doctor responsible for outpatient care diagnosis); to have been prescribed the continuous use of lithium carbonate; to be 18 years old or over and to be able to verbally communicate in Portuguese. Only 36 people assisted in this period fulfilled the inclusion criteria of this study.

For the collection of data, a review of medical records and structured interviews were performed, using a guide developed by the authors of the study with questions about socio-demographic information and patients' treatment, as well as a test evaluating patients' adherence to drug therapy[13] including lithium carbonate, and a scale to evaluate the interviewees' knowledge concerning the prescribed drug therapy[14]. The participants were interviewed in a private room at the healthcare center subject of this study.

The level of adherence was defined by Morisky and Green test[13]. This test allows to identify the patients' level of adherence and to discriminate whether the eventual non-adherence is due to an intentional behavior (questions: "do you ever fail to take your medication when you feel well?" and "do you ever fail to take your medication when you feel unwell with it?") and/or unintentional behavior (questions: "have you

ever forgotten to take your medication?" and "are you ever careless with the times to take your medication?"). The test was validated, translated and used in Brazil[15].

To each answer, the value of (0) zero or (1) one was assigned, being the value of (1) one designed for negative answers or for positive answers in which the frequency stated was once a month or less, and the value (0) zero for positive answers with other frequencies. The patients who scored four points on the Morisky and Green[13] test were classified as "adherent" and those who scored from zero to three points as "non-adherent".

In order to identify the level of patients' knowledge in regards to the medication prescribed to them, the Stape scale was used[14]. The mentioned instrument shows how to translate into percentages the quantity (numbers) of information that patients have and directs the classification of this knowledge.

This instrument assumes that the level of someone's knowledge about each aspect related to the medications (name, dosage and frequency of use) can be scored from 0 to 100% and classified into regular ranges which represent the following categories: no knowledge (0%), very little knowledge (0% ⊣ %25%), little knowledge (25% ⊣ %50%), regular knowledge (50% ⊣ %75%) and good knowledge (75% - %100%).

Patients' answers were compared to the information contained in the medical records. Each question's answer was classified as right or wrong considering the assessed items for each prescribed medication. The answer "I do not know" was classified as wrong. In this way, if ten medications were prescribed to a person who could accurately inform the name of five of them, their level of knowledge about the drugs' names would be of 50% and included on the "little knowledge" category, which corresponds to the points ranges 25% ⊣ %50%. This procedure was used with each variable related to the prescribed medication.

The number of blood tests to measure lithium levels in the blood carried out since the beginning of the patients' treatment at the place of study was identified through review of medical records. After double entry of the data collected in an Excel spreadsheet, the descriptive statistics for analysis was used.

Results

Features of the participants in the study

In 2009, 36 people with BD and continuously using lithium were assisted at the place of study. All of them met the inclusion criteria and agreed to participate in

the study. The features of the participants can be seen on Table 1 below.

Table 1 – Features of participants with affective bipolar disorder. Ribeirao Preto, SP, Brazil, 2009

Variable	N	%
Gender		
Female	23	63.9
Male	13	36.1
Total	36	100
Age		
20 – 30 years old	04	11.1
31 – 40 years old	06	16.7
41 – 50 years old	10	27.8
51 – 60 years old	07	19.4
61 – 70 years old	07	19.4
71 – 80 years old	02	5.6
Total	36	100
Marital status		
Married	14	38.9
Single	14	38.9
Divorced	04	11.1
De facto	04	11.1
Total	36	100
Time of diagnosis		
0 – 05 years	02	5.6
06 – 10 years	05	13.9
11 – 15 years	08	22.2
16 – 20 years	03	8.3
21 years or more	09	25.0
Do not know	09	25.0
Total	36	100
Occupation		
Retired	09	25.0
Unemployed	01	2.8
Employee (registered)	06	16.7
Contractor	08	22.2
Stay-at-home	07	19.4
Others	05	13.9
Total	36	100

At the time of data collection, three (8.3%) people had already shown suicidal tendencies and three (8.3%) had a history of suicide attempt. The number of hospitalizations varied between zero and 12. It is noteworthy that eight (22.2%) people had never been hospitalized, 19 (52.8%) patients were hospitalized between one and four times, six (16.7%) were hospitalized between five and eight times and three (8.3%) had been hospitalized more than eight times.

According to the interviews, ten (27.6%) patients used to drink alcohol before starting drug therapy and, in the period of data collection, this number was reduced to two (5.6%) people.

Among the participants, 20 (55.6%) had a monthly income of less than four minimum wages. Although

35 (97.2%) patients obtained some of the medication through the public system, it was possible to identify two (5.56%) people who had monthly expenses with the purchase of some psychotropic medication and five (13.9%) with the purchase of non-psychotropic medication. In case of failure of the public system in supplying medications, 24 (66.7%) people stated that they bought or would buy the medication.

Prescribed drugs

Regarding the types of prescribed medication, 11 (30.6%) patients were undergoing monotherapy with lithium. In relation to the others, 12 (33.3%) used two types of medications, eight (22.2%) people used three types of medications and five (13.9%) had prescriptions for four different medications.

In the participants' prescriptions, the number of tablets to be daily taken varied from one to 13, being that 17 (47.2%) took more than four tablets a day. It should be mentioned that 21 (58.3%) participants used medication three times a day.

It was possible to identify that 21 (58.3%) patients reported to have some side effect caused by the prescribed drug(s). The most mentioned side effects were: weight gain, headache, drowsiness, lethargy, shivering, dizziness, gastrointestinal discomfort and dry mouth.

Adherence to drug therapy

The adherence to all prescribed medications, including lithium, was assessed through the Morisky and Green test.

Of those interviewed, only eight (22.2%) had adhered to the prescribed drug therapy, 15 (41.7%) had not adhered to it as a result of unintentional behavior, while 13 (36.1%) were considered non-adherent as a result of intentional and unintentional behavior. It can be highlighted that, among the 11 patients undergoing monotherapy with lithium carbonate, six (54.5%) were considered non-adherent.

Participants' knowledge concerning drug therapy

The patients' level of knowledge about the name, dosage and frequency of prescribed medications is presented in Figure 1.
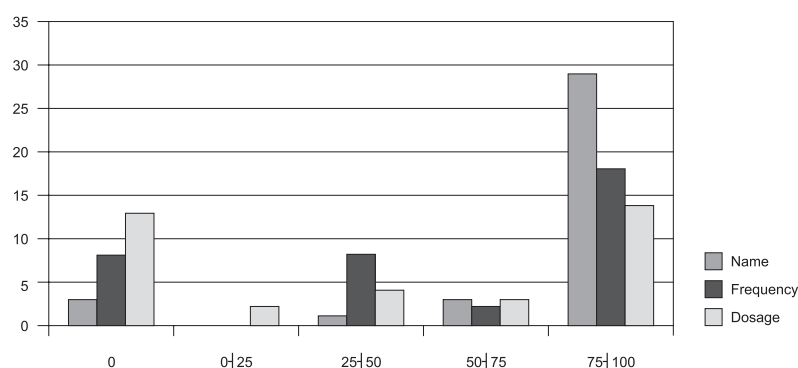

Figure 1 – Distribution of participants according to the level of knowledge about the name, frequency and dosage of the prescribed medications

Based on Figure 1, it could be noted that the name of the prescribed medications was the most known item among the participants, as 29 (80.6%) of them had "good knowledge" in relation to it, that is, they were within the range of 75% to 100% in the scale that assesses the level of knowledge. In the assessment of knowledge related to the names of medications, the answers that identified the prescribed medication, either by its generic name or by any commercial name, were accepted as correct.

Concerning the frequency of these medications, it was identified that half of the participants had "good knowledge" about this issue.

It was found that 19 (52.8%) patients had little knowledge in relation to the daily dosage of the medications, since their knowledge had been classified into the categories "no knowledge" (0%), "very little knowledge" (0%⊢25%) or "little knowledge" (25%⊢50%).

In assessing the abovementioned information in relation to the medication dosage, the answers that identified the quantity, in units of measure (gram, milligram and milliliter), to be taken at each time or in a period of 24 hours, in accordance with medical prescription, were considered correct.

Proportion of tests to measure lithium levels in the blood performed at the psychological healthcare service per year

To identify the proportion of tests to measure lithium levels in the blood performed at the psychological healthcare service per year, the number of tests performed with each patient was divided by the number of years of lithium treatment at the psychological healthcare service in study.

None of the participants in the present study achieved the proportion of two tests performed per year at the psychological healthcare service in study. The proportion of one test performed per year was achieved only in relation to seven (19.4%) patients.

Of all interviewed participants, 14 (38.9%) started lithium treatment prior to the period they began to attend the psychological healthcare service.

Discussion

As regards the classification of the participants of this study, most of them were female. The literature points out that men and women are equally likely to develop this disorder. The fact that there is a greater number of women undergoing treatment for BD control may be due to women more often seeking healthcare assistance and adhering to treatment better than men[8].

The present study identified the same proportion of married and single people diagnosed with BD. The literature indicates that there are less married people among the population with BD than among the general population, which can be a consequence of the disorder's symptoms[16].

It was noted that only six (16.7%) participants stated to have an employment relationship. A study suggests that people with BD may have lower productivity at work, lower cognitive performance and less favorable economic situation than people with depression or people without psychological disorders[16]. However, when compared to people with other disorders, those with BD show high academic performance and desire to work, although they are faced with the problem of unemployment[17].

During the period of data collection, alcohol consumption was identified in two (5.6%) patients. The literature states that the consumption of alcohol is higher in patients with BD than in the general population[18], and emphasizes that this behavior is related to poor prognosis and low adherence to medication[3,19].

Suicide is one of the most damaging consequences of BD[9,20]. In this study, three (8.3%) patients who had already tried to commit suicide some time in their lives were identified, while other three (8.3%) showed suicidal tendencies. It is noteworthy that the percentage identified in this study is lower than that stated by the literature, which points out that between half and one quarter of patients with BD had tried to commit suicide[9,20]. The fact that all participants were taking lithium could be a possible explanation for such result, since this medication has an important role in reducing the risk of patients with BD committing suicide[3,9].

Most participants obtained medications through the public healthcare system and 24 (66.7%) interviewed participants stated that they would buy the medication if the supply by the public system failed. The guarantee of access to medication through the public system is of utmost importance to the treatment adherence[3] and is the subject of concern for patients and their families, especially when there are financial constraints that preclude the purchase of the prescribed medication[21].

In relation to the therapeutic framework, 25 (69.4%) participants made use of other medications besides the lithium. Most patients took their medications three times a day and ingested three or more tables daily.

The literature reveals that bipolar patients use three medications in average and this aspect increases the chances of drug interactions[7]. Simultaneous use of medications can be a problem in following a medical treatment, as it increases the chances of side effects, the difficulties of self-administration of prescribed medications and, consequently, it increases the probability of non-adherence[22].

The majority of the participants in this study reported having side effects to the prescribed drugs. Indeed, lithium causes side effects such as drowsiness, fatigue, lethargy, cognitive problems, weight gain, gastrointestinal disorders, shivering, hair loss, polyuria, polydipsia, among others[10]. These effects may compromise the patients' quality of life, which can be an important hurdle to adherence to this drug therapy[3,23].

Most patients with BD did not adhere to drug therapy, as identified in previous studies[3,22,24]. The majority of those who did not adhere to it, had this behavior unintentionally, and this is also corroborated by the literature[24].

Treatment adherence is closely related to the manner in which a person follows medical recommendations[25]. Low adherence to medications is associated with worse prognosis, high recurrence rate[9], hospitalization

and suicide[4], besides contributing to treatment ineffectiveness and socio-economic damage[7]. As for lithium, the unintentional non-adherence may favor the administration of medications at random times, thus increasing the risk of intoxication resulting from dosage overlapping.

Patients' knowledge concerning the therapeutic framework is a basic condition for the conduction of the treatment if they are responsible for self-administrating the drugs[22]. In the present study, it was possible to note that patients expressed difficulties in adequately reporting the dosage of the drugs prescribed and this fact can compromise their safety in the use of these medications.

Such aspect is compounded by the fact that families of people with BD also have little knowledge about the medications prescribed to patients, which limits their ability to intervene in order to assist patients in maintaining therapeutic drug levels[21].

The lack of knowledge about the drug dosage can contribute to the ineffectiveness of the treatment, as a result of the use of medications below therapeutic levels, and can increase toxicity risk, particularly in relation to lithium, which is a drug with a narrow therapeutic range and severe toxic effects. Therefore, the level of knowledge concerning the therapeutic framework and the lithium is related to better adherence and lower toxicity risk[5].

The serum level of lithium considered therapeutic ranges from 0.6 mEq/l to 1.2mEq/l, representing a narrow therapeutic range. At levels above this range, toxicity signs and symptoms start to appear, such as nausea, vomiting, diarrhea, strong shivering, blurred vision, muscle contractions, lethargy and confusion[10]. Patients need to receive information from the healthcare team in order to identify these toxic side effects because the toxicity caused by lithium brings serious complications and can be deadly[5,10,12].

In this context, nurses can effectively intervene through psycho-educational strategies. In addition to improving the understanding about the treatment, psycho-education can promote better management of the disorder, adherence to treatment, better *insight*, early recognition of the symptoms, a healthy lifestyle, management of stressful situations and repression of abuse drugs. This therapeutic approach also helps to reduce relapses and hospitalizations and favors a better social functioning[26].

In the studied healthcare service, the assessment of the proportion of tests performed for each individual to measure lithium levels in the blood per year revealed that none of the participants had achieved the proportion of two tests per year, being that, for most of them, not even the proportion of one test per year was achieved. The test to measure lithium levels in the blood in patients undergoing lithium treatment must be performed at least every six months if the patient has a stable condition[10]. Therefore, none of the participants had an appropriate frequency of tests in accordance with the minimum recommended by the literature.

An aggravating factor for these findings is the fact that 22 (61.1%) participants had lithium prescribed when they were already being assisted at the place of study. Although in some cases the medication may have been prescribed during hospitalization, it is possible that some patients had started taking lithium at the place of study.

For those starting the treatment, the number of tests recommended is even higher, to allow a safe adjustment to the dosage[7,10]. Furthermore, depending on patients' health conditions, lithium treatment can be started with high dosages, and this requires strict monitoring to avoid exceeding the therapeutic limit[7].

Serum monitoring of lithium levels enables to verify adherence to treatment, assists with the adjustment to dosages and the detection of variations in serum concentration of this substance. The provision of these tests at healthcare services is an important conduct to ensure the safety of patients using lithium.

Final considerations

This study featured 36 patients with affective bipolar disorder who are medicated with lithium and assisted at a psychological outpatient care center. In this research, the sample includes only people with BD assisted at only one public service of a country town located in the state of Sao Paulo, Brazil, but it is possible that the problems identified herein are common to patients in other contexts.

In this study, several patients were submitted to complex therapeutic methods, had limited knowledge about the prescribed medication, especially in relation to the dosage, and presented low adherence to the drug therapy. None of the participants in this study had achieved the minimum proportion of tests per year to measure lithium levels in the blood recommended by the literature for the treatment and maintenance of treatment with lithium.

These limitations indicate the risks in following the drug therapy, especially in relation to medications with

narrow therapeutic range such as lithium, which can considerably compromise people's prognosis.

As part of the multidisciplinary team, nurses should invest in strategies to minimize such limitations of healthcare services. Among possible strategies, the psycho-educational approach, on an individual or group basis with patients and families, should be highlighted. Such an approach may contribute to improving patients' knowledge about drug therapy, promoting adherence and active participation in the treatment. With greater understanding and co-responsibility, patients can contribute with the correct administration of medications, performance of regular tests, management of side effects to lithium and early detection of intoxications.

Therefore, the present study contributes to the practice and research in the field of Professional Nursing Activity and psychological health, as it points out the factors that may compromise the safety of people with BD when undergoing drug therapy. It is recommended that further studies implementing and assessing managers' and healthcare teams' strategies aimed at educating, supervising, motivating adherence and ensuring tests for patients undergoing treatment are developed.

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