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BIBLIOGRAPHIC STUDY OF FACTORS THAT INFLUENCE THE NON-ADHESION TO TREATMENT IN PATIENTS WITH BIPOLAR AFFECTIVE DISORDER

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ABSTRACT

Review of clinical studies dealing with bipolar affective disorder (BD) in order to identify the main factors that contribute to non-adherence to treatment, as well as to identify proposals and suggestions that can minimize this problem. The methodology used is based on the Scielo, BIREME and Pubmed databases. 35 studies were selected that were related to the theme non-adherence to treatment in bipolar patients, referring to the period from 2005 to 2019. In the analysis of the data obtained, the determining factors of non-adherence to treatment were grouped into three categories: drug therapy; patient's own characteristics, life history and personality, family dynamics and cultural insertion; and, related to the institution, the psychiatrist and the engaged multiprofessional team. It is concluded that non-adherence is part of the course of treatment for bipolarity, varying between services, but it is not exclusive to it, since, in general, other clinical diseases of a chronic nature also present with varying degrees of non-adherence. Therefore, the interdisciplinary team must be available and accessible to the patient to answer questions and discuss their treatment. BD is considered to be a biopsychosocial problem and requires frequent, multidisciplinary interventions from the perspective of multidisciplinary psychoeducation, as a key element of better adherence to treatment.

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INTRODUCTION

According to the Diagnostic and Statistical Manual of Mental Disorders 5 (DSM-V), 2013, Bipolar Affective Disorder (BD) is classified into: type I bipolar disorders (one or more manic episodes or mixed episodes); type II (one or more major depressive episodes accompanied by at least one hypomanic episode); cyclothymics (chronic and fluctuating mood disorder) and those with no other specification (Tan *et al*., 2019). Its prevalence in the world population is about 1.5%, being a serious public health problem. This mental illness is associated with a high risk of mortality, such as violent causes and suicides. It appears that approximately 25% of patients attempt suicide at some stage in their lives and, of these, about 11% are successful (Hamann *et al*., 2014). It was observed that the concept of adherence to treatment is variable among authors, in general the concept that adherence is patients' obedience to the prescriptions made by doctors is used, so terms such as: obedience and adherence are used.

In addition, Santin defines that adherence to treatment is characterized as following the recommendations made by the doctor. Partial compliance is when patients omit doses at least 30% of the time. In addition, the various methods of adherence measures stand out, among them: self-report, therapeutic monitoring of the drug or metabolites (serum dosages), measurement of physiological parameters, refills, pill count, electronic monitoring and adherence scales. For mood stabilizers, the most used method is drug monitoring (Santin *et al*., 2005). Even using all the techniques to monitor adherence to treatment, there is a gap between the effectiveness and the effectiveness of mood stabilizers, since, of the total of patients investigated under ideal research conditions, 66% of patients treated with lithium respond to treatment, but only half of them have clinical benefits. Another aspect to be considered is the residual symptoms and the recurrence of the disease, generating frustration and non-adherence to treatment, which are marked characteristics in 40% of patients with BD being treated (Chakrabarti, 2016).

Thus, the importance of investigating non-adherence to treatment by patients with Bipolar Affective Disorder (BD) is emphasized.

MATREIALS AND METHODS

A bibliographic study was carried out from the "Lilacs" databases; "BIREME" and "PUBMED", corresponding to publications within the period from 2005 to 2019, considering the theme of non-adherence to treatment in patients with Bipolar Affective Disorder. The descriptors were used: "patient compliance"; "Affective disorders", "psychotic"; "Bipolar disorder". 62 publications were found, 55 in the Pubmed database and 16 in the Lilacs and Bireme database. Studies in Portuguese, Spanish and English were included. Of these, 35 studies were selected, in which the factors involved in non-adherence to treatment were identified and analyzed, as well as proposals and suggestions to minimize this problem. Thus, in this survey, 12 research texts were selected in Brazilian populations, 4 research texts in foreign populations, and 4 bibliographic surveys carried out by Brazilian authors. After analyzing the data obtained, the determinants of non-adherence to treatment were grouped into three categories: drug therapy; patient's own characteristics (life history and personality, family dynamics and cultural insertion) and the institution, the psychiatrist and the engaged multiprofessional team.

RESULTS AND DISCUSSION

Bipolar affective disorder (BD) is a chronic, recurrent disease associated with high rates of mortality and socioeconomic losses, with environmental stressors, somatic and personality disorders as potential risk factors. Accompanied by the positive history of bipolar disorder in the family, the unstructured socioeconomic situation and families with high emotional expression (Bahrini *et al*., 2016). Thus, the key point in the treatment of bipolarity is around mood stabilizers and anticonvulsants. Lithium, carbamazepine and valproic acid are the most used mood stabilizers, and olanzapine, aripiprazole and lamotrigine can also be used, with only lithium available in the Brazilian Unified Health System (Santin *et al*, 2005). Given this multiplicity of therapeutic options considered effective, one could imagine a very optimistic scenario for patients suffering from BD. However, it is observed that most of these patients, even following regular and adequate treatment, have an unfavorable evolution. In the United States, BD is responsible for 5% to 15% of the longest psychiatric hospital admissions, and inadequate treatment is seen as a villain in the management and adequate control of the disease, as it involves major depressive episodes and severe manic episodes that culminate with hospitalization (Silva *et al*., 2017). In addition, a worrying fact about the rates of non-adherence (or poor adherence) to the treatment is that they can increase the recurrence of mania, since about 60% of the patients hospitalized with Acute Mania had flaws in the use of the medication in the month before his hospitalization (Greenhouse *et al*., 2000). It is also worth mentioning that the understanding of psychological aspects is extremely important in addressing treatment adherence. Based on the above, it is observed that adherence to treatment consists of a psychological phenomenon as self-knowledge, self-criticism and insight develop, associated with the evolutionary character - which means that, at the beginning of treatment, adherence is lower than when compared to the later stages of treatment, being progressively higher over time. The authors report their own experiences in which family and group support, as well as cognitive-behavioral therapies encourage treatment adherence (Levin *et al*., 2020). Adherence to treatment in bipolar patients has been studied based on the following scales: The Illness Concepts Scale (ICS; Linden, Nather, & Wilms, 1988), The Lithium Attitudes Questionnaire (LAQ; Harvey, 1991) and the Schedule for Assessment of insight-Expanded Version (SAI-E; Dantas and Banzato, 2007). The ICS scale was developed to access the understanding of the disease in schizophrenic patients, focusing on confidence in their medications and psychiatrists, guilt, control, negative expectations regarding the disease, susceptibility, aggravations and idiosyncratic beliefs. However, it is worth saying that these scales fail when they do not assess bipolar patients, whose manic and hypomanic manifestations - such as grandeur and high mood - cause them pleasure (Chakrabarti, 2016). In view of this, BD is a disease whose polarity, severity, time of evolution, insight and number of depressive episodes influence patients' adherence to treatment. Factors linked to medications, such as adverse effects, drug interactions, particular pharmacokinetics and complex dosing regimens, are responsible for low adherence. Still, factors related to the doctor, such as the therapeutic alliance, are also fundamental for maintaining the treatment (Mazzaia and Souza, 2017). In this study, the factors that positively influence non-adherence to treatment will fall into three categories, the first of which is associated with drug therapy; the second related to the doctor and / or the institution and the third related to the patient and the family:

Regarding drug therapy: According to the Second Consensus of Granada on Drug Therapy Problems (2002), the three biggest obstacles to adherence to drug treatment were listed: (1) problems of need - the patient uses unnecessary drugs or when he does not use the necessary drugs ; (2) effectiveness problems - when the medication used does not produce the expected effect, whether or not it is dose dependent; (3) safety problems - when the patient uses unsafe medications, either due to the dose or side effects, the latter secondary to the dose and effectiveness (Miasso *et al*., 2008). The medications have therapeutic and side effects that, for some patients, can be intolerable or even fatal. For this reason, some strategies have been suggested to assist patients regarding these effects: increasing the number of health professionals aware of the implications related to the drugs in use; disseminate and develop control strategies in health programs; identify and define problems related to medications individually; goal plan to limit the progression of the problem, improve the criteria for drug use (Cereser *et al*., 2009). The treatment of bipolarity can be with lithium or other mood stabilizers or association of lithium with other mood stabilizers (anticonvulsants) and / or antipsychotics, as well as benzodiazepines. Brazilian bipolar patients use, on average, three psychotropic drugs, which considerably increases the chances of drug interactions. Such interactions can decrease or increase plasma lithium levels, leading to relapse or discontinuation of treatment due to toxicity, since the therapeutic and toxic range of lithium is quite narrow (Kasper, 2006). Bipolar affective disorder (BD) is associated with an increase in cardiovascular morbidity and mortality due to general medical conditions, such as cardiovascular disease, obesity and diabetes. Some studies have assessed the prevalence of metabolic syndrome (MS) in BD patients from different countries, reporting alarming rates ranging from

16.7% to 49%. In addition, several studies evaluating weight gain in a patient using psychiatric drugs, report obesity as a frequent side effect, which increases the chances of morbidity and mortality. Furthermore, it is postulated that, even in the presence of high levels of leptin, the hormone associated with the feeling of satiety, lithium, valproic acid and antipsychotics could reduce the sensitivity of the hypothalamus to the action of this hormone (Salzmann-Erikson and Sjodin, 2018).

Regarding the doctor and / or institution: When prescribing combined treatment, it is essential that the medical team and the institution to which the patient is treated monitor the pharmacological interaction, safety in pregnancy, the therapeutic efficacy - toxicity, side effects, impact on mortality, as well as the cost of treatment. All mood stabilizers should be administered in lower doses when given in combination, thus reducing the burden of side effects and increasing adherence to treatment (Santin, Cereser and Rosa, 2005). Care should not be restricted to drugs but involve psychosocial approaches that assist patients in the inter-crisis, this focus of the health team must, in addition to providing pharmacological adherence, improve the quality of life of patients globally. Psychoeducation allows access to a fundamental right, which is to be informed about your disease. It is a powerful instrument to improve the outcome of patients and to help them manage despair, fears, stigma and low self-esteem (Miasso *et al*., 2008). In this perspective, nursing can intervene by improving the quality of life of people with BD, using psychoeducational strategies, reinforcing information from the medical team about the characteristics of the disorder and the proposed treatment; training for supervised self-administration of medications aiming at patient autonomy after hospital discharge; development of handouts and / or leaflets with simple explanations that encourage patients to understand their drug therapy, acting as partners in the treatment, in addition to the adoption of home visits, especially for patients identified as at risk for non-adherence to drug therapy (Miasso *et al* ., 2009).

Psychoeducation aims to provide bipolar patients with a theoretical and practical approach to understand and deal with the consequences of the disease, which means trying to understand the complex relationship between symptoms, personality, interpersonal environment, side effects of medication and becoming responsible (but never guilty) in relation to the disease, collaborating with the doctor in some aspects of treatment. Improving insight into the disease is essential to successfully conducting a psychoeducational program. Understanding denial and learning the biological causes of the disease are an essential part of the first sessions. Another important issue is the distinction between (biological) causes and triggering factors such as extreme events of emotion, sleep deprivation, drug use and others (Machado at al., 2019). Basically, a psychoeducational program for bipolar patients and their families should include at least the following points: (1) Information about the high rates of recurrence associated with the disease and its chronic condition; (2) Information on trigger factors and personal training to help patients identify their own; (3) Information about psychopharmacological agents, their advantages and their potential side effects; (4) Training in the early detection of prodromal symptoms; (5) Composition of an "emergency plan"; (6) Training on symptom management; (7) Information on the risks associated with the use of illicit drugs, coffee and alcohol; (8) Emphasis on the importance of maintenance routines - especially sleep habits; (9) Promotion of healthy habits; (10) Training in stress management; (11) Concrete information on some subjects such as pregnancy and bipolar disorders and risk of suicide; (12) Dealing with stigma and other social problems related to the disease that bipolar patients cannot easily discuss with their "healthy" friends (Colom and Vleta, 2004).

Regarding to patients and their families: Bipolar Affective Disorder is a difficult diagnosis considering the first years of manifestation of the disease, because, in general, patients only present with depressive conditions, coming to manifest manic conditions many years later. The veracity of the diagnosis is given by the effectiveness of the treatment. However, it is worth noting that depressions are not adequately treated with conventional treatment, presenting hypomanic or irritability, worsening insomnia, without diagnosing bipolarity. Bipolarity is a chronic disease with high social costs due to absences from work, disability pensions, accidents, early clinical comorbidities as previously discussed, chemical dependency, expenses and excessive debts secondary to exacerbations of manic and hypomanic periods (Malhi *et al*., 2018). It is estimated that factors related to patients are considered to be more difficult to control. From this perspective, in a study on adherence to treatment in bipolar patients, the reasons given for not using mood stabilizers were: the idea of having your mood controlled by medication, accepting the fact of having a chronic disease, feeling good if medication is needed, they feel less attractive to their spouse and friends, they miss periods of greater productivity and creativity in hypomanic episodes, they feel depressed, less creative and productive (Almeida *et al*., 2018).

When we consider diseases with a chronic course, it is clear that they are characterized by symptoms that occur over time in an acute or gradual, constant or recurrent manner. The result can lead to death or have a reduced life expectancy or be disabling. When a family member has a chronic illness, it can produce some emotional and relational characteristics due to the impact generated by the patient on his family group. Agudelo *et al* introduces some psychological concepts related to the observation of patients with chronic diseases and their families. The expressed emotions are defined as the individual attitudes or predispositions that facilitate or interfere in interpersonal relationships and that constitute a relational process between patient and family (Agudelo *et al*., 2007). In the United States, they are defined as individual attitudes or concepts that interfere in interpersonal relationships and that constitute a relational process involving patients and their families. Criticism is defined as a negative filter that distorts a person's perception of himself and others. The "sobrenvolvimento" is the lack of appropriate emotional boundaries between members of a family. It is a risk factor for relapses in patients with chronic psychiatric illnesses, in the case of BD, but also in depression and schizophrenia. Patients with a high degree of criticism do poorly on their treatments (Agudelo *et al*., 2007). Agudelo selected a sample of patients with diabetes, patients with bipolarity and healthy people, both groups with chronic pathologies, which can be defined as more criticized and censored, suffering more family intrusions when compared to the group of patients without pathologies, but the greater complaint of perception of criticism occurred in the group of bipolar patients. The author considers that family hostility may be greater when one thinks that patients are able to control the symptoms of the disease, becoming more intense

when dealing with a mental illness such as bipolarity. In hypomanic situations, restlessness, expenses, flirtations can often be forgotten as symptoms and treated as voluntary attitudes and character flaws in patients. Or the avolia, causing damage to hygiene or absence from work in depressive conditions can be seen as laziness by family members and treated with hostility and impatience (Agudelo *et al*., 2007). Bipolar patients have difficulties in perceiving their own symptoms, this characteristic being a sign of inability of the executive function. The severity of the condition, association with drug and alcohol abuse and personality disorders are associated with poor adherence to treatment. According to Johnson and Fulford, the phenomenon of poor adherence to treatment is poorly understood by researchers, who believe that poor adherence is determined by several factors acting simultaneously (Chang *et al*., 2015).

In a study that inquired about the main concerns of patients regarding taking the prescribed medications, the most frequently cited reasons were "feeling dependent", "feeling that taking the medications is a slavery", "feeling afraid", concern about long-term side effects and "feeling ashamed". It is noteworthy that all of these reasons have to do with the lack of information, whereas other reasons traditionally considered by psychiatrists as side effects have been cited by less than 5% of patients (Colom and Vleta, 2004). Still, according to Health Belief Models, patients who believe they are sick tend to follow their prescriptions more adequately to stay healthy, some patients may see the number of medications prescribed as an indicator of health status (Rosenstock *et al*., 1988). In addition, difficulties in including medication in the daily routine is associated with non-adherence to treatment in bipolar patients. In addition, predictable daily routines and a social rhythm compatible with medication are important steps in the cooperation of patients with treatment adherence (Goodwin *et al*., 2016). Interventions that encourage a more structured lifestyle can help improve compliance, especially for young patients. The expectation of side effects is a stronger predictor for non-adherence than the side effects actually experienced by patients. Knowing these beliefs and fears, both on the part of patients, as well as family and friends are part of a proposal to optimize adherence to treatment. Concerns about future commitments as well as accessing patients' satisfaction and acceptance of treatment are determinant for adherence (Sousa *et al*., 2016).

Likewise, the importance of an individualized approach for patients is emphasized, as beliefs bring peculiarities to each patient. These characteristics can be perceived when listening to the patient in a doctor-patient relationship or, if possible, in the relationship between a multidisciplinary team and the user. Multidisciplinary teams are not always formed, but this is a more complete model of assistance, allowing more opportunities for listening and solutions. Some studies show that a psychoeducational approach, which makes it easier for the patient to deal with stigma, promotes insight into their condition, teaches patient and family how to perceive prodromal manifestations, stimulates healthy lifestyle habits and avoids drug abuse reduce number of hospitalizations in targeted populations (Pellegrinelli, Roso and Moreno, 2010). In view of the above, when analyzing the studies carried out with populations in the period selected for this bibliographic survey, it is observed that the results of adherence were better than those reported in the literature cited in the studies themselves, a fact that leads us to conclude that the patients who had a closer monitoring by the multidisciplinary team and accepted with the diagnosis of bipolar - to the point of being involved in studies where they would have to report the use of medications regularly associated with self-observation regarding their mood and sleep and other aspects - suggests that this type of attitude encourages adherence. A very interesting and peculiar aspect of bipolarity is that the number of mood stabilizers in use was related to better adherence, possibly because it contained residual symptoms. Eutymia is a key moment for better adherence to treatment, as well as observation of the patient's lifestyle and the adequacy of the posology to be proposed. It is during eutymia that the insight will be formed and that the patient will be able to clear his doubts and receive the relevant information for his treatment and self-observation. The family has a fundamental role in the observation of prodromal signs of hypomania and depression. Therefore, it deserves attention from the multidisciplinary team in order to be trained and instructed on these signs. The professional also has to be alert to families that do not accept the diagnosis of relatives, or because they hostile the symptoms without understanding that they are part of the manifestations of bipolarity and blame the patient for “not controlling themselves”. Likewise, family members, because they believe that the drugs of continuous use or the large number of pills per day can harm you, discourage the treatment of patients, so consultation with family members is important. Allowing family members to clear their doubts is also important.

Another important aspect that was expressly mentioned in some works was the expression “frustrating” for professionals with regard to relapses, being noticeable that this does not depend on adherence, which is up to the health professional is to support, to perceive the prodromes early so that the conditions are as low as possible and shorten the periods of relapse. So that, the feeling of frustration for professionals must be perceived and supervised so that this perception does not harm the technical performance in care as a patient. Before acting with the burden of frustration, doctors should ask themselves why this feeling is present and observe how it manifests itself in care as a non-adherent patient. It is important that a supervisor is present to guide and present the attitude of the attending physician so that the patient continues to receive the best care possible. Being flexible is the best word when dealing with life, and other people's decisions are a goal to be pursued without compromising the patient's well-being, without jeopardizing stability.

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