Original Research Article

Management of Bipolar Affective Disorder: Drug Interactions and Toxicity

ABSTRACT

Aims: This study evaluates the most prescribed medications for bipolar affective disorder (BAD) at the Psychosocial Care Centre – Alcohol and Drugs (CAPS-AD) in Palmas, Tocantins, alongside their potential drug interactions. It also investigates lithium carbonate toxicity in a control group.

Study design: Field research at CAPS-AD; experimental laboratory research using the Osmotic Fragility Test; and bibliographic/documentary analysis

Place and Duration of Study: CAPS-AD, Palmas, Tocantins, Brazil, from December 2021 to March 2022.

Methodology: We investigated the toxicity of carbonate of lithium in a control group and in three different concentrations, being 0.12; 0.06; 0.03. Therefore, documentary research was carried out in Tocantins to carry out an osmotic fragility test, with subsequent statistical analysis, with ANOVA and Tukey's test, with a significance of 95%.

Results: The study confirmed lithium carbonate toxicity at all tested concentrations compared to the control group. Absorbance measurements revealed significant hemolysis across all concentrations, except for 0.06 mg/mL at NaCl levels of 0.48% and 0.72%.

Conclusion: Based on the tests and studies conducted in this work, it is possible to confirm the existence of lithium-associated toxicity. The toxic effects may result in severe health impairments for affected individuals, making it essential to perform regular tests according to specific clinical requirements, as well as monitoring serum lithium levels (lithiumemia) and renal function.

Keywords: Bipolar affective disorder, lithium carbonate, toxicity, mental health.

1. INTRODUCTION

Bipolar Affective Disorder (BAD) is a chronic and recurrent mental health condition that significantly affects an individual's quality of life, leading to functional and cognitive impairments, as well as an increased risk of premature death (GRANDE et al., 2016). It is characterised by the occurrence of manic episodes (bipolar mania), hypomanic episodes, and depressive episodes (bipolar depression) (MCINTYRE; CALABRESE, 2019). According to the latest International Classification of Diseases (ICD-11, 2018), this disorder is defined by mood dysregulation, with the presence of manic episodes (type I) or hypomanic episodes (type II), and major depression in both diagnoses, alongside the possibility of mixed episodes.

Unipolar depression, also referred to as Major Depressive Episode, is the primary cause of morbidity in patients with bipolar disorder and is associated with higher morbidity and mortality rates compared to patients with bipolar mania. Depressed individuals are at a higher risk of suicide, panic attacks, inter-episode symptoms, and psychosis (KAPCZINSKI; QUEVEDO, 2016). This condition is characterised by a depressed mood or loss of interest/pleasure in nearly all activities for at least two weeks, accompanied by four or more additional symptoms, which may include changes in sleep and/or psychomotor speed, feelings of guilt and worthlessness, fatigue, and a reduced ability to think or concentrate (BOSAIPO; BORGES; JURUENA, 2017).

Initially, treatment for Bipolar Affective Disorder (BAD) involves the use of mood stabilisers, anticonvulsants, or atypical antipsychotics, which, when combined with psychosocial interventions such as individual or group psychotherapy and psychoeducation groups, have been shown to significantly benefit patients (ROSA; LEÃO, 2022). To ensure effective treatment adherence, it is crucial that medication is combined with psychosocial interventions. Although pharmacotherapy remains the primary treatment for BAD, it provides only partial symptom relief when used in isolation.

Another critical point is that prolonged management with mood stabilisers can also impair adherence and lead to psychosocial harm, highlighting the importance of combining pharmacological treatment with psychosocial interventions to promote patient autonomy (OLIVEIRA et al., 2019). Lithium is one of the first-line drugs for managing both acute manic and depressive episodes in BAD (BOSAIPO; BORGES; JURUENA, 2017). However, in addition to its effects on the central nervous system, lithium has systemic impacts on multiple organs, including the kidneys, heart, motor plate, and the thyroid and parathyroid glands. It may cause hypothyroidism, hyperthyroidism, goitre, ophthalmopathy through various mechanisms, nephrogenic diabetes insipidus, and other disorders. The adverse effects are typically reversible after discontinuation of the drug.

However, some patients may experience irreversible renal damage due to chronic interstitial nephropathy (LERENA et al., 2022). Symptoms of lithium toxicity include tremor, polyuria, polydipsia, bradycardia-tachycardia syndrome, oedema, ataxia, dermatological conditions (such as acne and psoriasis), increased appetite, dysentery, emesis, and decreased thyroid function (MALHI et al., 2020; PARIZOTTI et al., 2021). Therefore, it is essential to assess adherence to lithium treatment, for which lithium serum levels (lithium monitoring) are measured. Despite this, it is well known that lithium, at high concentrations, can be toxic to the human body due to its narrow therapeutic index, making frequent monitoring of serum levels necessary (WON; KIM, 2017).

Given the risks associated with the primary medication used, it is crucial to have a more comprehensive understanding of other medications recommended for the treatment of BAD, including potential drug interactions. It is also important to investigate the effects of lithium carbonate on human blood cells, ensuring that patients neither abandon their treatment nor suffer from physiological and biochemical harm. The osmotic fragility test emerges as an ideal option, as it is low-cost, simple to perform, and a widely accessible laboratory screening method commonly used to assess the resistance or fragility (lysis) of erythrocytes when exposed to variations in the osmotic concentrations of sodium chloride.

2. MATERIAL AND METHODS

This study employs a variety of methods, divided into three phases: field research at the CAPS-AD in Palmas-Tocantins, experimental research in the laboratory using the Osmotic Fragility Test, and documentary/literature research.

2.1 Medication Survey – CAPS-AD

Initially, a survey was conducted with the pharmacy team at the Psychosocial Care Centre – Alcohol and Drugs (CAPS-AD) in Palmas, Tocantins, through a guided visit. Medications prescribed for the treatment of Bipolar Affective Disorder (BAD) were selected. Data collection took place from December 2023 to March 2022, with approval from local supervision. As these were secondary data, the medication list was organised in a table. A documentary and bibliographic comparative study was then conducted to gather relevant information, including dosage forms, therapeutic indications, potential drug interactions, and side effects of medications used to treat BAD.

2.2 Osmotic Fragility Test

Following the medication survey at CAPS-AD, lithium carbonate was selected for an experimental toxicity study ex vivo, where biological material is obtained from a living organism. The osmotic fragility test was employed to determine whether this medication affects the cell membrane of human erythrocytes. This technique is based on a simple, low-cost method that assesses the variation in the resistance of red blood cells when exposed to saline solutions with decreasing concentrations (PARDINI, 2015). Male participants were selected for peripheral blood collection, with inclusion criteria requiring that they were free from licit or illicit drug consumption in the 48 hours preceding collection. Participants were recruited based on availability and voluntarily.

The collection process took place at the Basic and Health Sciences Laboratory (LACIBS) at the Federal University of Tocantins (UFT), which adheres to biosafety guidelines. The laboratory is equipped for blood collection, technique development, and result analysis. For the erythrocyte osmotic fragility test (FOE), a 5 mL sample of peripheral blood was collected by venipuncture from the research participants, using a Vacutainer® kit with an EDTA-containing tube as an anticoagulant. The collection was performed by a registered nurse and a qualified pharmacist.

Aliquots of 50 µL of blood were exposed to increasing concentrations of the medication (0.03, 0.06, 0.12 mg/mL) diluted in 0.9% NaCl. After a 60-minute exposure to the medications, the blood was then exposed to increasing NaCl solutions: 0.12%, 0.24%, 0.48%, 0.60%, 0.72%, and 0.9%, homogenised, and incubated in a controlled water bath at 37 °C for 60 minutes. After incubation, the tubes were centrifuged at 1500 rpm for 10 minutes, and the supernatant was analysed using a Thermo Scientific® Genesys 10S UV-VIS spectrophotometer at 540 nm.

From the data obtained by spectrophotometry, hemolysis curves for each individual were constructed. These were used for statistical analysis of the osmotic fragility of erythrocytes to compare all variables. Using the FOE data from the groups, statistical analysis was performed for comparisons between the groups (SILVA, 2015).

2.3 Medications Indicated by the Unified Health System – SUS

Based on the medication data for BAD from CAPS-AD, a documentary search was conducted through Ordinance No. 3, dated March 9, 2015. A comparison was then made between the medications used at CAPS-AD and those recommended by the SUS. Descriptive analysis was applied to the statistical analysis of the medication comparisons, and for the experimental test, the data were subjected to normality analysis followed by ANOVA, with Tukey's post-hoc test at a 95% significance level. All processes were carried out at the Basic and Health Sciences Laboratory (LACIBS) at the Federal University of Tocantins, Palmas-TO campus. The study was submitted to and approved by the Ethics Committee (nº. 066/2013).

3. RESULTS AND DISCUSSION

Bipolar Affective Disorder (BAD) is a complex psychiatric condition with an unknown cause, often characterised by sudden mood swings ranging from depression to manic episodes. It is essential to inform patients that Bipolar Disorder is typically chronic and progressive, with frequent recurrences and, at times, severe episodes (YATHAM et al., 2018). In this context, the family plays a crucial role as a support and safety network. When integrated with community involvement and the healthcare team at the Psychosocial Care Centre (CAPS), a comprehensive support network is formed, including activity workshops, meetings, and integrative practices aimed at reintegrating the individual into society (SANTANA, 2021).

A support network encompasses interpersonal relationships and the strategic recognition and enhancement of bonds, which can be categorised into two systems: the Informal System and the Formal System. The Informal System includes family, friends, neighbours, and civil society institutions (NGOs, religious organisations, associations, and clubs) that provide social support to individuals affected by health conditions. The Formal System comprises public institutions and services offering care, support, and assistance to individuals and society, including health services (Family Health Strategy - FHS, Psychosocial Care Centres - CAPS, outpatient clinics, and hospitals), social assistance services (CRAS, CREAS, shelters, and hostels), child protection councils, courts, schools, INSS, housing departments, among others (FUSTER, 1997; FUSTER, OLAIZOLA, & OCHOA, 2002).

The Psychosocial Care Centres (CAPS), established by Ordinance No. 3088 of 23 December 2011, are strategic components of the Psychosocial Care Network (RAPS). CAPS serves as a space for rehabilitation, open to the community, primarily designed for individuals experiencing mental distress or disorders. Family involvement is integral, and the multidisciplinary team focuses on the user's rehabilitation within their health territory. The Psychosocial Care Centre – Alcohol and Drugs (CAPS-AD), restructured by Ordinance No. 130 of 26 January 2012, provides care for individuals facing intense psychological distress caused by the use of crack, alcohol, and other substances. It also addresses adverse clinical situations that hinder the establishment of social connections and life projects.

3.1 Medication Overview

At the CAPS in Palmas, TO, it was reported that patients with Bipolar Affective Disorder (BAD) often use multiple medications. Commonly prescribed drugs include bupropion (150 mg), lithium carbonate (300 mg), clonazepam (2 mg and 0.5 mg), chlorpromazine (25 mg and 100 mg), quetiapine (25 mg and 100 mg), sertraline (50 mg), and sodium valproate (500 mg and 250 mg) to stabilise mood or address episodes of bipolar depression. However, it is recommended to use only one medication for the treatment of BAD or associated depression, avoiding polypharmacy whenever possible.

Table 1. Medications most frequently used for the treatment of BAD at CAPS-AD in Palmas, TO, including their names, usual dosages, indications, posology, and associated drug interactions.

Medications / dosage	Indications	Posology	Drug interaction
Bupropion/ 150mg	Treatment of Major Depressive Disorder (MDD) and alcohol dependence.	Initial dose for most adults is one 150 mg tablet per day. The physician may increase the dose to 300 mg (two tablets) daily if symptoms do not improve. Do not take more than one tablet at a time. Doses should be spaced at least 8 hours apart. Avoid taking the medication near bedtime as it may cause insomnia.	Herbal medicines or supplements (e.g., vitamins), monoamine oxidase inhibitors (MAOIs), and other medications should be monitored.
Lithium Carbonate 300mg	Manic episodes in bipolar disorders; prevention of recurrent mania; prophylaxis of depressive phases; and treatment of psychomotor hyperactivity.	Variable and typically ranges from 900 mg to 1800 mg per day, divided into two doses. A single daily dose is not recommended during initial treatment or when doses exceed 1800 mg/day. Dosages should be tailored individually and adjusted as needed. Plasma lithium levels (lithiumemia) must be monitored to achieve therapeutic levels, generally between 0.8 and 1.4 mEq/L.	Nonsteroidal anti-inflammatory drugs (NSAIDs) such as indomethacin and phenylbutazone, as well as diuretics like hydrochlorothiazide and chlorothiazide.
Clonazepam 0.5mg and 2mg	Anxiolytic and anticonvulsant for epilepsy, infantile spasms (West syndrome), anxiety disorders, mood disorders, psychotic syndromes, restless legs syndrome, burning mouth syndrome, vertigo, and balance disorders.	For mood disorders, the dosage ranges from 1.5 mg to 8 mg/day. Recommended dose: 2.0 to 4.0 mg/day.	Central nervous system depressants, alcohol, antidepressants, sleep medications, certain analgesics, antipsychotics, anxiolytics, anticonvulsants, gastrointestinal drugs, and grapefruit juice, as they may enhance medication effects.
Chlorpromazine 25mg and 100mg	Treatment of acute psychiatric conditions and control of chronic psychoses.	Ranges from 25 mg to 1600 mg/day, depending on clinical needs. Initial treatment should start with low doses (25 to 100 mg), repeated 3–4 times daily, as needed, to achieve symptom control (maximum dose: 2 g/day).	Levodopa, lithium, and sultopride are contraindicated or not recommended due to interactions.
Quetiapine 25mg and 100mg	Schizophrenia; monotherapy or adjunctive therapy for manic episodes in bipolar disorder; depressive episodes in bipolar disorder; and maintenance treatment of bipolar I disorder.	Dose titration is as follows: Day 1: 50 mg; Day 2: 100 mg; Day 3: 200 mg; Day 4: 300 mg. Doses may increase to 400 mg by Day 5 and up to 600 mg by Day 8. Antidepressant efficacy has been demonstrated at doses of 300–600 mg, with no additional benefit observed above 600 mg during short-term treatment.	Alcohol, medications affecting brain function or behavior, drugs causing electrolyte imbalance or QT prolongation, anticholinergic agents, and certain antifungals, antibiotics, and antivirals.

Sertraline 50mg	Depression (including depression with anxiety), panic disorder, post-traumatic stress disorder (PTSD), social anxiety disorder, and premenstrual dysphoric disorder. Indicated for adults and children aged 6 years and older in cases of obsessive-compulsive disorder (OCD).	Oral administration, once daily, preferably at the same time each day, with or without food. Maximum recommended dose: 200 mg/day.	Monoamine oxidase inhibitors (MAOIs), pimozide.
Sodium Valproate 500mg and 250mg	Monotherapy or adjunctive therapy for partial complex seizures, whether isolated or associated with other types of seizures.	Initiate with 10–15 mg/kg/day, increasing by 5–10 mg/kg/week until the optimal clinical response is achieved. Optimal response is generally observed at doses below 60 mg/kg/day.	Liver disease or significant hepatic dysfunction, mitochondrial disorders caused by POLG gene mutation (e.g., Alpers-Huttenlocher syndrome), children under 2 years with suspected POLG-related disorders, urea cycle disorders, porphyria.

The treatment of this condition is often compromised primarily due to misdiagnosis, leading to the inappropriate prescription of medications that do not directly address the underlying issue. This can exacerbate the patient's clinical condition or simply delay effective treatment (SILVA; DIAS; ROSALINO, 2017). Lithium, a natural element and metal, plays a significant role in the pharmaceutical industry and is commercially available as lithium carbonate. For five decades, lithium carbonate has been predominantly used for the treatment of Bipolar Affective Disorder (BAD), demonstrating efficacy in prevention and reducing the likelihood of recurrence (KENDALL et al., 2016; FERENSZTAJN-ROCHOWIAK et al., 2021).

It is estimated that 70% to 80% of patients with BAD receive lithium as an adjuvant treatment, primarily for suicide prevention and recurrence reduction. Frequent monitoring of lithium levels through lithium serum testing is necessary to ensure therapeutic efficacy, as lithium is not always used as monotherapy (PENHA et al., 2019; PARIZOTTI et al., 2021; LOPES, 2019). In another CAPS facility in Mutuípe, BA, medications such as carbamazepine (200 mg), risperidone (3 mg), haloperidol (5 mg and 2 mg/mL), clonazepam (2.5 mg/mL), valproic acid (50 mg/mL), and long-acting haloperidol decanoate (50 mg/mL, intramuscular) were dispensed as part of the therapeutic regimen (SANTANA, 2021).

Interactions between antipsychotics and antidepressants may lead to harmful adverse reactions in patients, such as agitation and motor disturbances. These undesired effects often contribute to non-adherence to treatment or withdrawal from care. At the CAPS 'Esperança' in Recife, PE, therapeutic workshops combined with pharmacological treatment were reported as effective and satisfactory by users in terms of the guidance provided. However, most patients remained on polypharmacy regimens (BARROS; DUARTE, 2020).

In a study by Balen et al. (2017), 7.4% of severe potential drug interactions involved the combination of chlorpromazine and haloperidol. Such interactions represent significant health risks, including reduced efficacy or excessive potentiation of the expected therapeutic effect, as well as increased treatment costs (FRIEDRICH; BLATTES, 2022). Liu et al. (2017) further noted that for each additional capsule taken by a patient, the risk of non-adherence to treatment increases by 12%.

3.2 Osmotic Fragility Test

The most commonly used medication for Bipolar Affective Disorder (BAD), as observed in both studies and at the Alcohol and Drug Psychosocial Care Centre in Palmas-TO, is lithium carbonate, which is considered the most effective treatment for this condition to date. This medication is effective in both the prevention and recurrence of BAD (PEREIRA et al., 2019; LOPES, 2019). Despite sometimes failing to achieve the desired mood stabilisation, lithium carbonate is the only medication proven to directly prevent suicide (SARAI et al., 2018).

To evaluate whether lithium carbonate is toxic to human erythrocyte membranes, the Osmotic Fragility Test (OFT) or Osmotic Fragility Curve remains a widely used laboratory screening method. This test assesses the resistance or fragility (lysis) of erythrocytes when exposed to varying osmotic concentrations of sodium chloride (QUADROS; BRITO JUNIOR, 2022). In this study, the results of the tests performed are detailed in Figure 1.

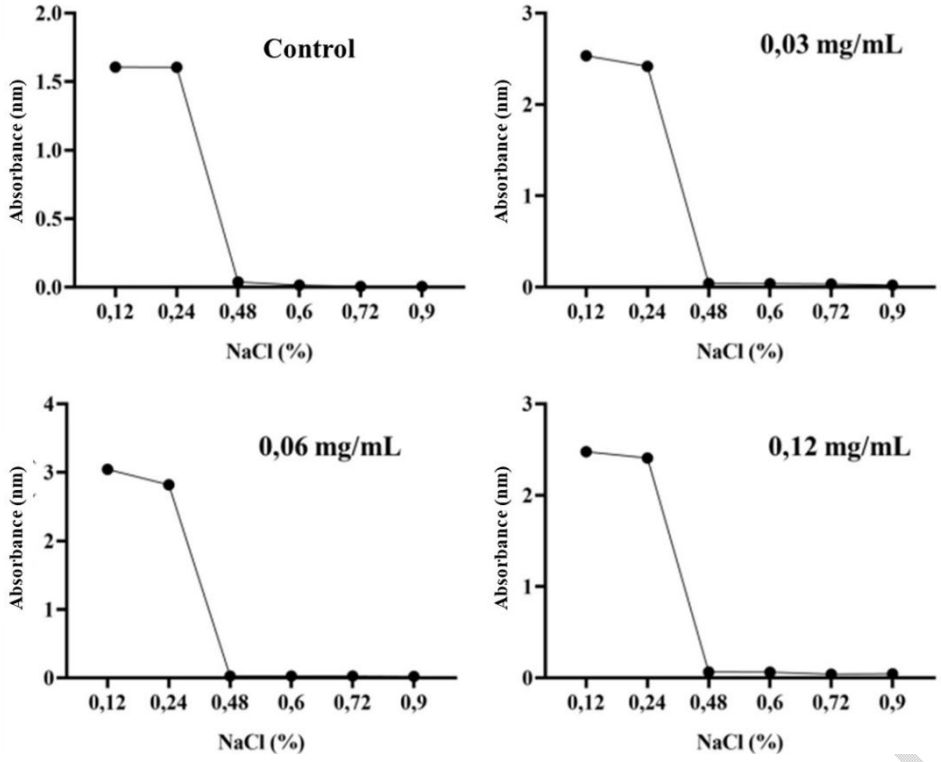

Fig. 1. Absorbance results from the Osmotic Fragility Test on human erythrocytes (n=3) in the control group and drug-treated groups (0.03, 0.06, and 0.12 mg/mL).

The absorbance data indicate that haemolysis occurred after administering the tested medication, as absorbance correlates with the amount of light absorbed, which increases with higher haemoglobin levels—a marker of erythrocyte rupture. Haemolysis was observed across all medication concentrations when compared to the control group, except at NaCl concentrations of 0.48% and 0.72% in the 0.06 mg/mL group, where no differences were detected compared to the control group. Lithium exhibits a bioavailability of 80–100% and is primarily excreted via the kidneys. However, due to its similarity to sodium or sodium deficiency, lithium is reabsorbed in place of sodium, leading to elevated plasma levels and nephrotoxicity (ALVES, 2021; MCKNIGHT et al., 2019). As a renally excreted drug, reduced glomerular filtration rates and lithium excretion can increase serum levels, leading to toxicity. Lithium has a narrow therapeutic index, with safe and effective doses typically ranging from 300 mg/day to a maximum of 1800 mg/day, with lower doses recommended for older adults due to decreased renal excretion, which increases adverse effects.

Even at therapeutic doses, lithium can cause adverse effects, including nephrotoxicity, oedema, nausea, vomiting, polyuria, and tremor—frequent complaints that reduce treatment adherence (ÖHLUND et al., 2018; MELEIRO, 2018; ALASTANOS; POTTER; CROUSE, 2019). Co-administration with antipsychotics or non-steroidal anti-inflammatory drugs (NSAIDs) may result in neurotoxicity and nephrotoxicity (ALMEIDA, 2020; CÂMARA et al., 2019; ALVES, 2021). Lithium intoxication can arise from chronic kidney function decline or acute accidental overdoses, even when serum levels are within the therapeutic range (EL BALKHI et al., 2017; BAIRD-GUNNING et al., 2016; PERRONE, 2020). Frequent drug interactions also contribute to lithium toxicity. For instance, Pasqualoto et al. (2018) found that 75% of prescriptions involved drug interactions, with 44.4% classified as high risk, 23.9% as moderate risk, and 6.5% as low risk.

Gradual and progressive symptom onset characterises lithium toxicity. There is no specific detoxification treatment; instead, symptomatic management is provided. Common symptoms include tremors (which can be alleviated with adjuvants like propranolol and atenolol), polyuria, polydipsia (potentially indicative of diabetes insipidus or nephrotoxicity), bradycardia-tachycardia syndrome, oedema, ataxia, dermatoses (e.g., acne and psoriasis), increased appetite, diarrhoea, emesis, and reduced thyroid function (MALHI et al., 2020; PARIZOTTI et al., 2021). Lithium can also cause electrocardiogram (ECG) abnormalities and elevated cardiac markers indicative of cardiac injury. Post-bariatric surgery pharmacokinetics can increase lithium toxicity with neurological repercussions (HAMID et al., 2020; FIGUEIREDO; LEMOS, 2020). Co-administration with antipsychotics or NSAIDs exacerbates lithium toxicity by reducing glomerular filtration rates and lithium excretion, raising serum levels (ALVES, 2021).

In conclusion, lithium toxicity may result from excessive doses or reduced renal excretion. Drug interactions are a significant contributor to increased lithium toxicity, which can occur even at low doses and is a common cause of treatment discontinuation (MOTA et al., 2021). Lithium is often combined with selective serotonin reuptake inhibitors (SSRIs)—citalopram (25%), escitalopram (25%), and sertraline (50%)—or antipsychotics such as chlorpromazine and haloperidol, which may lead to additional side effects (BALEN et al., 2017; PEREIRA et al., 2019). Observed symptoms include rigidity, stupor, dyskinesia, oliguria, and an increased risk of cardiotoxicity (SEEMAN; GONZÁLEZ-RODRÍGUEZ, 2018; SADOCK; SADOCK; SUSSMAN, 2018). Antidepressants can also cause rebound effects, leading to manic episodes and treatment discontinuation (ELISABETSKY et al., 2021; TUNC; TUNC, 2022).

To minimise patient harm and enhance adherence, nurses play a critical role in administering medications at separate times from antidepressants or anticonvulsants, ensuring proper hydration, educating families about environmental control and safety, fostering family involvement, monitoring risky behaviours, promoting well-being, maintaining a calm demeanour, providing patients with adequate time to respond, and establishing a trusting relationship. Additionally, the multidisciplinary team must align with the family to ensure cohesive care (JANSEN et al., 2022). It is crucial to monitor for signs of lithium toxicity and balance its use with patient safety.

3.3 Medications Recommended by the SUS

The treatment of bipolar depression should preferably involve monotherapy, considering prior response history, tolerability, and contraindications. However, combinations may be employed in cases of refractoriness, contraindications, or intolerance to lithium, such as fluoxetine with olanzapine, lithium carbonate, or valproic acid. Lamotrigine and quetiapine are first-line monotherapies, with quetiapine being the second most evidence-based medication. Lithium carbonate remains a Level 1 recommendation for all phases of BAD treatment, including bipolar depressive episodes (BRASIL, 2016). The Ministry of Health has approved medications for the direct treatment of BAD within the Brazilian Unified Health System (SUS), including clozapine, lamotrigine, olanzapine, quetiapine, and risperidone. These medications, initially used for other health conditions within the SUS, were incorporated for the treatment of BAD per the official announcement on March 10, 2015 (BRASIL, 2015).

Other drugs, such as carbamazepine, haloperidol, and fluoxetine, are also included in BAD treatment. The primary goal of pharmacological therapy remains symptom remission, followed by maintenance therapy to prevent recurrences (BRASIL, 2016). However, inadequate or unnecessary combinations can increase costs and delay patient recovery (BRASIL, 2015). Many CAPS facilities do not fully adhere to SUS protocols, which undermines treatment efficacy. Inconsistent access to recommended medications can lead to ineffective treatments, prolonged recovery, and an increased risk of relapses and severe episodes.

4. FINAL CONSIDERATIONS

Through the tests and studies conducted in this work, it is possible to affirm that lithium toxicity exists. It is well established that toxic effects can cause severe health impairments for individuals experiencing this condition. Therefore, regular testing based on specific needs, as well as the monitoring of serum lithium levels and renal function, is indispensable. Healthcare professionals caring for patients using lithium carbonate must remain vigilant for symptoms indicative of toxicity to promptly adjust dosages and provide symptomatic treatment. Another critical aspect is educating patients about adverse reactions, symptoms of toxicity, and the potential need for dose adjustments. This knowledge is essential for ensuring effective treatment and encouraging adherence. While these factors often contribute to treatment discontinuation, proper guidance and information can support the patient's commitment to psychiatric care. It is evident that further testing and research are needed for this essential chemical element, which requires careful attention.

Finally, it is crucial to establish effective protocols for the treatment of Bipolar Affective Disorder (BAD), including psychotherapeutic interventions combined with medication and family involvement, to truly restore the user's quality of life. Nurses play a vital role in effectively integrating and linking users to healthcare services. This includes monitoring signs and symptoms of toxicity risk and implementing an individualised care plan based on the Nursing Care Systematisation (NCS). This approach aims to safeguard the patient’s well-being and encourage adherence to treatment, rather than compromising their integrity.

DISCLAIMER(ARTIFICIALINTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

CONSENT AND ETHICAL APPROVAL

Ethical approval for tris study was granted by the Research Ethics Committee for Human Subjects at the Federal University of Tocantins (approval number: 066/2013). Additionally, written informed consent was obtained from all participants involved in the clinical trial. The privacy and confidentiality of participants' data were strictly maintained during and after the study.

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