International Journal of Health Science

Acceptance date: 08/11/2024

IN THE STORM OF BIPOLAR DISORDER

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Abstract: Bipolar disorder (BD) is a chronic condition characterized by alternating episodes of mania, depression and hypomania, which significantly affect patients' quality of life. Lithium stands out as one of the most classic mood stabilizers in the treatment of BD, being widely used both in acute crises and in the prevention of new episodes. This study conducted a literature review to investigate lithium's mechanisms of action, its therapeutic efficacy and the challenges associated with treatment, including side effects and the need for continuous monitoring. Lithium was found to have neuroprotective properties against self-destructive attacks with a proven effect in reducing the risk of suicide. In addition, it is important to adjust doses and monitor serum levels to minimize adverse effects and optimize adherence to treatment. Despite the challenges, lithium remains an essential treatment for BD, representing an effective short- and long-term therapeutic option for patients facing this psychiatric condition.

Keywords: Mood stabilizers. Lithium. Bipolar disorder.

INTRODUCTION

Bipolar disorder is a chronic and recurrent psychiatric condition, marked by extreme mood swings that alternate between episodes hypomania, depression and mania, interspersed with periods of remission. This disease is considered one of the main causes of functional disability, especially in young adults, as observed by Bosaipo; Borges; Juruena (2017) and Reis et al. (2015). Early diagnosis, combined with appropriate treatment, is crucial to improving prognosis, since bipolar disorder is strongly related to high rates of comorbidities, such as anxiety disorders and substance abuse (Almeida; Nascimento Júnior; Cardoso, 2023).

Among the therapeutic options available, lithium stands out as the most important mood stabilizer in the management of BD, being the first line of pharmacological treatment (Nicola, 2019). Its effectiveness in controlling both manic and depressive episodes is widely recognized, and it is even the only drug with proven antisuicidal properties, helping to prevent relapses and reduce associated mortality (Reis *et al.*, 2015; Nicola, 2019).

Considering this therapeutic alternative, this study aims to investigate the mechanisms of action of Lithium in the context of bipolar disorder and identify biomarkers that can predict the response to treatment, reviewing its efficacy, adverse effects and possible risks. The aim is to optimize and personalize therapeutic interventions. Understanding the mechanism of action of Lithium in the treatment of bipolar disorder represents an important contribution to personalized medicine and public health, since it influences the neural processes responsible for stabilizing mood and preventing new depressive and manic episodes.

METHODOLOGY

This study consists of a literature review on the theme "Lithium: awakening in the storm of bipolar disorder". The literature search was conducted using the following descriptors: "Bipolar disorder", "Lithium" and "Mood stabilizers". The research was carried out on the PubMed, Google Scholar and VHL Regional Portal platforms, which integrate databases such as the Scientific Electronic Library Online (SCIELO) and the Latin American and Caribbean Literature on Health Sciences (LILACS), among others. Articles published between 2010 and 2024 in Portuguese, English and Spanish were included, resulting in the identification of 785,000 documents.

Inclusion criteria were applied to select studies that directly addressed the central focus of this research, with full text availability. After eliminating duplicate materials and those that did not meet the inclusion requirements, 37 articles remained, which served as the basis for this Final Paper.

The structuring and formatting of the work followed the current institutional manual of methodological standards (Morais, 2018), which follows the ABNT guidelines for academic work and scientific articles.

THEORETICAL BACKGROUND

BIPOLAR DISORDER: OVERVIEW

Definition and subtypes of bipolar disorder

Bipolar disorder is a psychiatric condition that can significantly impact an individual's functional capacity and quality of life, and is considered one of the most disabling illnesses, with severe mood swings. It causes episodes of mania, depression and hypomania which alternate with periods in which the mood remains stable (Bosaipo; Borges; Juruena, 2017; Lima, 2018). Several studies (Bosaipo; Borges; Juruena, 2017; Cunha, 2023; Facchin, 2022) establish two subdivisions for bipolar disorder: type I and type II.

According to the *Diagnostic and Statistical Manual of Mental Disorders: DMS-5* (APA, 2014), bipolar disorder type I is a psychopathology in which the person experiences at least one episode of mania, which lasts at least seven days or requires hospitalization due to its severity. Although most individuals with this diagnosis also have episodes of depression, these are not required to confirm the disorder.

Type II bipolar disorder is a subtype of bipolar disorder in which the person experiences episodes of depression alternating with episodes of hypomania, but without ever having a complete manic episode.

Etiology and risk factors

The etiology of TB is complex and multifactorial, resulting from the interaction between genetic, neurobiological and environmental factors (Bosaipo; Borges; Juruena, 2017). Goodwin (2016) reports that TB has a strong genetic predisposition, with a heritability rate of up to 80% in identical twins and significant prevalence in first-degree relatives of diagnosed patients.

Bipolar disorder is characterized by significant alterations in the neurochemistry of the brain, particularly in neurotransmitter systems such as serotonin, dopamine and noradrenaline, which are fundamental in regulating mood and behaviour. In the disorder, an imbalance of these neurotransmitters occurs, with studies indicating a reduction in serotonin levels during depressive episodes and an increase in dopaminergic activity during manic phases (Alves *et al.*, 2023; Cordeiro *et al.*, 2024).

In addition, Cordeiro *et al.* (2024) report that there is evidence of gray matter atrophy in important areas such as the prefrontal cortex and hippocampus, regions associated with emotional control and memory.

These neurochemical changes are strongly linked to the symptoms of bipolar disorder, such as extreme mood fluctuations. And understanding them is key to developing more effective treatments aimed at regulating these imbalances. Structural neuroimaging studies also identify changes in brain volume, such as enlargement of the lateral ventricles in some individuals (Cordeiro *et al.*, 2024).

Although bipolar disorder has an important genetic component, Carneiro and Soratto (2016) point out that environmental and psychosocial factors also play a crucial role in its manifestation and evolution. Research suggests that stressful events, such as trauma or significant losses, can trigger manic or depressive episodes. Stress can also alter the functioning of the hypothalamic-pituitary-adrenal axis, con-

tributing to hormonal dysfunctions associated with the disorder (Rocha *et al.*, 2023).

Another relevant factor is psychosocial aspects, such as family and social support, which influence both the frequency and severity of episodes. The combination of genetic predisposition and adverse environmental factors is a key aspect in the development of bipolar disorder (Carneiro; Soratto, 2016).

Symptoms and diagnostic criteria

Episode of mania

According to the Diagnostic and Statistical Manual of Mental Disorders: DMS-5 (APA, 2014) and Fernandes et al. (2016), the manic episode is marked by a period in which the patient's mood becomes abnormally elevated, expansive or irritable and this change lasts for at least a week. During this time, the person experiences intense and prolonged joy, with a feeling of euphoria and excess energy. The individual may start several activities at once, but fail to complete them, displaying grandiose behavior and an exaggerated confidence in their abilities. When challenged or contradicted, the patient can become extremely irritable. In addition, there is a significant reduction in the need for sleep, with the person feeling refreshed after only a few hours of rest. Other characteristics include: excessive and accelerated speech, rapid and scattered thoughts and a tendency to be easily distracted.

The patient may also adopt impulsive and reckless behaviors, such as spending money wildly, increasing sexual desire and engaging in risky activities. These behaviors can be inappropriate and even dangerous, affecting both the person themselves and those around them. These changes are serious enough to cause damage to the individual's social or professional life and, in some cases, may require hospitalization to prevent risks (Fernandes *et al.*, 2016).

Episodes of hypomania

Hypomania is characterized as an elevated or irritable mood state that is less intense than mania, but still results in noticeable changes in the person's behaviour. Symptoms include mood swings such as euphoria or significant irritability, increased energy, hyperactivity, impulsivity and decreased need for sleep. During hypomania, the individual may feel more active, start multiple activities at the same time, be more sociable, talk excessively and engage in impulsive behavior, such as overspending. Unlike mania, hypomania does not include psychotic symptoms such as delusions or hallucinations, which differentiates it and reduces its severity (Moreno; Moreno; Ratzke, 2005; Bosaipo; Borges; Juruena, 2017).

According to the DSM-5, in order to diagnose an episode of hypomania, the patient must be in an abnormally elevated, expansive or irritable mood for at least four consecutive days, accompanied by at least three additional symptoms, such as grandiosity, decreased need for sleep, rapid speech, flight of ideas, increased goal-directed activity or excessive involvement in pleasurable activities with a high potential for negative consequences (APA, 2014).

These symptoms must represent a marked change in the individual's usual behavior, but not be severe enough to cause significant social or occupational dysfunction or require hospitalization. In addition, the episode must not be induced by substances or other medical conditions (APA, 2014).

Depressive episode

A depressive episode is characterized by five or more symptoms present over a twoweek period, which represent a change from previous functioning. At least one of the symptoms must be depressed mood or loss of interest or pleasure. Symptoms of a depressive episode include: depressed mood most of the day (almost every day) indicated by an individual's report of feeling sad, empty or hopeless or by others' observation of the same symptoms. In children and adolescents, the mood can be irritable. There is also a marked decrease in interest or pleasure in all, or almost all, activities most of the day, almost every day (APA, 2014).

As cited by Bosaipo; Borges; Juruena (2017), sleep disorders are recurrent in this episode, manifesting themselves in the form of both insomnia and hypersomnia. Agitation or psychomotor retardation are frequent and can be perceived by others. Fatigue or a feeling of loss of energy is an almost constant occurrence, as are feelings of worthlessness or excessive and inappropriate guilt, which can reach delusional levels. Thoughts of death, suicidal ideation, or specific plans to commit suicide are serious symptoms that occur during the episode. These criteria constitute a major depressive episode, common in bipolar disorder type I, but not necessary for the diagnosis of this disorder.

Impact and course of the disease

Bipolar disorder is a chronic condition marked by oscillations between episodes of mania, depression and hypomania, with periods of stability between crises. This fluctuating course can be characterized by recurrent episodes and extreme mood swings (Parizotti; Alves Filho; Peder, 2021).

The use of lithium as a mood-stabilizing treatment is effective, especially in preventing new episodes and reducing the severity of symptoms. However, the fluctuating course of the disease requires continuous monitoring, with treatment adaptations for each phase. Many patients require therapeutic combinations for more efficient control, as monotherapy is often not enough to maintain stability (Missio, 2019).

Patients with bipolar disorder often have psychiatric and clinical comorbidities. Among the most common psychiatric comorbidities are anxiety disorders, such as panic disorder and obsessive-compulsive disorder, as well as substance abuse (Dellazari, 2023; Garcia; Melgaço; Trajano, 2022). Obsessive-compulsive disorder, in particular, can precede the first mood episodes, making it difficult to correctly diagnose bipolar disorder (Dellazari, 2023).

Substance use, such as alcohol, is significantly more prevalent in bipolar patients, with substance abuse rates three to five times higher than in the general population (Garcia; Melgaço; Trajano, 2022).

According to the studies by Félix, Mello and Silveira (2021), other medical conditions, including hypothyroidism, hypertension and diabetes are also observed in these patients, and the presence of comorbidities is associated with a worse response to treatment. Comorbidities need to be managed concomitantly, as they can not only interfere with the effectiveness of mood stabilizers, but also increase the risk of clinical complications (Rocha *et al.*, 2023).

Parizotti, Alves Filho and Peder (2021) state that bipolar disorder is one of the psychiatric conditions with the highest risk of suicide. It is estimated that around 15% of patients with bipolar disorder commit suicide at some point in their lives. The risk is particularly high among young males, patients with a history of suicide attempts and those with concomitant use of psychoactive substances (Félix; Mello; Silveira 2021).

Lithium therapy has been shown to be effective in reducing this risk and is one of the few drugs with proven efficacy in preventing suicide in patients with bipolar disorder. Continuous follow-up and monitoring of associated conditions are crucial to identifying suicidal behavior early and implementing appropriate interventions (Félix; Mello; Silveira, 2021).

LITHIUM: HISTORY AND MECHANISM OF ACTION

History of Lithium use

In 1817, the Swedish chemist Johan August Arfvedson identified lithium as a chemical element while studying the mineral petalite, but its medicinal use only began to be explored in the 19th century (Frota; Lima, 2024). The first medicinal use of lithium was by the British doctor Alfred Baring Garrod in the treatment of gout between 1847 and 1859. He observed that these salts could dissolve urate crystals, thus initiating research into its use in medical conditions (Zung; Michelon; Cordeiro, 2010; Frota; Lima, 2024).

It wasn't until 1949 that Australian psychiatrist John Cade rediscovered lithium as a mood stabilizer and published studies on its efficacy in the treatment of mania (Frota; Lima, 2024). Cade observed that Lithium gave manic patients a great improvement and suggested its use as a mood stabilizer, which established the basis for its large-scale use in modern psychiatry (Zung; Michelon; Cordeiro, 2010).

As reported by Moreira and Matos (2014), over time, understanding of the mechanism of action of Lithium has evolved, especially with the research of Mogens Schou in the 1950s, which corroborated its efficacy not only in the treatment of manic episodes, but also in the prevention of relapses in bipolar disorders.

But it wasn't until 1970 that Lithium was recognized by the *Food and Drug Administration* (FDA) in the United States as an effective treatment for acute manic crises in patients with bipolar disorder, an important moment in psychiatric medicine. Soon after, in 1974, Lithium received a new approval, becoming the first official treatment to prevent the recurrence of manic and depressive episodes in people with bipolar disorder, consolidating its position as a long-

term treatment option (Parizotti; Alves Filho; Peder, 2021; Tondo *et al.*, 2019).

Mechanisms of action of lithium

According to Parizotti, Alves Filho and Peder (2021) and Guariento (2016), lithium influences the treatment of bipolar disorder by modulating neurotransmitters such as dopamine, GABA, glutamate and serotonin, stabilizing communication between neurons and regulating intracellular mechanisms. It reduces the concentrations of Inositol and Diacylglycerol (DAG) which act as intracellular messengers, reducing the cellular hyperactivity associated with the disorder. Lithium also inhibits the GSK-3 enzyme, which is associated with increased neuronal death, promoting neuroprotection neuroplasticity. These effects result in mood stabilization, reduced symptoms of mania and depression and suicide prevention (Parizotti; Alves Filho; Peder, 2021).

According to the studies by Silva Júnior and Gonçalves (2019) and Parizotti, Alves Filho and Peder (2021), the mechanism of action of Lithium in the treatment of bipolar disorder is based on the inhibition of the phosphatidylinositol cycle and the enzyme GSK-3B (Glycogen Synthase Kinase-3 Beta), which play a fundamental role in intracellular signaling. This promotes the regulation of neurotransmitters and mood stabilization, resulting in a positive therapeutic effect. Although Lithium can cause adverse effects, careful dosage adjustments are necessary to improve its efficacy and adherence to treatment.

Impact on the neurobiology of bipolar disorder

Lithium is widely recognized as a first-line mood stabilizer in the treatment of bipolar disorder. It helps regulate the release of neurotransmitters, such as serotonin and dopamine, which are dysregulated in the disorder.

Lithium's action results in a reduction in manic and depressive episodes, promoting long-term mood stability. In addition, the use of mood stabilizers, such as lithium, modulates neural activity, which contributes to the prevention of relapses and frequent mood swings in individuals with bipolar disorder (Rocha *et al.*, 2023).

Horita (2013) and Rocha *et al.* (2023) indicate that lithium is uniquely effective in reducing the risk of suicide among patients with bipolar disorder. This is due to its ability to regulate the neurotransmitter systems associated with mood and impulsivity, as well as its neuroprotective properties that mitigate self-destructive behavior. The use of Lithium is associated with a significant decrease in suicide rates in bipolar patients, when compared to other mood stabilizers and antidepressants.

According to Alves *et al.* (2023), bipolar disorder is associated with various neuroanatomical alterations, such as a reduction in the volume of the hippocampus and alterations in the prefrontal cortex, which are fundamental for emotional regulation, and an increase in the volume of the amygdala. Lithium has a neuroprotective effect, preserving brain structure and even reversing some of these alterations.

EFFECTIVENESS OF LITHIUM IN BIPOLAR DISORDER

Effectiveness at different stages of treatment

Lithium is one of the first-choice treatments for bipolar disorder, being effective both in the acute phases and in preventing future episodes. During bouts of mania and hypomania, lithium acts as a mood stabilizer, helping to control symptoms of euphoria and irritability. However, its stabilizing effect can take one to three weeks to fully manifest, which often leads to the need to combine it with other drugs, such as antipsychotics or

antidepressants, for faster control of acute symptoms (Reis *et al.*, 2015).

Lithium's effectiveness in treating acute manic crises is directly related to the drug's serum concentration in the body. According to Queiroz *et al.* (2021), the substance is effective in approximately 73% of patients when administered in doses that generate high concentrations in the blood. Despite this, treatment with lithium in the acute phase presents some challenges, such as its latency of effect and the risk of adverse effects at higher doses.

In the maintenance phase, lithium helps prevent new mood swings, both manic and depressive, over time. Its continuous use has been shown to be effective in preventing recurrent episodes, providing long-term stabilization (Moreira; Matos, 2014). Adherence to treatment can be optimized by monitoring serum lithium levels, ensuring therapeutic efficacy and preventing toxicity (Félix; Mello; Silveira, 2021).

However, according to Souza and Geta (2011), after stopping Lithium, recurrence rates can reach 80%, while continuous treatment significantly reduces this risk. However, prolonged use of Lithium requires regular monitoring due to the risk of side effects, such as tremors and kidney dysfunction (Reis *et al.*, 2015).

Even with competition from other mood stabilizers, such as Lamotrigine and Valproic Acid, Lithium remains the most effective treatment, especially in preventing manic episodes (Souza; Geta, 2011). In short, Lithium is essential for the maintenance phase of bipolar disorder, ensuring long-term stability and significantly reducing the risk of suicide (Porto et al., 2023).

In addition to its efficacy in controlling acute phases and preventing relapses, Lithium has a proven antisuicidal effect, and is the only mood stabilizer to have this property in such a robust way. Reducing the risk of suicide in patients with bipolar disorder treated with lithium is one of the main benefits of continuous use of this medication. According to the literature, treatment with Lithium can reduce the risk of suicide by up to five times and the risk of suicide attempts by ten times (Reis *et al.*, 2015).

This reduction is particularly important considering that up to 50% of adults with bipolar disorder attempt suicide at least once in their lifetime (Souza; Geta, 2011). Factors such as substance abuse, family history of affective disorders and severe depressive episodes are commonly associated with an increased risk of suicide in patients with bipolar disorder. Adequate treatment with lithium, then, has mitigated these factors, contributing significantly to reducing mortality rates among these patients (Queiroz *et al.*, 2021).

Comparison with other mood stabilizers

Lithium is widely recognized as the gold standard mood stabilizer in the treatment of bipolar disorder, being particularly effective in preventing manic episodes and reducing the frequency of relapses in the long term (Guimarães *et al.*, 2024). In addition, studies show that, despite its side effect profile, Lithium excels at maintaining mood stability over time, significantly reducing the risk of episodes recurring. However, it is important to note that its effectiveness is slightly greater in preventing manic episodes than depressive episodes (Missio, 2019).

Valproate is another mood stabilizer which, according to Lange *et al.* (2024) and Missio (2019), is widely used and effective in the acute phase and maintenance of bipolar disorder. Compared to lithium, valproate has shown greater tolerability in some studies, with fewer adverse effects, especially in the short term. Despite its good response in controlling symptoms, valproate is often combined with lithium to improve the therapeutic response in patients who do not respond adequately to monotherapy (Lange *et al.*, 2024).

Carbamazepine is also used as a mood stabilizer, especially for patients who do not respond well to lithium or valproate (Guimarães *et al.*, 2024). Comparative studies indicate that both the combination of lithium and valproate and lithium and carbamazepine have similar results in the treatment of acute episodes of bipolar disorder (Missio, 2019).

However, Carbamazepine may have metabolic advantages over Valproate, such as less weight gain, for example. In terms of efficacy, both combinations (Lithium + Carbamazepine and Lithium + Valproate) are effective, with no significant differences in terms of relapse prevention. However, it is known that Carbamazepine may be preferred in specific cases due to its tolerability (Lange *et al.*, 2024; Missio, 2019).

According to Lange *et al.* (2024), Lamotrigine is used in the treatment of bipolar disorder, with proven efficacy mainly in preventing depressive episodes. Its efficacy in the manic phase, however, is lower than that of lithium and valproate. The combination of Lithium and Lamotrigine has also been studied, but tends to be less effective when compared to the combination of Lithium and Valproate or Carbamazepine.

Atypical antipsychotics, such as Quetiapine, have shown efficacy in both the acute phase and maintenance therapy of bipolar disorder, especially in patients with manic symptoms. The combination of Lithium with atypical antipsychotics, such as Quetiapine, has been shown to be effective in reducing the recurrence of episodes, with a good cost-effectiveness ratio in Brazil's Unified Health System (SUS). However, this class of drugs is not without side effects and can trigger weight gain and metabolic risk. Even so, in cases of inadequate response to monotherapy, atypical antipsychotics are an important option (Zimmermann *et al.*, 2015).

SAFETY AND SIDE EFFECTS OF LITHIUM

The use of lithium in the treatment of bipolar disorder, as reported by Mota *et al.* (2021), is associated with a series of common side effects, especially when used long-term. Among the most frequent are gastrointestinal disorders, namely nausea and vomiting, as well as effects on the renal system, such as a decrease in the ability to concentrate urine and the risk of nephrotoxicity.

Studies such as those by Félix, Mello and Silveira (2021) and Mota *et al.* (2021) also show a reduction in glomerular filtration rate (GFR) and an increased risk of chronic renal failure. According to Mota *et al.* (2021), these effects can be monitored with periodic tests to minimize the risks associated with the continuous use of Lithium.

In addition to the effects already mentioned, prolonged use of Lithium can cause a series of impacts on the nervous system. Guariento (2016) reports that neurological toxicity is one of the main risks associated with Lithium, due to its narrow therapeutic range. Symptoms such as lack of motor coordination, fine tremors, mental confusion and, in severe cases, seizures and coma, can occur if serum levels are not properly monitored. These symptoms are directly related to Lithium's ability to interfere with neuronal excitability and the conduction of nerve impulses (Guariento, 2016).

Lithium also has an influence on neurotransmitters, promoting mood stabilization by increasing serotonin synthesis and regulating its reuptake in synapses. However, it can reduce noradrenaline and dopamine levels, which can lead to chemical imbalances that result in depressive or manic symptoms (Guariento, 2016).

In addition, patients taking lithium may experience symptoms such as drowsiness, cognitive difficulties (memory and concentration problems) and fine tremors, which, although generally transient, can compromise adherence to treatment (Reis *et al.*, 2015).

Rubí-González *et al.* (2023) report dermatological side effects. Among the most common are the exacerbation or induction of psoriasis, which manifests itself in a way that is resistant to conventional treatments. Lithium can induce psoriasis in patients with no previous history or exacerbate pre-existing conditions, making it more resistant to conventional treatments such as corticosteroids and ultraviolet light therapy.

In addition, lithium-induced acne is frequent, especially in young patients, with lesions on the trunk and extremities. Rubí-González *et al.* (2023) describe that acne associated with lithium use is characterized by monomorphous papules and pustular lesions, with a higher incidence in men, due to the role of testosterone in the pathogenesis. Another observed side effect is alopecia, which can occur in up to 10% of patients. This manifestation is usually reversible after discontinuing treatment.

Although these effects are generally not serious, they can compromise adherence to treatment due to the aesthetic impact. Ferreira *et al.* (2017) also point out the importance of monitoring the adverse effects of Lithium, as conditions such as acne and alopecia can affect patients' adherence to treatment.

Monitoring these effects includes adjusting the dose of lithium and using dermatological treatments. Rico-Castrellón (2024), in this regard, highlights the importance of adjusting the dose to minimize adverse effects and ensure patients' therapeutic compliance.

FINAL CONSIDERATIONS

Just as dawn brings the hope of a new day after the darkness of night, Lithium has emerged as a promising and effective therapeutic solution for patients facing the emotional storms of bipolar disorder. Throughout this research, it has become clear that Lithium not only stabilizes extreme moods, preventing manic and depressive episodes, but also has a protective effect against the risk of suicide, one of the most worrying aspects of this disorder.

Lithium's efficacy, proven over decades of clinical use, is due to its mechanisms of action that promote neuroprotection and chemical stability in the brain. These mechanisms are comparable to the breaking of dark clouds, allowing light to shine through and brighten the lives of patients living with bipolar disorder. However, like any treatment, the

use of lithium presents challenges, especially in relation to its side effects and the need for continuous monitoring, aspects that can make it difficult for patients to adhere.

It is essential that new research continues to look for ways to optimize the use of Lithium for the purposes mentioned here, improving its safety and efficacy and thus offering an even more personalized treatment adapted to the needs of each patient.

In this way, Lithium remains a fundamental pillar in the management of bipolar disorder, being essential for transforming emotional storms into moments of stability and light. With continued advances in research and understanding of its mechanism, it is hoped that Lithium will continue to represent the dawn for many who face the difficulties of bipolar disorder, bringing not only symptom control, but also a significant improvement in patients' quality of life.

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