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# BIPOLAR DISORDER: RECENT ADVANCES IN PHARMACOLOGICAL AND PSYCHOTHERAPEUTIC TREATMENT

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**Abstract:** Bipolar disorder (BD) is a chronic and debilitating mental health condition characterized by alternating episodes of mania/hypomania and depression, with a high risk of comorbidities and suicide. Management of the disease is complex and multifaceted, requiring an integrated approach. This narrative review explores recent advances in treatment, highlighting pharmacotherapy as a central pillar. Lithium remains the gold standard treatment, with strong efficacy in acute mania and relapse prevention, complemented by other mood stabilizers (valproate) and atypical antipsychotics (quetiapine, lurasidone), the latter being crucial for the treatment of the challenging depressive phase. For severe or refractory cases, neuromodulation therapies such as electroconvulsive therapy (ECT) offer high efficacy. Essentially, psychotherapeutic interventions, such as cognitive-behavioral therapy (CBT) and family-focused therapy (FFT), are indispensable adjuvants for improving adherence, functionality, and preventing relapses. It is concluded that the best approach is a personalized and continuous combination of pharmacological and psychosocial strategies.

**Keywords:** Bipolar Disorder; Pharmacological Treatment; Lithium; Mood Stabilizers; Psychotherapy

## INTRODUCTION

Bipolar disorder (BD) is a common, chronic, and recurrent mental health condition characterized by episodes of elevated mood (mania or hypomania) and depression (Marzani et al., 2021). Affecting more than 1% of the global population, the disease has a significant debilitating impact, with high rates of comorbidities, including

anxiety disorders, substance use disorders, and chronic medical conditions (Marzani et al., 2021; Mutz, 2023). Suicide risk is a prominent concern, with about one-third of patients attempting suicide during their lifetime (Marzani et al., 2021). The management of BD is complex, as few therapeutic options have demonstrated efficacy in all phases of the disease—mania, depression, and mixed states—in addition to the maintenance phase (Mutz, 2023). The therapeutic approach is multifaceted and based on three main pillars: pharmacotherapy with mood stabilizers, psychotherapeutic interventions, and, in selected cases, neuromodulation therapies (Marzani et al., 2021; Mutz, 2023). The complexity of the clinical picture, especially in populations such as children and adolescents, requires a comprehensive and individualized therapeutic approach to improve long-term prognosis and functionality (Post et al., 2021).

## METHODOLOGY

This study consists of a narrative review of the literature, whose scope is to consolidate and critically evaluate current scientific evidence related to recent advances in the pharmacological and psychotherapeutic treatment of bipolar disorder. The bibliographic survey was conducted in the PubMed database, using the descriptors ‘Bipolar Disorder’, ‘Diagnosis’, and ‘Treatment’. These terms were combined using the Boolean operators AND and OR, following the terminology of Medical Subject Headings (MeSH). Publications from the last five years, available in full in Portuguese or English, that addressed the topic in a direct and y manner were selected. Studies that were not directly related to the central theme, duplicate publications, narrative reviews with

low methodological rigor, and articles not indexed in the database used were excluded. The selection of studies was conducted in two stages: screening of titles and abstracts, followed by evaluation of the full texts to confirm relevance. The information extracted was organized and presented in a descriptive manner.

## RESULTS AND DISCUSSION

The treatment of bipolar disorder (BD) is structured according to the phase of the disease (mania, depression, or maintenance) and aims not only at the remission of acute symptoms but also at the prevention of new recurrences, which occur in more than 70% of patients within five years (Marzani et al., 2021).

### Pharmacological Treatment

Pharmacotherapy is the basis of TB treatment, and its continuation for an indefinite period is recommended to minimize the risk of relapse (Marzani et al., 2021). Lithium, considered the gold standard treatment, has demonstrated robust efficacy in acute mania, including cases with psychotic symptoms, and is particularly effective in the prophylaxis of manic episodes (Fountoulakis et al., 2022). Its efficacy in preventing depressive episodes is less clear, although some studies suggest a positive effect (Fountoulakis et al., 2022). In children and adolescents, lithium also shows positive data for the treatment of acute mania and maintenance, with naturalistic follow-up studies suggesting better long-term outcomes compared to other mood stabilizers (Post et al., 2021).

In addition to lithium, other mood stabilizers, such as valproate and carbama-

zepine, and several atypical antipsychotics are first-line options (Marzani et al., 2021). For acute mania, valproate and some antipsychotics are effective as monotherapy, and the combination of lithium or valproate with an atypical antipsychotic is also a highly effective strategy (Marzani et al., 2021). The treatment of bipolar depression is particularly challenging; quetiapine and lurasidone (the latter in combination with lithium or valproate) are among the few options with robust evidence of efficacy (Marzani et al., 2021; Fountoulakis et al., 2022). Lurasidone has also been shown to be effective in bipolar depression in children and adolescents aged 10 to 17 years (Post et al., 2021). The use of antidepressants as monotherapy is contraindicated in type I BD and in episodes with mixed features, due to the risk of inducing mania (Marzani et al., 2021). In many cases, especially in the pediatric population, monotherapy is insufficient, and combination therapy is necessary to achieve mood stabilization (Post et al., 2021).

## Neuromodulation Therapies

For severe or refractory cases of TB, neuromodulation therapies are a valuable alternative. Electroconvulsive therapy (ECT) is highly effective for the treatment of acute mania and severe bipolar depression, including cases with psychotic symptoms or catatonia (Marzani et al., 2021; Mutz, 2023). Meta-analyses confirm remission rates of around 53% in bipolar depression, similar to those observed in unipolar depression (Mutz, 2023). Other brain stimulation techniques, such as transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS), are being rapidly researched. High-frequency TMS over the left dorsolateral prefrontal cortex shows

promise for bipolar depression, although the evidence base is still limited compared to ECT (Mutz, 2023). Invasive therapies, such as deep brain stimulation (DBS) and vagus nerve stimulation (VNS), are reserved for the most treatment-resistant patients due to their surgical nature (Mutz, 2023).

## Psychotherapeutic and Educational Approaches

Psychotherapy is an essential component that complements pharmacotherapy, improving treatment adherence and social functioning and reducing hospitalization and relapse rates (Marzani et al., 2021). Interventions such as basic psychoeducation and cognitive behavioral therapy (CBT) are evidence-based approaches (Marzani et al., 2021). In young people with BD or at risk for the disorder, Family Focused Therapy (FFT) has been shown to be highly effective, with meta-analyses documenting its benefits in stabilizing depression, reducing the risk of recurrence, and improving psychosocial functioning (Post et al., 2021). Educating patients and family members about the chronic nature of the disease, environmental triggers (such as changes in the sleep-wake cycle), and the importance of early intervention is critical for long-term management (Marzani et al., 2021).

## CONCLUSION

In summary, it is stated that bipolar affective disorder remains one of the greatest challenges in contemporary psychiatry, not only because of its chronic and recurrent nature, but also because of its multiple facets of manifestation in each patient (Marzani et al., 2021). From this perspective, pharmacological treatment remains a central strate-

gy, especially with lithium established as the gold standard, which is primarily effective in cases of acute mania and in preventing relapses (Fountoulakis et al., 2022). It should also be noted that the combination of mood stabilizers, atypical neuroleptics, and adjuvant therapies has proven effective in the face of the clinical complexity of the condition (Marzani et al., 2021; Fountoulakis et al., 2022). In light of these considerations, for the management of the depressive phase, evidence highlights the importance of therapeutic agents such as lurasidone and quetiapine, especially when combined with active ingredients such as lithium or valproate.

In this regard, it should be noted that in cases refractory to traditional pharmacological treatment, neuromodulation therapies—such as transcranial magnetic stimulation (TMS) and electroconvulsive therapy (ECT)—emerge as promising alternatives, with good efficacy and tolerability rates (Mutz, 2023). Furthermore, it is worth highlighting the crucial role that psychotherapeutic interventions play in treatment adherence, relapse prevention, and overall functional improvement of the patient, with the following interventions standing out: cognitive-behavioral therapy and family-focused therapy (Post et al., 2021).

Despite the progress achieved, gaps remain in clinical approaches, especially in the management of bipolar depression, in younger populations, and in the individualization of treatments based on biological markers and psychosocial factors (Salvi et al., 2021; Post et al., 2021). Finally, in this context, it is clear that the most promising path is the integration of pharmacological, psychosocial, and neurobiological strategies, combined with early detection and longitudinal follow-up, as an approach capable of

optimizing prognosis and reducing morbidity and mortality associated with bipolar affective disorder (Marzani et al., 2021; Fountoulakis et al., 2022; Mutz, 2023).

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