A survey on the management of bipolar disorders

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ABSTRACT — OBJECTIVE: *The aim of the study is to conduct a statistical survey among 49 psychiatrists in order to explore the most common pharmacological approaches used in clinical practice for the treatment of Bipolar Disorder (BD) and the occurrence and the management of the related unwanted effects.*

MATERIALS AND METHODS: *The survey was conducted by using a Google Form.*

RESULTS: *The collected results reveal that valproic acid is the most used treatment, aiming to stabilize patients' mood keeping it in a balanced range. However, this pharmacological therapy may expose patients to several adverse effects that can worsen their quality of life and adherence to the therapy.*

CONCLUSIONS: *Clinicians commonly use valproic acid in clinical practice and most of them do not intervene on the management of the related side effects, considering them as part of the therapy. Therefore, considering both the lack of strategies for counteracting adverse effects in medical practice and Myo-Inositol positive effect on reported pathological conditions, a concomitant supplementation with Myo-Inositol may be suggested in the management of these patients.*

KEYWORDS
Psychiatry, Bipolar disorder, Adverse effects, Mood stabilizers.

INTRODUCTION

Mood stabilizers and anticonvulsant drugs are the first line treatment in the management of chronic neuropathological conditions affecting brain functionality, including bipolar disorder (BD). Specifically, BD is a chronic psychiatric condition referred to a disorder of mood, characterized by extreme changes in energy levels and alternating episodes of mania and depression[1]. Considering the nature of the disorder, BD is a chronic condition with increasing disability and reduced quality of life (QoL) regarding both the affected patients and their relatives[2,3].

Notably, the pathogenesis of BD involves various biochemical and pathophysiological mechanisms, including the abnormal activation of the neuronal phosphoinositide signalling pathway[4]. This pathological condition is characterized by an excessive Inositol trisphosphate/Calcium signalling that drives the neuronal excitatory-inhibitory unbalance, which is involved in the firing of manic phases. Previous evidence indicated altered levels of inositol, especially Myo-Inositol (Myo-Ins), in the brain of BD patients: in detail, they reported significantly higher levels of Myo-Ins during the manic phase and significantly lower levels during the depressive one[5,6].

Consistent with these findings, drugs mostly used in BD, even though structurally dissimilar, exhibit as a common outcome the depletion of inositol in the central nervous system (CNS), thus reducing the overactive signalling involved in pathological mechanisms and giving rise to the "inositol depletion hypothesis"[7].

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Noteworthy, the administration of these medications is not devoid of risks and complications, and interestingly most of the adverse effects were associated with altered inositol metabolism in the involved peripheral tissues[8]. Such pathological effects include Polycystic Ovary syndrome (PCOS)[9], hypothyroidism[10,11], alopecia, hormonal, and metabolic imbalances, like weight gain, dyslipidaemia, hyperinsulinemia[12,13]. All these complications occurring during the pharmacological treatment, may worsen patients QoL and weaken their adherence to the therapy, leading to a poor compliance and a poor prognosis. The statistical survey investigates drugs mostly used in clinical practice in the management of BD and the occurrence of the most common side effects. The aim of this marketing research is to point out possible medical strategies to ameliorate the management of chronic neuropathological conditions, like bipolar disorder, and consequently to ensure patients the best possible QoL.

MATERIALS AND METHODS

The survey was performed by using Google Forms, in order to conduct a marketing research about the management of psychiatric conditions and the most common related side effects. We collected information from 49 psychiatrists, who could choose more than one answer, and were divided by age as follows: the 36.7% is 40-50 years old; 28.6%, 50-60 years old; 26.5%, 30-40 years old; 36.7%, 40-50 years old; and 8.2%, ≥ 61 years old. Most of the professionals, the 30.6%, included in the survey work in private clinics, while the 24.5% in hospitals and the 22.4% in both rehabilitation for addiction services and hospitals.

RESULTS

The conducted survey firstly revealed that psychiatrists mainly use valproic acid (VA) to treat extreme mood swings, including emotional highs (mania or hypomania) and lows (depression), associated with bipolar disorder in clinical practice. All the interviewed psychiatrists (100%) stated that they frequently prescribe valproic acid, with different ranges of dosage: the 59.2% of clinicians decides high dosage (≥750 mg), the 46.9% an intermediate dosage (500-750 mg), and the 8.2% a low dosage (<250 mg).

Regarding the frequency of medical examinations, about the half of clinicians (51%) reported that they visit patients every month, while the 30% of professionals reported medical checks every three months, ensuring a careful monitoring of patients.

Noteworthy, one of the questions of the survey evaluated the occurrence of the most common side effects following the administration of valproic acid. Only the 4% of psychiatrists do not observe any side effects related to VA therapy. The 91.8% of psychiatrists reported that patients exhibit weight gain as the most frequent side effect, the 26.5% observed alopecia, the 18.2% reported Polycystic Ovary Syndrome, the 6.1% reported acne. Only the 4% of psychiatrists reported adverse effects like drowsiness and psychomotor decline, and the 2% of them reported hypothyroidism. The 4.1% of professionals reported no side effects (Figure 1).

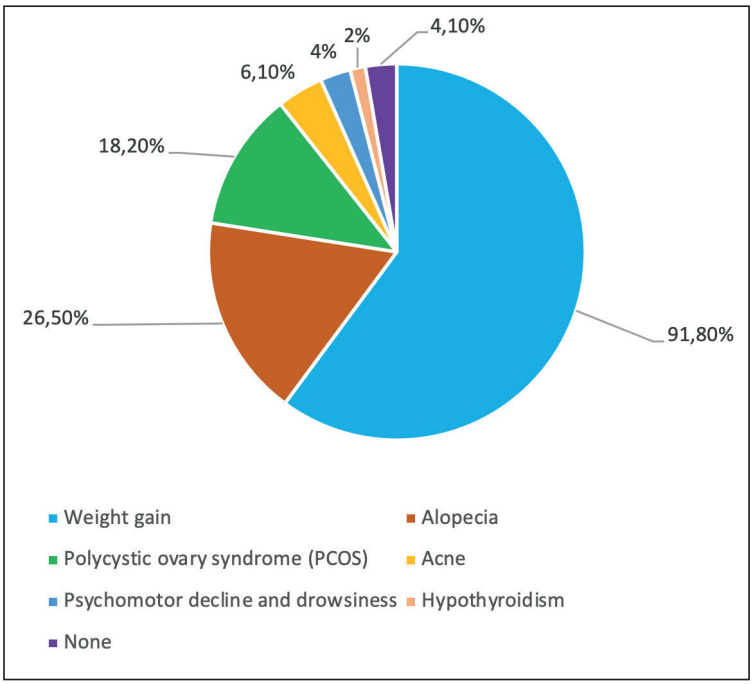

Figure 1. Valproic Acid Reported Side Effects.

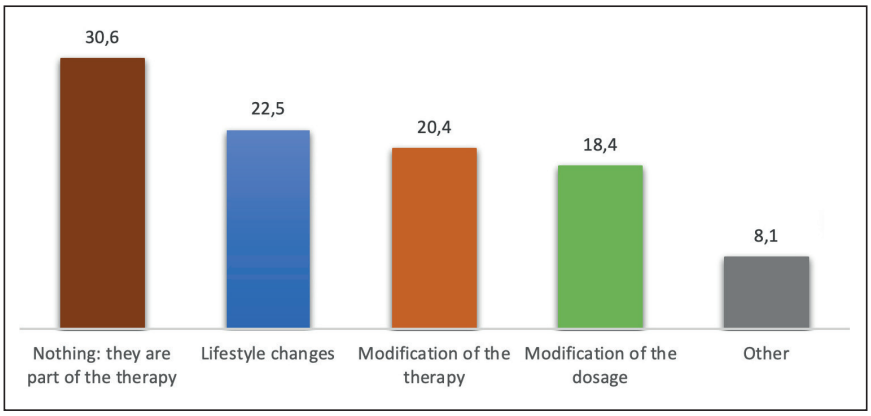

Figure 2. Valproic Acid Side effects management.

Furthermore, the survey inquired the management of the above-mentioned side effects (Figure 2). Notably, about the 18.4% of clinicians choose to modify the dosage, while the 20.4% of them modify the therapy by replacing valproic acid with alternative drugs, like lithium (51%) and atypical or second-generation drugs (40.8%). In addition, other psychiatrists recommend life-style changes including physical activity and an adequate diet (Figure 3). Noteworthy, a great portion of psychiatrists (30.6%) stated to not intervene in counteracting side effects, considering them as part of such therapies (Figure 2).

DISCUSSION

Several studies in literature reported that the main compounds with mood-stabilizing effects, approved especially for treating the manic phase, include lithium and anticonvulsants, such as valproate, carbamazepine, lamotrigine, along with some atypical antipsychotics, such as quetiapine, olanzapine, risperidone, ziprasidone and aripiprazole.

Notably, experimental and clinical evidence indicated that mood stabilizers and anticonvulsant drugs may expose patients to various side effects related to pathological conditions such as PCOS, hypothyroidism, hormonal and metabolic unbalances, including weight gain, hirsutism, dyslipidaemia[8-13]. Studies in patients taking valproic acid revealed that weight gain is one of the most common effects occurring in up to 50% of patients, followed by PCOS (0.5-4% of patients) and hypothyroidism in 25% of patients[8].

Our investigation among 49 psychiatrists pointed out that the most used drug in clinical practice is valproic acid for the treatment of bipolar disorders. The survey further confirmed that the administration of this drug is not devoid of risks and complications. Indeed, most of psychiatrists indicated weight gain, PCOS and alopecia as the most frequent side effects, while only a small portion of clinicians indicated hypothyroidism, drowsiness and psychomotor decline.

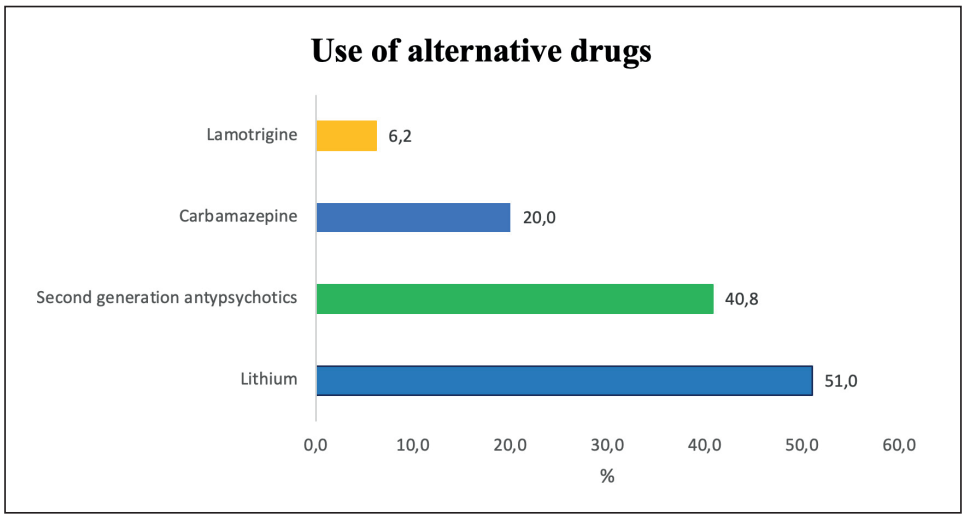

Figure 3. Use of alternative drugs.

Noteworthy, professionals do not intervene in the effort to counteract side effects accounting them as part of the therapy. For this reason, considering the chronic course of the disorder and the long-term therapies required[1-3] in BD patients, it is crucial to proper monitor related side effects in order to counteract, or altogether avoid them, improving patients' QoL.

Interestingly, the observed side effects were mostly associated with altered Inositol metabolism in the involved peripheral tissues. Notably, Sherman and colleagues reported that the Inositol depletion occurring in the CNS after mood stabilizer administration can reflect reduced Myo-Ins levels in peripheral tissues, such as kidney and testes[14], confirming the correlation between central and peripheral depletion of Myo-Ins.

In addition, several evidence reporting safety and beneficial effects of Myo-Ins administration in various pathological conditions previously described, including hypothyroidism[10], PCOS, metabolic and hormonal unbalances[9,12,13]. Furthermore, some studies indicated the positive effect of Myo-Ins administration on the adverse effects in patients taking mood stabilizers, without affecting the therapeutic central effect. For instance, studies on patients taking lithium and concomitantly exhibiting adverse effects such as polyuria and psoriasis[15-17], revealed that the administration of Myo-Ins in a controlled dosage (up to 6 grams/daily[16]) can improve such side effects without dampening the central therapeutic action. Therefore, considering that Myo-Ins poorly crosses the blood brain barrier[18] and considering its beneficial effects on the described pathological conditions, its administration in a controlled dosage may open the possibility to a concurrent supplementation with the pharmacological therapy, in order to counteract side effects and improve patients' QoL.

CONCLUSIONS

The survey conducted among psychiatrists pointed out that valproic acid is the most used drug to treat BD in clinical practice. Nevertheless, this pharmacological therapy may expose patients to various side effects, including weight gain, alopecia, PCOS, hypothyroidism. These conditions may worsen patients' adherence to the therapy and compromise quality of life of both patients and their relatives. However, to date clinicians do not intervene to counteract such side effects, they only attempt to change dosage or therapies, without a proper management of the related adverse effects.

For this reason, considering both the lack of strategies for counteracting adverse effects in medical practice and Myo-Ins positive effect on reported pathological conditions, a concomitant supplementation with Myo-Ins may be suggested in the management of these patients.

The presented survey gathered information on psychiatric clinical practice, with the aim to pave the way for new strategies that can ameliorate the management of chronic neuropathological conditions, like BD, and consequently ensure patients the best possible quality of life.

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Conflict of Interest:
All authors declare their conflict of interests as employees of companies, manufacturers of food supplements containing myo-inositol.

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