Pharmacological Management of Bipolar Disorder

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Abstract

Bipolar disorder is a mental pathology that has been known since ancient times and has its origin in the concept of “mania,” a term that comes from the Greek “µανία,” meaning “madness” or “frenzy”. Bipolar II is a history of at least one hypomanic episode plus at least one episode of major depression. Drug treatment for bipolar disorder has three symptom targets such as manic symptoms, mixed episodes, or depression and is usually given in stages. Lithium salts showed great efficacy in the treatment of manic disorder and they did so in a short period of time within several days. Lithium is the drug of choice in treating recurrent bipolar affective disorder (i.e., manic-depressive illness). Lithium was also relatively effective in treating manic manifestations in early dementia.

Keywords: Bipolar disorder; management; pharmacological

Introduction

Bipolar disorder is a mental pathology that has been known since ancient times and has its origin in the concept of “mania,” a term that comes from the Greek “µανία,” meaning “madness” or “frenzy” [1-2]. Bipolar disorder, largely due to its chronic and recurrent course, poses an important burden for the patient, the family and the society and its treatment is essential to avoid the main complications of the disease. In developed countries, bipolar disorder is ranked among the top 10 causes of disability. According to the World Health Organization (WHO), bipolar disorder is the fourth cause of neuropsychiatric disability in people aging 15 to 44 years. Additionally, the use of health resources that bipolar patients make is greater than that of patients with depressive or chronic medical conditions [3, 4]. Bipolar disorder is classically described as clinically significant episodes of depression and elevated mood (mania or hypomania) with intervening periods of normal mood (euthymia) [5, 6]. The substantial morbidity of bipolar disorder arises primarily from the depressive episodes, and there is frequent comorbidity with anxiety disorders and substance misuse [7, 8]. Based on American Psychiatric Association’s Diagnostic and Medical Manual of Mental Disorders, Fourth Edition –IV or DSM – IV: bipolar disorders classified as follows bipolar I have a history of at least one episode of mania. Nearly all patients with bipolar I disorder also have episodes of major depression, but these are not required to make the diagnosis; bipolar II is a history of at least one hypomanic episode plus at least one episode of major depression; bipolar disorder not otherwise specified is a bipolar features that do not meet criteria for bipolar I or II disorder, eg, a history of episodes of hypomania with no history of major depression. This disorder is sometimes called bipolar spectrum disorder; cyclothymic disorder is a mild episodes/chronic; rapid cycling is many cycles of mania and depression each year. Four or more episodes a year; schizoaffective are combinations of affective and schizophrenia; intermittent explosive disorder: marked by sudden, unpredictable acts of violent, aggressive behavior in otherwise normal persons; mixed states are the signs of depression and mania at the same time [5, 7]. The prevalence of morbidity from, and mortality and costs associated with bipolar disorder make its effective treatment and, ideally, prevention important goals within psychiatry [9, 10]. Drug treatment for bipolar disorder has three symptom targets such as manic symptoms, mixed episodes, or depression and is usually given in stages. In acute treatment, the objective is to resolve an episode that has already developed. In maintenance treatment, the objective is to delay the occurrence of future episodes, minimize the severity of episodes that do occur, and reduce the severity of symptoms between episodes [11-13].

Lithium: Lithium is coined from the Greek “lithos,” meaning stone. Chemically, lithium is the simplest drug among those used in psychiatric therapy, as it is the lightest metal in nature. Lithium salts showed great efficacy in the treatment of manic disorder and they did so in a short period of time within sev-
eral days. Lithium is the drug of choice in treating recurrent bipolar affective disorder (i.e., manic-depressive illness). Lithium was also relatively effective in treating manic manifestations in early dementia. Lithium is less effective in treatment of mixed and rapid cycling. Three of the six most agitated schizophrenic patients became eased and calm and were docile and treatable for the first time in years. All of them returned to their original state when lithium was stopped. The recommended therapeutic Lithium blood levels for the treatment of acute mania range from 0.6–1.2 mEq/L, whereas maintenance levels could be lower, ranging from 0.6 to 0.9 mEq/L. Levels higher than 1.2 mEq/L are potentially toxic. When treating a patient with lithium, creatinine clearance is regarded to be the most reliable marker of kidney function to take into consideration. The adverse effects of lithium therapy have two digestive system (nausea, vomiting, diarrhea, abdominal pain, etc.) and nervous system (tremors, dizziness, asthenia, depression, etc.) categories of side effects, which were disappeared quickly in 2 to 4 days) after lithium discontinuation; renal problems either acute or chronic; hypothyroidisms; cardiac problems. Drug-drug interactions: angiotensin converting enzyme inhibitors, loop diuretics, metronidazole and thiazides decrease lithium dose by 50%. If lithium coadministered with iodine salts perhaps escalated the risk of hypothyroidism. Sodium containing preparations, theophylline, chlorpromazine etc perhaps reduced the serum levels of lithium. If lithium administered coincidentally with sibutramine perhaps escalated the pitfall of serotonin syndrome [14-17].

Valproate: Valproic acid is FDA approved for the treatment of acute manic episodes. Patients respond relatively rapidly (within 1–2 weeks and often a few days). Valproate appears to have a more robust anti-manic effect than lithium in rapid cycling and mixed episodes. Therapeutic serum levels range between 50 and 150 mg/mL. Side effects of valproic acid are gastrointestinal effects, tremor, sedation, pancreatitis, liver toxicity, increased appetite, hallucinations, hyperammonemia, hepatotoxicity (fatal adverse effects), pancreatitis, blood dyscrasias, weight gain and polycystic ovarian syndrome. Drug-drug interactions: Rifampicin, phenytoin, phenobarbitone etc decreased valproic acid levels. Aspirin and felbamate increases the valproic acid levels [18, 21].

Carbamazepine: Carbamazepine is approved by the FDA only for the treatment of bipolar mania. The response rate against acute mania is close to 50% (similar to that of valproic). However, the response rate against bipolar depression appears to be lower (roughly 30% or less). Carbamazepine seems to be less effective in the prophylaxis against depression than against manic/mixed episodes and less effective than lithium. Carbamazepine has been shown to be effective in the treatment of manic-depressive illness and aggression due to dementia in the elderly. Adverse effects are dose-related and include double or blurred vision, dizziness, sedation, ataxia, agranulocytosis, aplastic anemia, hepatic failure, stevens-johnson syndrome, and diplopia, vertigo, gastrointestinal disturbances, cognitive impairment and hematological effects. Drug-drug interactions: Carbamazepine decreased the efficacy of oral contraceptives if given concurrently. Carbamazepine decreased the half-life of doxycycline. Carbamazepine reduces the tolerance to alcohol [22-25].

Lamotrigine: Lamotrigine, at a daily dosage of 50–200 mg may be effective in the treatment of acute bipolar depression but not mania. Treatment should be initiated slowly; 25 mg daily for the first 2 weeks and then 50 mg for another 2 weeks, followed by slow increases, in order to avoid a moderately high incidence of rash. It was also found to be effective in preventing relapse in a six-month study of rapid-cycling BD II patients, most of who suffered from recurrent depressions. Adverse reactions to lamotrigine can include a serious skin rash in a small percentage of patients, which if unchecked can progress into Stevens-Johnson syndrome and toxic epidermal necrosis; dizziness, leucopenia, headache. Drug-drug interactions: Enzyme inducing medications such as phenytoin, carbamazepine, phenobarbitone, rifampicin, etc enhanced the metabolism of lamotrigine. Valproic acid decreases the metabolism of lamotrigine [26-29].

Antipsychotics: First generation (typical) antipsychotics are considered to be the traditional first-line treatment for acute mania. Mostly haloperidol, have been used for long and are generally regarded to act faster than mood stabilizers. Haloperidol is highly binding to dopamine 2 receptors, then cause more extra pyramidal symptoms and higher incidence of tardive dyskinesia. Unlike First generation (typical) antipsychotics, second generation (atypical) antipsychotics do not induce depression. Olanzapine, risperidone, quetiapine, ziprasidone and aripiprazole have already been approved by the food and drug administration for the treatment of acute mania. Second generation (atypical) antipsychotics adverse drug reactions are more cognitive problems such as more sedation and more anti-cholinergic side effect; more cardiovascular side effect and other side effect [30-34].

Other agents such as antidepressants (currently, fluoxetine, as part of the fluoxetine plus olanzapine combination, is the only antidepressant medication officially approved by the food and drug administration for the treatment of bipolar depression) and lurasidone is the first antidepressants whose efficacy in bipolar disorder was studied in the treatment of the depressive phase exclusively) [35]; other modern antiepileptic agents such as gabapentin was one of the first third-generation antiepileptic drugs to be studied for bipolar disorder and as almost all of them, it was initially evaluated for the treatment of mania [36].

Conclusion

Bipolar disorder, largely due to its chronic and recurrent course, poses an important burden for the patient, the family and the society and its treatment is essential to avoid the main complications of the disease. In developed countries, bipolar disorder is ranked among the top 10 causes of disability. The prevalence of, morbidity from, and mortality and costs associated with bipolar disorder make its effective treatment and,
ideally, prevention important goals within psychiatry. Lithium is less effective in treatment of mixed and rapid cycling. Three of the six most agitated schizophrenic patients became eased and calm and were docile and treatable for the first time in years. All of them returned to their original state when lithium was stopped.

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