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Overview of Bipolar Disorder (Manic Depression) and Its Management Approaches

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Abstract: **This review aimed to focus in discussing the Bipolar disorder from different psychological aspects, but mainly emphasizing the proper treatment approaches of this disorder, in addition to diagnostic procedures that can be done to evaluate the Bipolar disorder. Comprehensive search of literature was performed using MEDLINE/PubMed and Google Scholar, and was restricted to studies published in the past up to the November, 2016. The search terms included "bipolar disorder," "mania," "bipolar depression," "mood stabilizer," "atypical antipsychotics," and "antidepressants," and "treatment," or "therapy." we included studies that focus on diagnosis, treatment, of bipolar disorder, articles were selected with restriction to English language and human subject's inclusion. References found in each study were manually searched for more relevant articles to be included in this review. Accurate medical diagnosis and prompt, appropriate treatment are presently our best wish for decreasing this disease problem. It is for that reason important that clinicians thoroughly screen depressed patients for bipolar disorder and understand confusing comorbid disorders, such as anxiety disorders and substance abuse. The possibility of manic episodes in undiagnosed bipolar disorder treated with antidepressant monotherapy must also be kept in mind, given that these episodes may assist point the clinician toward a right diagnosis. Since bipolar depression is often refractory to treatment, aggressive therapy might be required. The substantial residual disease morbidity even in greatly treated patients suggests that new agents and combinations of agents might be needed for the effective management of bipolar depression.**

Keywords: **Bipolar Disorder, Manic Depression, Psychological Aspects.**

1. INTRODUCTION

The concept of bipolar illness outgrew Emil Kraepelin's classification of manic depressive madness, which was postulated around completion of the 19th century. Descriptions of mad activity associated with the manic state can be found in the writings of Hippocrates and as far back as the ancient Egyptians. In 1957 Leonhard coined the term 'bipolar' for those patients with depression who likewise experienced mania [(1)]. Bipolar illness is a mental disorder characterized by significant shifts in state of mind, thinking, behavior, and energy, are a significant public health issue [(2,3)].

The combined frequency of bipolar I (episodes of mania and hypomania) and bipolar II (hypomania only) condition has normally been estimated to range roughly between 0.5% and 2% [(4,5,6)]. Nevertheless, a variety of detectives have actually recommended that bipolar affective disorder makes up a larger spectrum of conditions connected with scientifically substantial morbidity [(7,8)]. Lifetime prevalence of bipolar I disorder is 1% to 2% in both females and guys; frequency of bipolar II condition is at least 2% and may be undervalued due to the possibility of recall predisposition in reporting hypomania [(6,10)]. Quotes of the prevalence of bipolar illness not otherwise defined vary widely, but the overall lifetime prevalence of these 3 disorders is at least 2.4% to 6% [(6,10)].

Although such syndromes seem attenuated, they have a high risk of suicide attempts, comorbidity with stress and anxiety, impulse control and compound utilize disorders, and conversion to frank bipolar disorder [(11)], as well as similar degrees of role disability to bipolar I and II condition [(12)].

Depression is the most typical complaint of patients with bipolar state of mind disorders, and many of these patients are treated with antidepressants, which have actually not been found to be more efficient than placebo for bipolar depression [13,14]. The concern has been discussed, antidepressants appear to have the prospective to induce hypomania or mania and to increase the rate of reoccurrence of depression, especially if any recurring hypomanic symptoms are present [14,15]. It is frequently more effective to stabilize mood (ie, to prevent additional manic and depressive reoccurrences) than to continue antidepressant treatment for any particular depressive episode for too long.

This objective can be accomplished with mood stabilizers, which are defined as treatments that both deal with and avoid recurrences of mania and depression [16]. The gold standard state of mind stabilizer versus which other treatments are compared is lithium [16], which has advantages of daily dosing and a clear connection of serum level with clinical response. Nevertheless, lab tracking for hypothyroidism, hyperparathyroidism and possible nephropathy is necessary, and negative effects such as weight gain, cognitive impairment, tremor and gastrointestinal adverse effects are frequently bothersome [17].

This review aimed to focus in discussing the Bipolar disorder from different psychological aspects, but mainly emphasizing the proper treatment approaches of this disorder, in addition to diagnostic procedures that can be done to evaluate the Bipolar disorder.

2. METHODOLOGY

Comprehensive search of literature was performed using MEDLINE/PubMed and Google Scholar, and was restricted to studies published in the past up to the November, 2016. The search terms included “bipolar disorder,” “mania,” “bipolar depression,” “mood stabilizer,” “atypical antipsychotics,” and “antidepressants,” and “treatment,” or “therapy.” we included studies that focus on diagnosis, treatment, of bipolar disorder, articles were selected with restriction to English language and human subject’s inclusion. References found in each study were manually searched for more relevant articles to be included in this review.

3. RESULTS

Patients with bipolar illness have high rates of medical, psychiatric, and drug abuse disorders, which contribute to lowered life span and lower lifestyle [10]. A majority satisfy requirements for at least 1 other mental illness; stress and anxiety and drug abuse conditions are most common, with a 40% to 60% lifetime prevalence [18]. Compared to the basic population, patients with bipolar illness have greater rates of diabetes mellitus and liver and heart disease and experience increased special needs and death from these diseases [19,20].

- ***Etiology and Pathophysiology:***

There is not a single hypothesis that combines hereditary, biochemical, medicinal, anatomical, and sleep information on bipolar affective disorder [21]. Biochemical examinations are underway for transmitters (catecholamines, serotonin, gamma aminobutyric acid (GABA), glutamate and others), hormonal agents (brain-derived neurotrophic factor, thyroid and others), and steroids alone and in partnership. Imaging research studies, emerging throughout medication, may shed light [21].

Epidemiological evidence, particularly research studies of concurrence in identical and fraternal twins, indicates that affective conditions are heritable. For relative of bipolar probands, the morbid risk is between 2.9 and 14.5 percent for bipolar illness and 4.2 and 24.3 percent for unipolar disorder, depending on the diagnostic criteria used and the heterogeneity of the probands [22]. The degree to which bipolar I, bipolar II, hypomania, cyclothymia, and unipolar depression are unique or genetically related entities is unknown [21]. It stays unclear if state of mind disturbance (phenotype) is the best sign of a genetic etiology. Concerns of patients and their relatives can be dealt with through therapy.

A number of serotonin hypotheses have actually been proposed, in isolation, or in relationship to other systems. The "permissive hypothesis" of serotonin function states that low serotonergic function accounts for both manic and depressive states through defective dampening of other neurotransmitters (primarily norepinephrine and dopamine) [9]. Some utilize this as a description as to why some bipolar patients do better on such antidepressants, including unusual cases of mania that dissipate.

A wide variety of neuroanatomical and neuroimaging research studies are being performed to find out more about bipolar disorder [22]. Sores in the frontal and temporal lobes are most often associated with bipolar illness. Left-sided lesions have the tendency to be related to depression and right-sided sores with mania, though distinctions may be reversed in the posterior regions of the brain (e.g., the association of depression with right parietooccipital sores). No irregularities have actually been found regularly by means of computed tomography (CT) studies, though ventricular enhancement has been thought. Magnetic resonance imaging (MRI) research studies expose a boost in white matter strengths connected with bipolar illness and correlated with age [23], though the medical significance is unidentified. Overall, most functional imaging research studies (single-photon emission computer system tomography [SPECT] and positron emission tomography [ANIMAL] have actually kept in mind anterior and prefrontal paralimbic hypoactivity in bipolar depression, while preliminary studies of manic patients have yielded irregular findings [23].

- ***Diagnosis bipolar disorder:***

A diagnosis of bipolar disorder is obvious when a patient provides with florid mania but is challenging when the initial discussion includes depressive signs; research studies normally report that 50% or more of patients at first present with depression [24,25]. Mainly due to the fact that unipolar depression is more common than bipolar depression, and due to the fact that bipolar depression does not have pathognomonic functions, bipolar affective disorder is often incorrectly identified as major depressive condition (MDD) [1]. Amongst patients who are eventually detected with bipolar illness, roughly 70% apparently had an initial misdiagnosis and more than 33% stayed misdiagnosed for 10 years or more [26]. Delay in diagnosis is a particular issue in ladies with bipolar affective disorder type II, because the signs of hypomania may not be really obvious [27]. Moreover, misdiagnosis during the postpartum period is common; in a study of 56 women referred for postpartum depression, 54% were later rediagnosed with bipolar illness [28].

The manic and depressive signs required for the DSM diagnosis of disorders of the bipolar spectrum (bipolar I, bipolar II, bipolar illness NOS, and cyclothymic condition) are summarized in (**Figure 1**) [29,30]. All of these disorders are defined by the presence of manic (bipolar I and bipolar NOS) or hypomanic (bipolar II and cyclothymic) episodes. In addition, they are all usually associated with depressive episodes. Depressive symptoms are not needed for the diagnosis of bipolar I or bipolar NOS, they are still frequently observed in these patients. In the Stanley Foundation Bipolar Network, more than 50% of patients with bipolar illness I stated that depressive signs had actually been their very first bipolar symptoms [31]. Amongst bipolar I patients, 76% reported more than 4 episodes of depression throughout the course of their disease, and 44% reported more than 20 episodes of depression [31]. A research study in which bipolar patients were followed for a mean of 12.8 years found depression to be the primary symptom [32]. The major difference in between disorders of the bipolar spectrum and major depressive condition, then, is a history of hypomanic or manic signs.

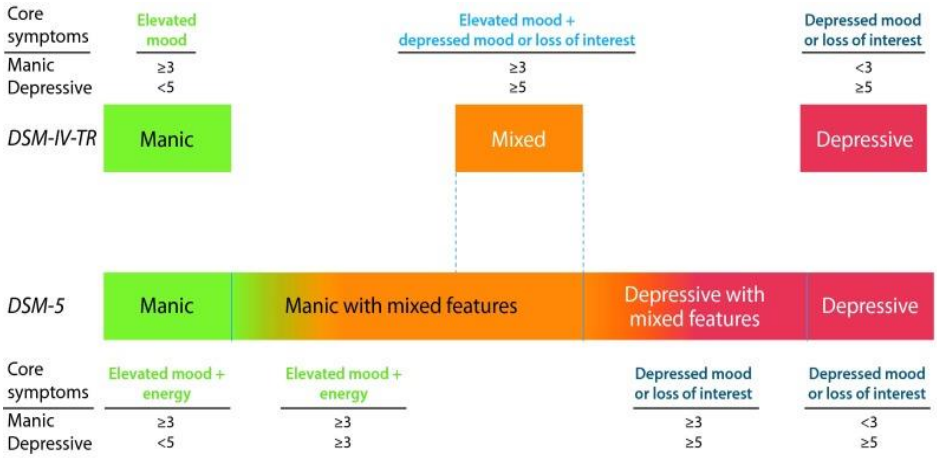

Figure 1: Conceptualization of Bipolar Mixed States in *DSM* [29]

Screening each patient for a history of mania and hypomania on their initial presentation of depressive signs is an early action towards the recognition of bipolar affective disorder [33]. Confirmed instruments that can be used consist of the Mood Disorder Questionnaire [34], the Composite International Diagnostic Interview [35] and the Primary Care Evaluation of Mental Disorders Patient Health Questionnaire [36]. Clinical screening can be supplemented with electronic health record (EHR)- based case findings, in which information gathered by self-report or a health care assistant is entered into the EHR and is evaluated for possible signs of bipolar affective disorder [37]. As a minimum of one-half of patients with

bipolar I condition and most patients with bipolar II disorder will at first present during a significant depressive episode, a mindful history to probe for previous manic or hypomanic signs is vital to guarantee an appropriate medical diagnosis [37]. To screen for historic manic or hypomanic symptoms that might otherwise be overlooked, the self-report Mood Disorders Questionnaire is a confirmed and beneficial instrument [38,39].

The initial evaluation should intend to gather laboratory and historical information that will help to dismiss other conditions and offer important information to ensure a safe and effective medication treatment strategy (**Table 1**) [40].

Table1: Initial Evaluation of Suspected Bipolar Disorder [4]

Tests to aid diagnosis	Thyroid function test, rapid plasma reagin test for syphilis, urine drug screen, B12 level, and careful history to screen for other secondary causes of mood symptoms	Consider neuroimaging for first episode, electroencephalogram if indicated, HIV test if applicable, and expanded toxicologic screen if suspicion of substance-induced episode is high
Tests to guide treatment and health maintenance	*General*: personal and family history of metabolic/cardiac disease; prior to lithium treatment: thyroid function test, complete blood count, urinalysis, electrocardiogram (≥ 40 y), electrolytes	Consider 24-hour urine creatinine for lithium treatment,evaluation for cataracts with quetiapine treatment, evaluation of menstrual irregularity with divalproex, initial screening for rash prior to lamotrigine treatment
	Prior to treatment with anticonvulsants: complete blood count, liver function, electrolytes, weight/body mass index	
	Prior to treatment with antipsychotics: screen for extrapyramidal/motor symptoms, metabolic syndrome (body mass index, waist circumference, blood pressure, lipid profile, fasting glucose)	

- ***Treatment approaches of Bipolar disorder:***

Treatment standards. The American Psychiatric Association (APA) established the Practice Guideline for the Treatment of Patients with Bipolar Disorder [29]. The concepts of psychiatric management are outlined in (**Table 2**) [29]. A healing alliance is crucial for understanding and handling the patient, identifying reoccurrence of health problem, improving adherence, and dealing with psychosocial stress factors. Patients require continuous education relating to the health problem, treatment options, and the impact of the disease on social and family relationships, vocation, and financial issues. Graphic representation of the health problem is a method to combine information (episode series, polarity, frequency, intensity, and relationship to stressors and treatment), inform the patient, and might help to establish an alliance [41]. For patients who are thinking about children or are pregnant, decision-making is finest done in the restorative relationship [42].

The Expert Consensus Guideline Series is another popular standard [43]. Medications may be functionally categorized as those who target mania, depression, mixed/cycling, sleep, and other signs. Levels of proof differ for all medications [44]. The 2005 CANMAT standards [45] (Canadian Network for Mood and Anxiety Treatments) are most equivalent to the Expert Consensus Guideline, and it advocates a chronic disease design incorporating patient, provider, and health delivery systems. Treatment selections are more based on effectiveness data than tolerability. The section for older grownups is considerably more in-depth compared to other standards.

Psychotherapeutic treatments, provided individually or through groups and households, are beneficial to nearly all patients with bipolar affective disorder and supply the context in which psychiatric management and pharmacotherapy work best [29]. Most patients struggle with psychosocial concerns (**Table 2**). Bipolar inpatients were surveyed about their informational needs in one research study, and they requested information about bipolar disorder, how to obtain support, how to manage symptoms (e.g., self-destructive ideation, anger), and ways to enhance social abilities [46]. Economic, social, and employment issues may happen for several years, even when patients do not suffer reoccurrence of health problem leading to hospitalization [47].

A summary of psychotherapeutic treatments exposes better outcomes and enhanced adherence to treatment [48]. Cognitive-behavioral, family-focused psychoeducation (likewise called behavioral family management), inpatient family, and group psychotherapy have actually been studied. Easy access to a primary nurse service provider increases outpatient utilization without increasing expenses [49].

Table 2: Summary of treatment guidelines for mood episodes in bipolar disorder [29,43,45]

EPISODE	APA [29]	CONSENSUS GUIDELINE [43]	CANMAT [45]	OTHER EVIDENCE
Mania - euphoric	Lithium	Traditional (non-AAP) MS: lithium or valproate	N/A	Lithium
Mania - mild or moderate	Lithium or valproate	Traditional (non-AAP) MS: lithium or valproate	N/A	Valproate and/or AAP(1)
Mania - severe	Valproate or lithium with AAP	Valproate and AAP	N/A	Valproate and/or AAP(1)
Mania - mixed	Valproate	Traditional and AAP	N/A	Valproate or AAP
Rapid cycling - depression	MS(1) and MS(2)	Lamotrigine or lamotrigine/ lithium	Lithium Lamotrigine Valproate	Lamotrigine
Rapid cycling-mania	MS(1) and MS(2)	Valproate or valproate/AAP	Lithium Lamotrigine Valproate	Valproate
Depression-mild or moderate (2)	Optimize MS	N/A	N/A	N/A
Depression-severe	MS(1) and SSRI, MS(2), or ECT	N/A	N/A	N/A

APA— American Psychiatric Association.

CANMAT—Canadian Network for Mood and Anxiety Treatments

AAP—atypical antipsychotic

MS—mood stabilizer

ECT—electroconvulsive therapy

1—Particularly if insomnia significant

2—If no mood stabilizer, initiate one

N/A—Not addressed

- ***Treatment of bipolar depression:***

The treatment of bipolar depression is a significant difficulty, with few treatments of proven efficacy and, in particular, considerable controversy about the role of antidepressant drugs. Authors of guidelines and agreement declarations on this topic often ponder why antidepressants are so frequently used regardless of the limited proof for effectiveness [50,51]. Until just recently, after the work of Emil Kraepelin, bipolar depressive episodes were considered phenomenologically and biologically just like unipolar depressive episodes. Even as late as the 1990s, inclusion and exclusion requirements in medical trials of antidepressants in patients with depressive disorder did not generally either select or stratify inning accordance with polarity. Earlier trials recommended that when given with antimanic treatment, selective serotonin reuptake inhibitor antidepressants were more reliable and no more likely to induce mania than placebo, and were less most likely to cause mania than tricyclic antidepressants [51]. In 2007, a big trial discovered no benefit associated with the

addition of paroxetine or bupropion to a mood stabilizer [52]; another reported that paroxetine was no better at achieving a durable healing than placebo [53].

The antiepileptic drug lamotrigine was examined in patients with bipolar depression after a scientific advantage was seen after treatment with the drug in patients with bipolar affective disorder [54]. A meta-analysis of private patient-level data from 5 trials of lamotrigine in bipolar depression reported a modest treatment impact; however, no one trial revealed statistically substantial advantages of treatment with lamotrigine in comparison with placebo. Therefore, the place of lamotrigine in intense treatment remains unsure [55].

Irregular antipsychotics have been examined in bipolar depression with variable outcomes [56]. Treatment with quetiapine causes more symptomatic enhancement in patients with bipolar depression than do lithium, placebo, and paroxetine [56]. Some evidence exists of a minimized risk of reoccurrence in patients who respond to acute-phase treatment and continue quetiapine rather than switch to placebo; hence, continuation could be of benefit in patients who can tolerate the drug's unfavorable results, including sedation and weight gain [57]. The fairly fast beginning of action of quetiapine is scientifically useful because it supplies clinicians and patients with a treatment that can be initiated early in the course of an aggravating depression in the same way that antipsychotics are utilized for emerging manic signs. Integrated olanzapine and fluoxetine results in more symptomatic enhancement than does olanzapine or placebo alone, which could suggest that fluoxetine is an efficient treatment of intense bipolar depression or that the combination of fluoxetine and olanzapine is synergistic [58].

4. CONCLUSION

Bipolar affective disorder is a long-lasting disease that is made complex by high comorbidity and risk of bad health results. The results showed that the presence of manic signs throughout depressive episodes was related to higher present and lifetime behavioral risk. Manic signs seem a dimensional element of bipolar depressive episodes, but might have a threshold of intensity related to increased impulsivity and associated behavioral threats. This might show a combination of depression with quality impulsivity. Depressive signs are an important component of bipolar disorder and are connected with minimized quality of life, impaired functioning, and increased death due to self-destructive acts. Accurate medical diagnosis and prompt, appropriate treatment are presently our best wish for decreasing this disease problem. It is for that reason important that clinicians thoroughly screen depressed patients for bipolar disorder and understand confusing comorbid disorders, such as anxiety disorders and substance abuse. The possibility of manic episodes in undiagnosed bipolar disorder treated with antidepressant monotherapy must also be kept in mind, given that these episodes may assist point the clinician toward a right diagnosis. Since bipolar depression is often refractory to treatment, aggressive therapy might be required. The substantial residual disease morbidity even in greatly treated patients suggests that new agents and combinations of agents might be needed for the effective management of bipolar depression.

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