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Bipolar Disorder: A Review

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Abstract

Bipolar Disorder (BD) is a chronic condition with periods of moderate to severe mood swings lasting for weeks or months. Mania escalates abnormal behavior, while depression is filled with thoughts of hopelessness. Unfortunately, studies have shown that individuals diagnosed with BD have higher illness severity than the general population, and there is no single factor associated with the cause of BD. Although studies have shown that BD is caused by many variables including the individuals brain structure, genes, family history which is not scientifically proven. Major barriers to BD treatment include individual adherence to treatment, family and community acceptance of the individual, resource availability, and provider/health care system barriers. However, the good news is that this disorder could be treated effectively with approved and evidence based pharmaceutical and non-pharmacological treatment modalities, couple with social, family, friends, and community support and tender loving care that is free of stigma. This is a review on bipolar disorder with current scholarly literature extracted from Medline, National Institute of Mental Health (NIMH), National Institute of Health (NIH), and other highly recognized journals. The data were analyzed and categorized based on bipolar background, prevalence, barriers to treatment and review in literature. Different types of bipolar disorders are defined, and multiple barriers preventing patients from receiving effective mental health treatment are highlighted. The manuscript concluded with the implications of this review to the nurse practitioners. It is important to note that this review has confirmed that there are gaps in knowledge on the part of the health care providers, including the psychiatrists. Health care providers need to update their knowledge on the current research, for them to deliver appropriate and effective treatment to their patients, improve their provider-client relationships, and enhance treatment adherence on the part of their patients.

Keywords: Bipolar; Depression; Mania; Mood swings; Psychiatric disorder; Mental health

Introduction

Bipolar disease is a manic, depressive, and chronic illness characterized by mood swings, increased energy and activity levels, with difficulties to carry out daily living activities [1]. Bipolar diseases are classified into different types; however, all the types have been shown to have overt symptoms. The mood change (manic episode) ranges from periods of energized activities to very sad periods known as depressive level. The hypomanic episodes are characterized by mild manic periods. The bipolar types are named based on their distinct manifestations:

Bipolar type - I or (BP - I): This type lasts for no longer than seven days and is defined by manic episodes. At times, the manifested symptoms are so severe that the individual may require inpatient care and be hospitalized. Depressive episodes occur more often with type I and may last at least two weeks. Mixed features, which alternates between depression and manic episodes may be seen at the same time in these individuals.

Bipolar type - II or (BP - II): This second type presents with lesser symptoms of manic episodes than those experienced with type I. This type of BD is characterized by both depressive and hypomanic episodes.

Cyclothymic: Also known as, cyclothymia presents in adults and lasts for about two years. This type of BD is characterized by multiple periods of hypomanic and depressive episodes but lasts for only one year in children and adolescents. However, they are not

categorized as either hypomanic or depressive episodes because the symptoms do not correlate with any of the above types.

Other types: Specified, unspecified, and related bipolar disorders which are defined by symptoms that exclude those mentioned earlier.

All the aforementioned types, are generally characterized by periods of abnormal intense emotion, sleep patterns, level of activities and behavior which are significantly different from the typical moods and behaviors of an ordinary individual without BD. These extreme changes correlate with the corresponding mood episodes. However, BD could present even when there are no severe mood swings. Individuals with mild symptoms of hypomania may presume that nothing is wrong with them, but family members and friends around these individuals may first recognize their symptoms as possibly being BD. This is why a support system, especially from the family, is crucial and variable for that individual's adherent to treatment. Without proper treatment by a specialist, individuals with hypomania may progress to develop a severe form of mania or depressive episodes.

There is no single causative factor linked to BD, rather, it has been reported that multiple variables may contribute to the illness or increased chances being diagnosed of BD, including brain structures. People with certain genes may have a higher chance of developing bipolar disorder when compared to others with disparate genes. Studies have shown that individuals with the same genes tend to develop bipolar disease; however, this has not been proven scientifically as studies have that identical twins have not always develop the same disorder, although they share the same genes. Similarly, most people from the same family of bipolar disorder do not have the same ailment.

The first step to assist anyone with BD is to advise the person to seek for a correct diagnosis and effective treatment because individuals with this disorder could lead healthy and productive lives if they could consult a health care provider or a specialist who could correctly identify the disease. If the problem persists, the health care provider could work in collaboration with an experienced psychiatrist for a psychological evaluation and treatment. Anxiety disorders, and specific mental health ailments may mimic BD, and similar symptoms have been observed with individuals diagnosed with BD [2].

Prevalence

In the United States, 5.7 million (2.6%) adults are affected with bipolar disease, 83% classified as severe with 0.4% to 1.6% lifetime rating. Approximately 25% individuals with BD had attempted suicide (164 per 100,000 person-years), a rate that is 10% higher than that of the general population. LaBouff also noted that individuals diagnosed with BD have 20% increased chance of committing suicide when compared with the general population [3]. Bipolar is evenly distributed across gender line with a lifelong onset between ages 14 to 30 years and a peak incidence in 20s. This disorder is not completely treated even when succinct diagnosis of BD is confirmed, and the affected individuals usually do not receive the care they deserve [4]. Even now, some researchers are not current with the updated guideline.

In 2018, Belizario, Silva, and Lafer observed that the Manic Predominant Polarity (MPP) correlated with an increased number of psychotic symptoms, and overt patients' hospitalization when compared with Depressive Predominant Polarity, known as DPP and Indefinite Predominant Polarity abbreviated as IPP. These results were observed over the study period which lasted for seven years. In a similar concept, the investigators further observed that the initial PP showed a difference in association with 67% of participants who retained their PP at pre and post evaluation periods, confirming that PP is a critical identifier for foreseeing the trend of BD [5].

In a nationwide, non-interventional study, Renes, Regeer, Hoogendoorn, Nolen, and Kupka, surveyed eight hundred and thirty-nine patients diagnosed with BD or another mental disease bipolar type. The results revealed that the group with a guideline was rated highest for the treatment been associated with a participation of a psychiatrist (98%) and for pharmacotherapy adherent (96%). The groups with lower percentiles included those that were treated with supplement -73.5%, emergency plan usage - 0.6%, use of psychotherapy - 52.2%, group psychoeducation - 47.2%, and mood monitoring - 47%. The investigators concluded that diagnosis of BP-1 versus BD-II, bipolar NOS, or schizoaffective disorder strongly associated with better outcomes as evidenced in the study results [6].

In a study of four hundred and sixty-four (464) subjects, forty-seven (47%) participants with BD retained functional recoveries and remissions after sustained treatment with once a month aripiprazole, while 63% remained till the completion of the study. Individuals who adhered and were treated, retained their symptomatic and functional sustainability for approximately one year. The investigators concluded that more than 33% of patients retained functionality while using the rigid grading scale. This study concluded that the treatment was harmless and well accepted by BD-I patients while confirming the monthly treatment option as treatment of choice for sustainability in BD-I patients [7].

Health care providers Continuing Medical Education (CME) is critical in recognizing and treating BD. Unfortunately, studies have revealed some knowledge deficits and competence in the assessment items used in the diagnosis and treatment of BD among health care providers. Correll, et al. [4] created a twenty-five-knowledge tool on adult patients' assessment. The study participants included 1,123 psychiatrists and 305 Primary Care Physicians (PCPs). Table 1 showed the outcome of their survey after the data was analyzed.

Assessment Item	Psychiatrists	PCPs
Correct use of a specific screening tool	43%	36%
Specific tool could improve the identification of BD in patients with depression	64%	51%
Most critical symptoms specific to the diagnosis of BD	76%	43%
Laboratory testing to rule out other causes for mood symptoms	52%	46%
Diagnosis of BD - I is strongly based on variation levels in activity, energy, and mood	73-75%	73-75%
Oral aripiprazole is not an approved SGA by FDA, for the maintenance of BD - I treatment	87%	76%
Aripiprazole monohydrate and risperidone microspheres are recommended to be used alone with BD – 1	19%	20%
According to guidelines, Lithium is the initial recommended medicine for BD - 1 maintenance	N/A	76%

Table 1: Knowledge gaps between the Psychiatrists and Primary Care Providers in BD treatment [4] Source: Correll, et al. (2019).

Available Resources

Many resources are available for individuals or families of individuals with BD, both online and otherwise, with medication side effects services by the federal government event reporting program. A report could be made on the website. Individuals and health care providers may also forward reports including basic information about medications or visit the National Institute of Mental Health webpage for the most up-to-date information on medications, side effects, and warnings. According to NIMH, National Institute of Health: "A family health care provider is a great resource and is considered the initial step in searching for assistance. In addition, the NIMH's help desk is also available for mental health information and resources are available online. A number to call for National Suicide Prevention Lifeline is available online as well. This hotline access is available round the clock, every day in a week to anyone and there is an assurance that all calls are kept confidential. Resources are available either for public data on psychiatric health or to locate rural services, or a number to call specific government agencies. Treatment and referrals helpline are available any time. The agency's website also has other tools and service locator that could search and identify treatment centers using the individual information, if needed." [1].

Barriers that Impede the Health of Individuals with Bipolar Disorder

There are multiple barriers to receiving effective mental health treatment. Combinations of variables affect the health of individuals who are diagnosed with BD. In 2001, Miller and colleague documented that individual with mental disorders, more especially the suicide victims have more difficulties in getting needed care when compared to individuals who died from other causes [8]. This finding is critical because it reveals why suicide could not be detected and prevented with adequate diagnosis and treatment before action is taken. It is also important to know that this finding is an awareness to enable a broader perspective of barriers to focus not only on suicidality but on risk factors and treatments as these two are intertwined.

Unfortunately, the barriers cannot be prevented in isolation, as these factors usually interact with and strengthen other potential barriers. According to LaBouff [3], the three major difficult barriers in BD afflicted individuals continuing treatments include the following:

Individual Barriers: This deals with the psychological barriers and knowledge deficit about the BD compounded with other physical and behavioral health. The investigator reported that psychological concerns are important variables of stigma. This is because mental diseases, be it mild, moderate or severe are still looked upon as something that are not diseases like cancer or heart disease, hence the fear. The individual would not like to be identified as an outcast, and as such, they tried as much as possible to blend in as though nothing is wrong with them, including not taking their medicines as prescribed. Unfortunately, lack of knowledge and education about mental illness is a huge barrier in treating individuals with BD effectively. Education is a very important variable in treating this disorder because prescribing the medicines without the patient knowing what the medications are for, their side effects, and adverse effects would not give this individual the motivation to adhere and follow up with the health care provider's instructions as required.

Family/Community Barriers: Family members, friends, and co-workers are usually at lost as these individuals are not provided with the means and resources that are available in the community to assist with patience adherence to treatment. Even when such resources are available, the tendency of ostracizing the BD patients is high. At times, family members knowledge deficit makes it impossible for these individual to choose to continue living as they are termed to be lazy, stupid and that it is all in their head. It has been reported that individuals who do not have social support and other required resources frequent the hospitals and have longer episodes and worse symptoms than their counterparts. With such barriers, individuals with BD may be frustrated and therefore may not adhere to effective treatment.

Health Provider/Health Care System: Unfortunately, many individuals with BD do not have health insurance, hence they rely

on the community health care services if fortunate enough to have them, as most health centers have decreases staff sustainability, resulting in disjointed treatment and decreased care for this special group, who need it most for sustainability. Unfortunately, there is always strained relationship with this population and their health providers, in these settings. This is due to the fact that patients have limited interactions with their health care providers, for effective treatment. In addition, the scheduling is mainly focused on medication management without any thorough assessment and patient education, to identify other comorbidities for effective referrals and treatments.

Review of the Literature

BD is a mental disease associated with mood swings and familial tendencies. The severity is believed to be genetic and systematically paralleled with circadian rhythms [9].

In 2019, Sayad, et al. worked on a comparative study using four different genes found in the blood of patients diagnosed with BD and healthy subjects. The study includes BD pathogenesis and their usage as biomarkers for patients suffering with the disease. The investigators reported that gene-4 yielded a better result in the differentiation of disease status between the study participants. However, gene-3 was identified to have the best sensitivity value, gene-4 had the best specificity values, while an enhanced diagnostic tool was enhanced with the combination of the four genes. This result concluded that genes have important role in the development of BD and could be used as identifier for BD [10].

According to King, et al. impairment in Bipolar type-I (BP-I) has been consistently found in the function, memory, and attention sections of the brain. No difference was found among BD-I and BD-II, in specific samples. Conversely, studies have shown that patients who experience both major depressive episodes and subthreshold states (SBD) showed the same profiles to BD - II and are found only in depressed state. However, SBD performed much better than both major depressive disorders and healthy controls in a euthymic sample. The investigators recommended further research on the behavioral state, method of patient selection, and brain testing [11].

Other research investigators have hypothesized that BD patients who are Lithium-Responsive (Li-R) showed specific results in different circadian rhythms when compared to those who are Lithium Non-Responsive (Li-NR). The results may have confirmed that circadian rhythms played a role in lithium sensitivity during the maintenance periods of BD [12]. The investigation showed that Li-Rs cells exhibited a shorter circadian period, which correlates between period and phase, and period shortening effects of lithium. These results suggested that similar genetic differences in the IP_3 signaling pathway may have resulted in some differences observed in the lithium effects on a specific rhythm [12].

In a similar study, it was shown that while planned social therapy, especially the rhythm treatments are useful for bipolar depression, non-structured psychosocial or pharmacological intervention have been shown to be just as efficacious. According to Gold and Kinrys, Lithium addresses circadian dysfunction in BD using color coded tools. The investigators documented that blue-blocking therapy are more effective for mania, while midday bright light is more suitable for depressed mode [2]. However, it is important to note that in contrast to pharmacotherapy, psychosocial treatments have limitations for implementation in everyday clinical practice in BD. Hence, a need for more effective non-pharmacological guideline recommendations for individuals with BD [6].

According to Adis medical, it is concerning that 60% of individuals with BD are not adherence to their medications even after it has been established that BD could be successfully sustained with other psychiatric medications and non-pharmacological treatments. Hence, barriers to medication adherence by patients could be decreased at all levels. Effective treatment with psychosocial and medication-related interventions are possible once the barriers to treatment are identified. This could also be used to enhance future medication adherence and treatment outcome [13].

In 2002, the Institute of Medicine outlined nine barriers to effective treatment and intervention of BD suicidal rate. The results showed that, in United States, more that 90% of individuals who completed suicide were diagnosable of mental disorder. Unfortunately, only about 50% of the individuals were diagnosed and treated appropriately [14].

Pharmacological and Non-Pharmacological Treatments

Pharmacological

There are different kinds of medicines which may assist individuals with BD in controlling their symptoms. These individuals are able to try different medicines before they could identify the ones that work best for them. The antipsychotic medicines are chlorpromazine, haloperidol, perphenazine, and fluphenazine. These are known as the first-generation medicines. While risperidone, olanzapine, quetiapine, ziprasidone, aripiprazole, paliperidone, lurasidone are referred as the second-generation antipsychotic medicines. Antidepressants and sedatives are prescribed as well. To prevent affective episodes, patients with BD are usually treated with mood stabilizers which included substances such as lithium, valproic acid, lamotrigine, and carbamazepine. Considerations are also given to the second-generation antipsychotics in pharmacological treatment. In one of their study, Hamms, et al. [12] reported on the lithium-induced neurogenesis. The results showed that the osmotic and physical effects of lithium could explain the volume changes in BD human brain. The investigators concluded that lithium spectroscopy, the pharmacokinetic differences between remitted and non-remitted bipolar patients may be future clinical research opportunities.

According to Reus [15], BD treatment could be categorized into acute and chronic. For clarity, the author of this paper would tabulate these medicines into acute and chronic by type, recommended medicines and comment as depicted in Table 2 and 3:

BD Type	Recommended Medicines/Dosages	Comment
Acute mania and mixed states	**First-line agents:** 1. Lithium 1500-1800 milligram per day 2. Valproate 1000-1500 milligram per day (50-125 nanogram per milliliter), 3. Carbamazepine 600-800 milligram per day (4-12 micrograms per milliliter), 4. Oxcarbazepine 900-2400 milligram per day, Olanzapine 10-20 milligram per day, Risperidone 2-4 milligram per day, 5. Quetiapine 350-800 milligram per day, Ziprasidone 80-120 milligram per day, Asenapine 10-20 milligram per day, or Aripiprazole 10-30 milligram per day.	"Treatment-resistant cases may respond to varying combinations of these agents or to the addition of clozapine"
Mania	Adjuncts to acute: Benzodiazepines. Lorazepam 1-2 milligram every four hours Clonazepam 1-2 milligram every four hours	The traditional antidepressants have been shown to enhance manic symptoms and increased mania in mixed episodes.
Bipolar depression	**First-line options:** lithium, lurasidone, and others	"Off-label agents with possible efficacy include modafinil, pramipexole, and intravenous ketamine."

Table 2: Acute Treatment of Bipolar Disorder by types, recommended medicines and comment [15].

BD Type	Recommended Medication	Comment
Mania	Best agents for prophylaxis: Lithium, quetiapine, aripiprazole, and olanzapine (valproate, carbamazepine/oxcarbazepine possibly beneficial)	1. "The goal of long-term treatment is to prevent of relapse or episode recurrence"
Depression	Used best as prophylaxis: Examples of the medicines include Lamotrigine and lithium	The advantages and disadvantages of the atypical antipsychotics and traditional mood stabilizers in BD sustainability is unclear
All	Long-term use of antidepressants may destabilize the patients and results into increased and frequent relapses. At times depression may outweighs mania as most severe over the life span.	"Bipolar disorder accounts for 7% of all disease-related disability-adjusted life years"

Table 3: Chronic Treatment of Bipolar Disorders by type and medications with comment [15] Source: Reus VI: Ferris Clinical Advisor (2019).

Non-Pharmacological Treatment

Electroconvulsive Therapy (ECT): With the ECT, it is very important to note that all medication management's method must be discussed with the individual's health care provider before initiation of such therapies. ECT is a treatment modality that could be used in place of other unsuccessful non-pharmacological treatments, pregnancy inclusive. Like any other treatment modality, ECT comes with limited side effects and memory loss. Individuals with side effects and adverse effects are encouraged to report such signs and symptoms to the health care provider immediately, to prevent further complications.

Psychotherapy has been shown to be effective if properly planned and executed with medication use. It could be used for individuals with BD when structured and used consistently and may be available in community health centers. Psychotherapy services that are available to BD individuals could be presented as support system, health education, and guidance. Other effective therapies are available for these individuals and their families. These psychotherapy modalities could also be found on the NIH psychotherapies webpage.

Use of Chart, known as life chart is used for documenting records of everyday symptoms and may assist individuals and their health care providers to track and manage their BD most effectively. Some individuals still experience episodes even with proper treatment management. Treatments could be more effective when the individual and the health care provider work closely together and establish a relationship which would make discussion more open for concerns and choices without any fear of been stigmatized.

Nurse Practitioners Implication for Care

It is very important for nurse practitioners to note that individuals with BD usually seek assistance when they are in a depressive mood than when experiencing mania or hypomania. Nurse practitioners should obtain complete medical and family history in order to ensure that individuals with BD are not mistakenly diagnosed with major depression. Complete family history is very critical, because individuals who have only depression do not experience mania, although, these individuals may simultaneously exhibit manic symptoms.

Nurse Practitioners (NPs) as health educators, especially those who specialized in psychiatry, should be aware of these differences. When collaborating with other specialists, the NPs are to learn new information from evidenced based studies, especially with the current genomic diagnosis in mental health, to enable them assist scientists better understand the clinical side of the BD, in order to deliver a disease specific treatment. This would help decrease the emergency room overload, with patients who are experiencing emergent BD symptoms. Unfortunately, these individuals would not know how to handle these abrupt symptoms except going to the emergency room for help. Nurse practitioners should also be involved with genomics typing for their patients who may present to their clinic with BD episodes. This would enable them to narrow down the symptoms and identify medications that works best for such episodes.

Nurse practitioners must make time to educate their patients who have BD. Patients should be encouraged to always talk to their psychiatrics and pharmacists to better understand the medicines' indications and side effects. They should be taught how to report any concerns about side effects to their health care providers right away as the medicines may be discontinued, changed to another dose or to a different medication. It is imperative that patients should be encouraged to avoid stopping a medication without talking to their health care providers first, as suddenly stopping a medication abruptly may results into severe symptoms. With no exceptions, all prescriptions in patients' possessions should be made known to the health care provider because taken some of these medicines with supplements may cause undesirable adverse effects.

Conclusion

In conclusion, as health care providers and educators, nurse practitioners have crucial role to play for mental health and suicidal patients in getting appropriate help immediately, by encouraging the individuals at risk to get help right away, or by their calling a specialist. Nurse practitioners should encourage this population to call their psychiatrist or personal health care provider, call 911 or go to the nearest hospital. The families should be part of the collaborative care team, and they should be encouraged to look after their love ones and never allow a suicidal individual to be alone. It is imperative that all harmful objects, firearms, and medications should be out of reach for at risk individuals.

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