Treatment and Diagnosis of Bipolar Disorder

By

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Declaration

It is hereby declared that

1. The thesis submitted is my/our own original work while completing degree at Brac University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
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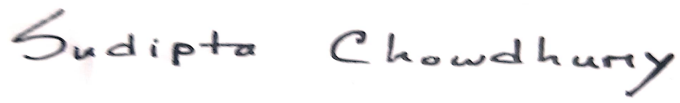

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Approval

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Ethics Statement

The study does not involve any kind of animal and human trial.

Abstract

Bipolar disorder (BD) is of a big concern to the world not only for the level of disability it can cause but also the increase of prevalence that has been observed in recent times. It is a kind of disease that often gets misdiagnosed and seldom reported in lower income countries due to the stigma it carries and lack of knowledge. The pathophysiology of BD is still unclear and a few effective treatment methods are available. The purpose of this review is to discuss the diagnosis and treatment methods currently available and mention some of the methods which have potential and should be further researched on.

Keywords: Bipolar Disorder, Borderline Personality Disorder, Attention Deficit/Hyperactivity Disorder, Lithium, Sodium Valproate, Atypical Antipsychotics, Conventional Antidepressants, Psychoeducation, Electro Convulsive Therapy, Benzodiazepine

Dedication

Dedicated to my parents.

Acknowledgement

With utmost respect, I would like to extend my heartfelt gratitude to all the people who have directly or indirectly helped me to complete of this paper. I am grateful to my supervisor for his patience, guidance and suggestions without which I would not have been able to complete this paper. Last but not the least, I would like to thank my family and friends for their undying love and support.

Table of Contents

List of Tables

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List of Acronyms

BD	Bipolar Disorder
BPD	Borderline Personality Disorder
ADHD	Attention Deficit/Hyperactivity Disorder
APA	American Psychiatric Association
SSRI	Selective Serotonin Reuptake Inhibitor
ECT	Electro Convulsive Therapy

Chapter 1

Introduction

How would you treat a person whose mood frequently shifts from extremely happy to severe sadness? While this is not a desirable trait to get included in a social circle, the actions might be a consequence of a condition rather than a choice. Bi polar disorder or BD is a condition which is considered as one of the most dangerous psychiatric disorders due to the extent of disability it causes to the patients and the suicide tendency it carries (Alda & Manchia, 2018). Patients with this condition undergoes severe manic and depressive episodes. The term bipolar was used for the first time in 1957 and was officially appropriated at 1980 due to the polarizing nature of the condition (Phillips & Kupfer, 2013).

The highest lifetime rate of bipolar disorder can be seen in United States which is 4.4%, and India has the lowest, with 0.1%. However, lack of reporting might be the reason behind the rate being so low as there are cultures where mental health problem is perceived as taboo. Studies show less than half of the patients get treatment from mental health professional and only a quarter of those happens in low income countries (Gardner, 2011).

Regardless of the variation in reports in different regions, this condition can cause severe problem and impairment by destroying a patient's social and personal relations. A patient with this condition is more likely to become a drug addict or commit suicide. This is why there should be more research and study regarding this condition.

1.1 BD and its type

BD is of 2 types based on Diagnostics and Statistical Manual 5(DSM 5). They are type I and type II.

Mania is an abnormally heightened psychological state where patients feel exceptional energy, restlessness and euphoria which in turn results in poor sleep, trouble concentrating and risky behavior. Hypo mania is a milder form of mania and depression is the complete opposite where patients experience extended period of extreme sadness and hopelessness.

A patient will be diagnosed with type I bipolar disorder if he experiences at least one manic episode and may or may not experience a major depressive episode. However, for type II bipolar disorder diagnosis, patient must experience a hypomanic episode and a major depressive episode lasting for no less than two weeks. In this condition, depression is the dominant state which is why type II bipolar disorder is often misdiagnosed with depression (Maassen et al., 2018).

1.1.1 Causes of BD

It is not clear what precisely causes BD. However, imbalance of neurotransmitters and hormones as well as abnormal physical characteristics of brain may be one of the causes. Moreover, a person is more likely to develop this condition if his parents or siblings have it indicating genetic reason. Furthermore, life events such as childhood abuse, severe stress, drug abuse, very upsetting experience etc. may cause BD (Hilty et al., 2006).

1.2 Prevalence of BD

In recent years, the rapid growth of mental health problem has been paralleled by prevalence of bipolar disorder. According to a survey, 32.7 million cases of bipolar disorder existed in 1990 (Ferrari et al., 2016). By 2013 the number has escalated to 48.8 million which is a 49.1% increase in prevalent cases. In Bangladesh, the prevalence is easy to miss as the awareness of BD is very low. A survey was done in Narail district of Bangladesh to assess the level of awareness regarding Mental Health Condition (MHC). Among 2425 participants, only 17 were fairly aware and 1365 participants had no idea about it. The awareness of depression, anxiety and psychosis was found to be 8.5%, 6.2% and 3.55 in order with the least awareness observed with Bi polar disorder which is 3.3% (Uddin et al., 2019).

A survey was conducted in Rajshahi where 279 married women were diagnosed for bi polar disorder. The study concluded that 2.5 % had BD and 7.2% cases were determined as probable case of BD. In comparison, 11 countries of America, Europe and Asia has prevalence of 2.4%, England has 2.0%, Canada has 2.2% and Singapore has 1.2%.

However, neighboring countries like India and Pakistan has an estimated prevalence of 8.6% and 14.3% in order (Abdul Wadood et al., 2020).

1.3 Pathophysiology of BD

The exact mechanism that leads to bipolar disorder is not clear. However, MRI studies have indicated structural and functional abnormality at the pre frontal cortex of bipolar disorder patients. A smaller left prefrontal grey matter volume as well as smaller right prefrontal grey matter volume was observed in patents with BD compared to a healthy person(López-Larson et al., 2002).

1.4 Methodology

All the information to write this review has been found in google scholar and pubmed. All the articles were acquired in full text, evaluated and reviewed.

Chapter 2

Diagnosis of bipolar disorder

One of the reasons it is difficult to diagnose bipolar disorder is that it requires extensive and detailed information gathering. It is important to understand the relationship between the personality of the patient and the condition itself. Moreover, gathering accurate information based on which the assessment is done can be very challenging if the patient is not cooperative. Furthermore, BD shares a lot of similarities with some other conditions making it difficult to distinguish (Hilty et al., 2006).

2.1 Diagnosis criteria

A healthcare team with adequate knowledge of BD is required for diagnosis. Only after a detailed history of manic or hypomanic and depressive episodes has been acquired, the clinical assessment should be done. Also, history of any prior drug abuse and history of this condition or similar condition in family members must be obtained beforehand. However, screening tool can be a useful asset. The most commonly used screening tools is Mood Disorder Questionnaire (Hilty et al., 2006).

There are multiple guidelines available for treating the different episodes of BD. APA(American Psychiatric Association) and Expert Consensus Guideline series are very well received guidelines (Hilty et al., 2006).

Table 1: Comparison of APA and Expert Consensus Guideline for different episodes of BD

Episode	APA	Expert Consensus
Euphoric mania	Lithium	Lithium/Valproate
Mild or moderate mania	Lithium/Valproate	Lithium/Valproate
Severe mania	Valproate/lithium + Antipsychotic	Valproate + Antipsychotic
Mixed mania	Valproate	Valproate/lithium + Antipsychotic
Rapid cycling mania and depression	Mood stabilizer	Lamotrigine Antipsychotic
Mild or moderate depression	Optimized mood stabilizer	Not available
Severe depression	SSRI Mood stabilizer ECT	Not available

Based on the clinical interview, the treatment trajectory and medication which might give optimum result is decided. Throughout the treatment, it is very important to gain the patients trust and make sure to identify any suicidal risk of the patient.

2.2 Difficulty Diagnosing

Patients with BD are often misdiagnosed with other psychiatric conditions. According to a study, only around 20% of patients with BD gets accurate diagnosis within the first year of seeking help and the average time it takes for BD to get diagnosed from the onset is 5-10 years (Phillips & Kupfer, 2013). What makes it so difficult to diagnose? The answer lies with the similarity is shares with conditions like BPD and ADHD.

2.2.1 BPD

Borderline Personality Disorder (BPD) is a condition where patients experience a frequent obdurate pattern of thoughts and sentiment which can sabotage a patients day to day life (Paris & Black, 2015). In other word, it is a condition in which patients are too sensitive to the way they are treated by other people. In a positive circumstance, a person with Borderline may feel overly enthusiastic, happy and loving. However, in an opposite scenario, the person may feel overly negative emotions like feeling extreme humiliation in a mildly embarrassing situation. Because of the mood swings patients with BPD is often misdiagnosed with BD and vice versa.

It is easier to distinguish BD I from BPD. Distinguishing BD II from borderline requires proper focus in specific area.

To begin with, a patient with BD is hereditarily linked and likely to have a first degree relative with the same condition whereas that is not the case with BPD. Furthermore, a patient with BPD will show a distinct sensitivity towards criticism while a patient with BD won't exhibit similar distinct personality trait. Moreover, the onset of BPD is generally late teenage years but borderline doesn't have clear onset. Besides, a change in environment can change the mood of a patient with borderline while the mood remains the same in case of BPD. Also, distancing from parent is a more likely scenario in BPD than BD.

Finally, the episode of BD react well to mood stabilizer and antipsychotic drugs while a very poor response can be seen with BPD making it even more important to be able to distinguish between these two conditions during diagnosis (Bayes et al., 2019).

2.2.2 ADHD

ADHD or Attention Deficit/Hyperactivity Disorder is a mental disorder responsible for an above average level of impulsion and hyperactive behavior which often starts at childhood and retains with age (Thapar & Cooper, 2016). The symptom of ADHD includes short attention span, forgetting task, having difficulty sitting still for a long time, increased energy, disorganization, rapid speech etc. Some of the symptoms of this condition shares resemblance with BD often making it difficult to differentiate during diagnosis.

To begin with, onset of ADHD is in childhood in all the cases whereas it is rare to observe such early onset in case of BD. Also, depression is a prominent feature in BD while that is not the case with ADHD. Moreover, BD patients experience psychosis during manic episodes but patients with ADHD do not. Furthermore, no suicidal tendencies can be observed in patients with ADHD whereas patients with BD have high suicide risk. Usually, BD patients requires reduced amount of sleep while patients with ADHD will experience fatigue if they sleep less. Finally, pretentiousness is seen in patients with BD but not in patients with ADHD (Brus et al., 2014).

Chapter 3

Treatment of BD

Treatment of BD is determined based on the severity of the episodes. Although, the ultimate goal is full recovery, objectives are set according to the phase the patient is in. If a patient is having acute episodes, the primary goal is to reduce the symptoms. For maintenance treatment, the primary objective is to prevent the episodes from recuring (Mccormick et al., 2015). All in all, a combination of pharmacotherapy, psychotherapy and adjunctive care has been proven effective for treating BD.

3.1 Pharmacotherapy

Mood stabilizers, atypical antipsychotics and antidepressants are medications approved by the FDA to treat different phases of BD.

3.1.1 Mood Stabilizers

Mood stabilizers are medications used to treat sustained and intense mood shifts. Lithium and valproate are two of the most commonly used mood stabilizers for BD.

3.1.1.1 Lithium

Initially lithium was the only medication which proved useful in cases of BD. Compared to latest medicines it has shortcomings like it takes longer time to onset while treating acute mania, poor response against bi polar depression and scarce therapeutic window (Geddes et al., 2004). Despite the limitations, Lithium is still relevant in the treatment of BD because Lithium is very effective in stopping manic episodes from reoccurring and it is the only medicine found to reduce the tendency of suicide in BD patients (Mccormick et al., 2015). Two placebo controlled studies conclude that 49% acutely manic patients responded to Lithium compared to 25% to placebo (Fountoulakis & Vieta, 2008).

The general dose of lithium is 600 to 2400 mg per day to achieve a serum level of (0.8-1.2) microgram per ml. Side effects like obesity, cognitive complication, skin problem etc. are associated with lithium. Lithium can cause severe toxicity in case of overdose (Hilty et al., 2006).

3.1.1.2 Sodium Valproate

Sodium Valproate is the most widely used mood stabilizer. It has a faster onset of action compared to Lithium but the efficacy is not up to the mark when used as maintenance treatment for mania (Mccormick et al., 2015).

Generally, a dose of 500 to 3500 mg per days is used in treatment. Usually the dose is separated into 2 doses but single dose delivery is used in case of Extended Release (Hilty et al., 2006).

Some of the side effects of valproate are hair loss, tremor, dizziness, obesity etc. Severe side effects like hepatotoxicity and pancreatitis might occur but it is rare.

3.1.2 Atypical Antipsychotics

Atypical antipsychotics or 2nd generation antipsychotics is a class of drugs that reduces or relieves symptoms of psychosis. All atypical antipsychotics have been proven risk free and demonstrates effectiveness when used to treat acute bipolar mania. However, only a few atypical antipsychotics have shown similar result against acute depression. Aripiprazole, asenapine, risperidone are the drugs approved as singular or as an addition to mood stabilizer for treating acute mania and maintenance treatment of BD. Only Quetiapine is approved as monotherapy to treat acute depressive episodes of both BD I and BD II. A specified combination dose of olanzapine and fluoxetine has approval for using to treat depressive episode of BD I (Mccormick et al., 2015).

3.1.3 Conventional Antidepressant

Antidepressants are medications used to treat depression and anxiety. There is a controversy surrounding whether or not antidepressants should be given to patients with BD. The reason is that antidepressants can trigger manic episodes especially in patients with substance abuse problem (Hilty et al., 2006).

SSRI is the class of medication which carries the least risk among antidepressants. A study concluded that fluoxetine shows positive feedback not only in acute phase but also maintenance phase in patients with BD II. It also reported that almost half the patients relapsed after 6 months treatment with fluoxetine compared to cent percent relapse while treated with placebo (Fountoulakis & Vieta, 2008).

On the other hand, antidepressants show different outcome when used as solo or in combination. A study suggests that 25% bipolar depressed patients switched to mania or hypomania when treated with antidepressant only compared to a 14% switch when antidepressant is used along with a mood stabilizer (Post et al., 2006).

However, there are recent studies which claim antidepressants are not useful in treating BD. A study took 179 patients and treated one batch with mood stabilizer and antidepressant while another batch was treated with placebo and antidepressants for 26 weeks. It came to the conclusion that the recovery rate was almost identical where for placebo treated patients the rate was 27.3% and for antidepressant treated patients the rate was 23.5% (Fountoulakis & Vieta, 2008).

3.2 Psychological Treatments

All the evidences point to the fact that psychological interventions are very effective in BD treatment. A recent study provided Cognitive Treatment to 52 patient for half a year and noticed a decrease in depression score and dysfunctional traits (Fountoulakis & Vieta, 2008). Psychoeducation especially family centered psychoeducation can be an excellent step as it will help the family members to recognize certain triggering factors of the episodes and appropriate steps can be taken based on it.

3.3 Other Agents

Benzodiazepine is a medicine which doesn't do anything against BD itself. However, it has antianxiety property which can help the patient. Though a definite conclusion can't be reached, some studies suggest ECT or Electro Convulsive Therapy is effective in acute mania. Inositol shows good result when used as additional treatment for patients with refractory depression (Fountoulakis & Vieta, 2008).

Chapter 4

Conclusion

BD is a condition which can make a person incapable of living in society if proper treatment and care is not provided. In this age when suicide rate is noticeably increasing it has become absolutely necessary to make people aware of how important taking care of mental health is. BD is the leading condition as far as suicide rate is concerned (Tondo et al., 2003). A study shows that about 15 to 20 percent BD patients commit suicide (Miller & Black, 2020). Another study shows about quarter to half of the BD patients try to take their life at least once in their lifetime (Latalova et al., 2014). Considering currently relies solely on psychological analysis to diagnose, awareness of taking mental health issues seriously is the right direction forward to control the circumstance.

A significant amount of work is done on BD to provide information and treatment. However, further studies and research are required to effectively control the condition so that the patients can live a normal life.

Chapter 5

Future Direction

Pattern recognition approach where artificial intelligence recognize complex pattern from a massive amount of data, is now being used to accurately diagnose BD. A combination of this and various neuro imaging techniques hold the potential to avoid misdiagnosis of not only BD but other similar disorders as well (Phillips & Kupfer, 2013).

Also, a decrease in melatonin is observed in BD patients. Melatonin plays an important role in maintaining circadian rhythm and has a huge impact on sleeping pattern. Melatonergic pathway in CNS is being considered a potential treatment target of BD. Moreover, mitochondrial pathway, cholinergic system, neuropeptide system etc.is being extensively studied to discover new drug to treat BD.

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