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Review Article

Clinical presentation, differential diagnosis and management of bipolar disorder in children and adolescents: a review

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ABSTRACT

Bipolar disorder is a mental illness that causes serious disabilities in both social and work function. The occurrence of this disorder in children and adolescent age group has gained the attention of research workers since the 20th century. The varied clinical presentation of this disorder in comparison to the adult population, as well as the management approaches have been a matter of debate for ages. The aim of the study was to put forward the diagnostic and treatment approaches of bipolar disorder in children and adolescent.

Keywords: Adolescent, Bipolar disorder, Children

INTRODUCTION

Bipolar disorder, also known as manic depressive illness, is a psychiatric illness that involves shifts in a person's mood, energy, activity levels, and the ability to carry out day-to-day tasks.[1,2] These disorders are characterised by depressive episodes alternating with mania or hypomania and are associated with essential impairments, economic distress, chronic and debilitating medical conditions, and a high risk for suicide.[3] Prior to the 1990's, bipolar disorder was rarely diagnosed in children and adolescents. About only 10% of child and adolescent discharges in the United States in 1996 had a primary diagnosis of bipolar disorder.[4]

Starting from 1995, articles began to appear in the academic literature suggesting that bipolar disorder manifests differently in children than adults. It was also seen that bipolar disorder is often under recognized and undertreated in children and adolescents.[3,5] The parameters for the treatment of bipolar disorder in children and adolescents was released by the American Academy of Child and Adolescent Psychiatry in the year 1997 and by the year 2004 the proportion of inpatient children and adolescents discharged with a bipolar disorder diagnosis increased considerably.[4,6]

There is no child- specific criteria for bipolar disorder in the current edition of Diagnostic and Statistical Manual of Mental Disorders (DSM 5). Children and adolescents may experience the classical Kraepelinian (1921) or DSM type bipolar disorder. However, many bipolar children and adolescents have very short and frequent periods of mania, hypomania, or depression and, more controversially, some have continuous mood lability and irritability.[7] More recent work by Biederman's group at Harvard suggests intriguing links between paediatric bipolar disorder and attention-deficit/hyperactivity disorder.[1]

Children and adolescents with bipolar disorder usually have poor psychosocial outcome, increased risk for suicide, substance use, and psychosis which is why there is a strong need for the proper diagnosis and adequate treatment of this illness.[3] The controversy has now shifted from a debate about whether it can be diagnosed in youth to how it is diagnosed, how it can be distinguished from other more commonly diagnosed childhood psychiatric disorders, and how it can be treated and prevented.[8]

History of bipolar disorder

Bipolar disorder is a surprisingly modern concept. The terms 'melancholy' and 'mania' used to describe the two extremes of bipolar disorder were first mentioned in Ancient Greek. Hippocrates described melancholia ('black bile') as a state of *"aversion to food, despondency, sleeplessness, irritability, and restlessness".* Greek physicians believed that the illness often arose from the substrate of the sombre melancholic temperament, which, under the influence of the planet Saturn, made the spleen secrete black bile, ultimately leading to mood darkening through its influence on the brain. Mania on the other hand is a state of raving madness with exalted mood. It was Aretaeus of Cappadocia, a physician and philosopher in the 1st century AD, who is credited with making the connection between the two major mood states. He wrote: "*It appears to me that melancholy is the commencement and a part of mania*".[1]

The modern psychiatric concept of bipolar disorder has its origins in the nineteenth century. It was in 1854 when Jules Baillarger and Jean- Pierre Falret first described the disorder as circular insanity (Jean-Pierre Falret's term) and folie à double forme (Jules Baillarger's term). The German psychiatrist Emil Kraepelin (1856-1926) distinguished this disorder from demence precoce (schizophrenia) and coined the term 'manic- depressive psychosis' to describe it. The term 'bipolar disorder' is thought to be less stigmatizing than 'manic- depressive illness' and has therefore largely superseded the latter.[9]

Prevalence

The prevalence of BD-I and BD spectrum disorders in adults is around 1% and 5%, respectively, and the majority of them had the onset of their mood symptoms before age 20 years.[10] An increasing number of studies have begun to estimate the occurrence of bipolar disorder in youth. Lifetime prevalence rates of bipolar disorder in youth range from 0.2 percent in the Great Smoky Mountains Study to 2.9 percent for bipolar I disorder or bipolar II disorder in the National Comorbidity Survey-Adolescent supplement (NCS-A). A few studies have also estimated 12 months prevalence rates of bipolar disorder ranging from 1.3 to 2.5 percent. The prevalence rate of mania ranges from 0.4 (12 months) to 2.0 percent (12 months); and the rates of hypomania range from 0.1 (lifetime) to 0.9 percent (6 months). The results of longitudinal studies converge in estimating the prevalence of bipolar disorder at between 1.4 and 2.1 percent, which approximates cross-sectional prevalence rates in adult samples. This was confirmed by a recent meta-analysis of epidemiologic studies of bipolar disorder in children and adolescents, which reported a mean prevalence of 1.8 percent.[1]

Various clinical studies have suggested that the rates of bipolar spectrum disorders in youth are equally common in males and females.[11] The WHO indicates that BD is the 6th leading cause of disability in the world. Bipolar disorder in youth is a significant public health problem that is often associated with dysfunction in family and peer relationships, poor academic performance, high rates of chronic mood symptoms and mixed presentations, psychosis, disruptive behaviour disorders, anxiety disorders, substance use disorders, medical problems (e.g., obesity, thyroid problems, diabetes), hospitalizations, and suicide attempts and completions.[12]

Age of onset

The age of onset of bipolar disorder is most commonly around 20 years of age. Bipolar men appear to have 4 to 5 years earlier onset than bipolar women. In more than half of the cases, onset is before the age of 20, frequently in late adolescence. The ages of onset of bipolar I disorder and bipolar II disorders are similar, but there is a slight tendency for higher age of onset in bipolar II disorder patients. Early onset BD is associated with a severe course of illness and poor outcome; children with prepubertal onset BD are reported as approximately 2 times less likely to recover as those with post-pubertal onset BD.[13,14]

Diagnosis and subtypes

Several bipolar disorder categories are included in DSM 5: bipolar I disorder, bipolar II disorder, cyclothymic disorder, substance/medication- induced bipolar and related disorder, bipolar and related disorder due to another medical condition, other specified bipolar and related disorder and unspecified bipolar and related disorder (DSM 5).[11]

There is a huge diagnostic dilemma and controversies in the diagnosis of bipolar disorder in children. It is a misfortune that there are no specific diagnostic criteria for bipolar disorder in the youth. The basic types have been tried to be explained in this article.

Bipolar I disorder

The first episode of bipolar I disorder could be manic, depressive, or mixed. A mild retarded depression or hypersomnia for a few weeks or months, which then switches into a manic episode, is a common presentation.[10,15] A mixed manic episode is when the child meets criteria for both mania and major depression during the same episode (simultaneously or in rapid sequence). To diagnose BD-I, both symptom criteria (3 or 4 symptoms in addition to elation or irritability, respectively) and duration criteria should be met in addition to the 'significant functional impairment or psychosis' during mania. The duration of manic episode should last at least seven consecutive days or the severity of symptoms should require an inpatient admission anytime during the episode.[16,17] Bipolar I disorder in children is not as rare as previously thought. It is seen that most reported cases are in boys, and mixed manic (dysphoric-explosive) and rapid-cycling presentations are the mode. Childhood-onset depression must also be

considered a major risk for ultimate bipolar transformation. This is based on the following characteristics: (1) early age at onset; (2) even sex ratio; (3) prominence of irritability, labile moods, and explosive anger, suggesting mixed episodes; (4) questionable response to antidepressants, hypomanic switches, or both;(5) high recurrence rate after depression; and (6) familial affective loading.[10]

Bipolar II disorder

Bipolar disorder-II is characterized by at least one major depressive episode and at least one hypomanic episode (hypomania should last at least 4 consecutive days).

Cyclothymia

It is characterized by numerous hypomanic episodes together with numerous periods of depressed mood or loss of interest or pleasure that do not meet all the criteria for a BD or a major depressive episode (1 year of duration of illness in youth, versus 2 years in adults, is required for the diagnosis).

Bipolar disorder unspecified

It is the type where the clinical features of hypomanic or mixed episodes are present but they do not meet the diagnostic criteria for any of the more specific BD subtypes. In a 4-years follow up study, 25% percent of youth with BD-II converted to bipolar I and 45% of those with unspecified bipolar disorder converted to BD-I or II.[16]

The diagnostic criteria for bipolar disorder in DSM 5 have included changes in mood and energy level. In addition to that, the DSM 5 no longer requires the full criteria for mania or hypomania and major depressive disorder to make a diagnosis of a mixed episode. Instead, it had added a specifier that is, "with mixed features" which can be applied to a current manic episode, hypomanic episode, or depressive episode. The mixed features for a manic or hypomanic episode could be applied when at least three of the following symptoms during majority of the days of the current or recent episode of mania or hypomania are present: depressed mood, loss of interest in activities, psychomotor retardation, easy fatigability, feelings of guilt, or suicidal ideas. Similarly, the specifier can be used when the individual experiences at least three symptoms of a manic episode during majority of the days of the current or recent depressive episode.[2]

More recently, the American Psychiatric Association has proposed a new diagnostic category, Disruptive mood dysregulation disorder (DMDD) in the DSM 5 which is characterized by 'atypical' polar symptoms specially temper tantrums which are out of proportion to the situation or the provocating stressor, along with a persistently irritable mood [American Psychiatric Association: Desk reference to the Diagnostic criteria from DSM-5 (2013). Bipolar and related disorders. Arlington, VA, American Psychiatric Association)].[11]

AETIOLOGY

The single best predictor of BD in youth is family history with rates of positive family history in up to 20% of cases. Current studies have indicated that multiple genes seem responsible for BD but so far they have not been identified.[5] Neuroimaging techniques have now indicated that neural circuits involved in emotion processing and regulation in BD youth are different from their healthy peers and also volume of amygdala in BD adolescents is found to be reduced compared to healthy controls; which may suggest the possibility of a developmental delay in the gray matter of subcortical regions in BD adolescents.[8] Some studies have also mentioned about an abnormality in the regulation of prefrontal-subcortical circuits.[18] However, important biological, emotional or social factors may precipitate BD or serve as protective factors in genetically predisposed youth.

CLINICAL PRESENTATION

The DSM 4- TR as well as DSM 5 symptom criteria for bipolar disorders are same for children, adolescents and adults (requiring an episodic change in mood lasting at least 4 days for hypomania and 7 days for mania); however, bipolar disorder in children and adolescent is often characterized by excessive episodic irritability with aggressive outbursts and violent behaviour. The children are usually angry or dysphoric in between the period of outbursts. These 'atypical' bipolar symptoms in children also include severe mood disturbance, temper tantrums, and high levels of distractibility and inattention. The cardinal symptoms of grandiose thoughts and euphoric mood of bipolar disorder is rare in pre-pubertal children. However, the symptoms of the manic episode in adolescent group are usually featured by delusions and hallucinations, which mostly involve grandiose thoughts about worth, power and relationships.[2]

Co-morbid disorders

Bipolar disorder in children and adolescent is rarely seen in absence of co morbid conditions. These additional disorders often make the diagnosis and treatment of bipolar disorder difficult and also worsen the prognosis. Co-morbid disorders frequently associated with BD in youth include Oppositional defiant disorder/Conduct disorder [ODD/CD], attention deficit hyperactivity disorder, substance use disorders, anxiety disorders (which includes panic disorder, posttraumatic stress disorder, obsessive-compulsive disorder), and pervasive developmental disorders.[17]

Therefore, the early diagnosis and appropriate management of bipolar disorder in this age group may prevent the emergence of these co-morbid disorders.[2]

Oppositional defiant disorder

Recent studies have reported that ODD is the second most common co morbidity after ADHD.[18] It is difficult to diagnose ODD in the context of BD as the symptom of ODD overlap with those of mania, with no specific symptomatology to distinguish ODD from mania. The occurrence of ODD may be secondary to bipolar illness or it may be a prodrome of bipolar illness. However, many children with ODD do not progress to bipolar illness in later period.[19] This issue therefore requires further evaluation. The treatment of ODD is primarily behavioural in nature. However, when it is co-morbid with bipolar disorder, pharmacological treatment often reduces the symptoms of ODD. Several studies have suggested that atypical antipsychotic Risperidone can be useful in reducing the aggressive features in ODD though further studies are warranted.[17]

Attention deficit hyperactivity disorder

It has been seen that ADHD as a co morbid disorder is more often associated with early onset bipolar disorder (<18 years) (Sachs GS et al, 2000). Owing to the similarity in the symptomatology of mania and ADHD such as distractibility, motoric hyperactivity and increased talkativeness, there is an unfortunate risk of over diagnosis.[20] Interestingly, children of bipolar parents have a high risk for ADHD and likewise relatives of ADHD children have an increased risk for BPD.[21] This may suggest a genetic association between the two disorders. The symptoms of ADHD such as inattentiveness, impulsivity, talkativeness etc, in BPD children may often become the second most severe complaint after the mood is well stabilized. The medication options for ADHD in youth with BD are amphetamine salts and atomoxetine which should be started after stabilizing the mood.[17]

Conduct disorder

Paediatric onset BPD is commonly associated with 'affective storms' and aggressive temper outbursts, which may lead to aggressive behaviour towards family members and other adults, teachers or even other children.[22] Also, some children show serious acting out behaviours such as stealing, vandalism, suspension from school, etc. These behavioural symptoms frequently meet the diagnostic criteria for Conduct disorder. There is a high incidence of Conduct disorder (60%) in youth with BPD and is associated with a complicated course of the disorder.[17]

Anxiety disorders

The presence of anxiety disorders is reportedly high in children and adolescents with bipolar disorder.[23] Due to the heterogeneous presentation of anxiety disorders, it is difficult to ascertain as to which anxiety disorder is associated with bipolar disorder. However, the most common of them is found to be panic disorder. Several studies have reported that patients diagnosed with bipolar disorder who have high levels of anxiety symptoms are prone to have higher risk of alcohol abuse and suicidal behaviour as adults.[17]

Treatment of bipolar disorder in children and adolescents

The goal of the treatment is to control or ameliorate the symptoms that are affecting the child's psychosocial functioning and endangering the child's life and also to prevent new episodes or recurrences. The treatment incorporates pharmacotherapy, psycho education and psychosocial interventions including the child's family and school to provide an optimum environment for the child's better adjustment and achievement.

Pharmacotherapy

The recent trend focuses on lithium, antiepileptic drugs with mood stabilizing effects (i.e.; divalproex sodium and carbamazepine), and second-generation antipsychotics (i.e.; risperidone, olanzapine, quetiapine, ziprasidone and aripriprazole) to treat mania in youths; however atypical antipsychotics and mood stabilizing agents are the agents most studied among them.[3] Lithium is the FDA approved drug to treat mania in children of or older than 12 years of age, whereas risperidone and aripriprazole are approved for children of 10 years age or older. The medications have showed better results in treating bipolar symptoms when used in combination, which may be multiple mood stabilizers, or mood stabilizers augmented with atypical antipsychotic medication However, the adverse side effects such as gastrointestinal distress (e.g. nausea, vomiting), cognitive dulling, headache, hypothyroidism, weight gain, tremors and extrapyramidal side effects, of these medications should be closely monitored.[24] The treatment of bipolar depression in youth has been sparsely studied which makes it a clinical challenge. The use of antidepressants should be done only in the presence of an antimanic agent.[25] Further, as there are quite a huge number of adverse effects of these medications, examination of alternative treatment options, such as flax seed oil and omega-3 fatty acids, is warranted.[26]

Psychosocial treatment

The psychotherapeutic interventions for childhood-onset bipolar disorder have focused on the role of high emotion expression in families (e.g., critical remarks, hostility, and overprotection) which negatively impact the children with bipolar disorder and may even encourage negative reactions them (e.g., temper tantrums, self-destructive behaviour).

The treatment focuses on educating families about the management of bipolar disorder, prevention of relapse, individual psychotherapy, social and academic functioning.[24] There are about five lines of overlapping psychosocial therapies for BD youth and their families,

designed to fit specific age groups and methods of intervention:

Child and family focused cognitive behaviour therapy (CFF-CBT)

It was specifically designed for 8-18 years old with BD.[27] This therapy is based on the principles of reward-based CBT.

Multi-family psychoeducation groups (MFPG) and Individual family psychoeducation (IFP)

Developed by Firstad as adjunctive treatments for bipolar and depressive spectrum youth. It emphasises on psychoeducation around the role of medications and coping strategies.[28]

Family focused therapy (FFT)

FFT is specifically for adolescents with BD (FFT-A) (manual version) focuses on reducing the symptoms through increased enlightenment on how to cope with the disorder, decreasing levels of expressed emotion, and improving family problem-solving and communication skills.[29,30]

Dialectical behavior therapy (DBT)

It is a psychotherapy initially designed for adults with borderline personality disorder has been adapted for the treatment of adolescents by Goldstein.[30-32]

Interpersonal and social rhythm therapy (IPSRT)

For adolescents with BD addresses the deficits in interpersonal functioning and management of affective symptoms to combat their negative influence on psychosocial functioning.[33,34]

The average duration of psychosocial treatment for BD in paediatric population has not been established; however, continuing psychosocial interventions for subthreshold symptoms may be helpful.[35,36]

The psychosocial treatment, when used as adjunct to the pharmacotherapy, has been shown to reduce the relapse rate and also improvement in depressive symptoms, manic symptoms and behavioural disturbance in paediatric BD (Sadock et al, 2015). Due to a dearth of studies, it is difficult to comment on the efficacy of psychosocial interventions alone, in combating the symptoms of bipolar disorder in children and adolescents.

CONCLUSION

As we have seen, bipolar disorder in the paediatric population is not rare as previously thought. Moreover, the disorder has a serious negative impact on the child's social and work function, which makes this age group a priority to look after. Since the beginning of 1995, bipolar disorder in children and adolescents has been extensively studied leading to a number of developments in this field. The paediatric population are now receiving the diagnosis of bipolar disorder, and new disorders such as DMDD, have come into the picture. Owing to the numerous numbers of studies in pharmacological interventions, there has also been development in the treatment of bipolar disorder in the paediatric age group. Some studies have also shown that psychosocial interventions are helpful in the management of this disorder. However, more studies are warranted in identifying the efficacy of these interventions in treatment of bipolar disorder in children and adolescents.

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