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Clinical picture and treatment of bipolar affective disorder in children and adolescents

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Summary

Bipolar disorder (BD) is characterized by pathological changes in mood as well as recurring episodes of mania, hypomania, depression and mixed symptoms. In recent years, the number of BD diagnoses has risen considerably in children and adolescents. It is believed that an average rate of prevalence of bipolar spectrum disorder in the pediatric population is 1.8%, and BD type I – 1.2%, and the prevalence of the disorder increases with the age of patients. Despite the same diagnostic criteria, there are premises that suggest that the symptoms of the disorder are present with a different frequency among children and adolescents than in adults. The most frequent manic symptom in persons with childhood-onset of the illness is thought to be irritability, and in adolescence – hyperactivity. BD in children and adolescent population is accompanied by a high rate of comorbid psychiatric conditions. Attention deficit hyperactivity disorder and borderline personality disorder constitute particular diagnostic challenges. Early onset of BP is linked with a more severe course of the illness, worse prognosis, and a higher suicidal rate. Pharmacotherapy of BD in the pediatric population includes 1st and 2nd generation mood stabilizers, while their efficacy and safety profiles are different than in adults. The American Food and Drug Administration recommends treating manic episodes in young persons with lithium, aripiprazole, quetiapine, risperidone, olanzapine and depressive episodes with a combination therapy of olanzapine and fluoxetine.

Key words: bipolar disorder, attention deficit hyperactivity disorder, therapy

Introduction

Bipolar disorder (BD) is characterized by pathological changes in mood as well as recurrent episodes of mania, hypomania, depression and mixed symptoms. Diagnosing BD in the child and adolescent population is based on the same diagnostic criteria that are applied in adults. However, the nature of the clinical picture of BD in the developmental period is linked with difficulties in formulating a proper diagnosis and applying an adequate treatment. In the last decades, we have observed a dynamic increase in the number of studies focusing on BD in the population below 18 years of age [1]. This paper provides a discussion of their results regarding epidemiology, clinical picture, diagnosis as well as treatment.

Prevalence of bipolar disorder in children and adolescents

It had been believed for decades that BD rarely occurs in the developmental period [2]. However, the frequency of BD in persons below 18 years of age was observed to grow in the generations following World War II, and the first episode of this illness was observed at an earlier and earlier age [3]. In the last two decades, BD has been diagnosed considerably more often among children and adolescents. Moreno et al. [4] state that the estimated number of BD-diagnosed adolescents who visit the doctors' offices increased from 0.0025% in 1994–1995 up to 1% in 2002–2003. On the other hand, Harpaz-Roten et al. [5] observed a significant increase of the percentage of young patients hospitalized due to bipolar spectrum disorder, i.e., bipolar I disorder, bipolar II disorder, bipolar disorder not otherwise specified and cyclothymia – from 11% in 1995 to 18% in 2000.

Holtzman et al. [6] state that among studied BD patients in 21.9% the symptoms of the illness were present at the age of 12 or earlier, and in 43% between 13th and 18th year of age. Baldessarini et al. [7] observed that BD was present in 5% of children aged below 12 and in 23.7% of persons aged 13–18. Also, Perlis et al. [8], while studying a big group of BD adults, often stated an early onset of the illness. According to them, in 27.7% of patients, the onset occurs at the age of 12 or earlier, and in 37.6% between the 13th and 18th year of age. Other studies which assess the prevalence of BD among children and adolescents estimated the prevalence at the following level: 0.1% at the age of 9–13; 1.2% in persons aged 8–19; from 2.9% to 6.7% in the group aged 14–18 [9, 10].

At present, approximately 30–60% of BD adults report the onset of symptoms before the 20th year of age. In the study of Goetz et al. [11] carried out in the Czech Republic, the average age of the first episode of BD was 14.9 years (14.6 for depression and 15.6 for hypomania), and 15% of the studied individuals experienced the first episode of the illness before the 13th year of age.

A series of studies suggest that the frequency of BD among children and adolescents differs in various countries. A clearly visible growth in the number of diagnoses in this population was observed in particular in the USA – from 0.42% in 1994 to 6.7% in 2003. However, in other countries, such as Canada, the Netherlands, Romania, Switzerland, an early-onset BD is diagnosed considerably less frequently than in the

USA. One of the studies which compared patients from the USA with those in Europe pointed that the onset of BD before the 13th year of age was 31.1% in the USA and 5.6% in Europe, while between the 13th and 18th year of age — 38.1% in the USA and 26.6% in Europe. In the USA, more than two-thirds of the studied individuals were diagnosed with BD in their childhood or adolescence, and in Europe only one third [12]. Bellivier et al. [13], who compared the patients from Pittsburg with patients from 10 European countries, observed that in the USA the patients with onset earlier in life constitute 63%, and in Europe — 25%. In the study carried out by Etain et al. [14], the sub-group with an early onset constituted 68% in the USA, while in France — 42%. Some researchers suggest that the factors responsible for the increase in the frequency of childhood-onset BD diagnoses in the USA include widening diagnostic criteria, i.e., "overdiagnosing", and also false coding related to refunds [12].

Van Meter et al. [15] carried out a meta-analysis which included 12 epidemiological studies (6 carried out in the USA and 6 in other countries between 1985 and 2007) covering 1622 individuals aged between 7 and 21. They showed that there are no significant differences in the average rate of BD prevalence in the USA as compared to other countries. The differences in the frequency of BD prevalence resulted mainly from a "narrower" definition of BD applied during qualification of patients to particular studies in countries other than the USA. Furthermore, BD prevalence in particular communities did not reveal a growing tendency. It was assessed that the average rate of bipolar spectrum disorder prevalence in the pediatric population was 1.8%, and the bipolar I disorder (with manic states) – 1.2%, while the prevalence rate increased in the groups of older patients.

The DSM-5 classification of the American Psychiatric Association, in the chapter devoted to depressive disorders, introduced the term Disruptive Mood Dysregulation Disorder (DMDD) [16]. It was done to prevent wrong diagnoses of BD in the population of children and adolescents and also to prevent diagnosing BD in young persons with chronic irritability, with persistent disturbances of anger control as a response to normal stimuli as well as some mania-like symptoms (yet without fulfilling all symptomatic criteria to diagnose manic or hypomanic episode). Long-term observation of the group of young persons with DMDD revealed that this disorder is likely to be a predictor of depression, anxiety and dysthymia in adulthood, but not BD. According to DSM-5, DMDD occurs in approximately 2–5% of children and adolescents, and it is more often diagnosed in boys [17].

The clinical picture of bipolar disorder in the population of children and adolescents

In ICD-10, the diagnostic criteria for BD are identical both for adults, and children and adolescents. Also, DSM-5 presents the same diagnostic criteria, regardless of a patient's age. The only exception is the depressive episode. Its criteria contain the additional information that in children and adolescents, instead of depressed mood – irritable mood may appear, and instead of body weight loss – a failure in obtaining the expected body weight.

Despite identical diagnostic criteria for all BD patients, there are premises that some symptoms of the illness are present with various frequency in the populations of children, adolescents, and adults. Between 2004 and 2016 four papers were published which analyzed the population of at least 250 patients and focused on the character of manic symptoms in particular age groups. Jerrell and Shugart [18] stated that in the child-adolescent population irritability and depressive symptoms were present more often than in adults. Birmaher et al. [19] compared 173 children (aged <12 years) with BD, 101 adolescents with childhood-onset of the illness and 90 adolescents with adolescence-onset. In the group of children and adolescents with childhood-onset, they observed a higher degree of irritability, mood lability and more frequent comorbid attention deficit hyperactivity disorder (ADHD). Furthermore in both groups of adolescents (in comparison with children) symptoms such as racing thoughts, increased productivity and impaired judgment were described during manic episodes, while during depressive episodes – more severe symptoms with higher frequency of atypical signs and suicidal attempts.

In the study covering a population of 1,106 patients, Safer et al. [20] revealed that as compared to adults, children and adolescents more often manifest aggression and irritability, while in adults cognitive functions abnormalities (logorrhea and disordered content of thoughts) are more frequently present. The meta-analysis of 20 research studies carried out by Van Meter et al. in 2016 [21] shows that the most frequent symptom of mania in childhood is increased level of energy (79%) and the second most frequent symptom is irritability (77%).

Recently, Ryles et al. [22] carried out a systemic review of the frequency and severity of mania in various age populations. The analysis included nine studies published between 1992 and 2012, except for the aforementioned analysis by Van Meter et al. [21]. The conclusions of the paper suggest that the most frequent manic symptom in persons with childhood-onset of the illness is irritability, in persons with adolescence-onset – increased levels of activity, and adulthood-onset – pressure of speech.

Numerous studies carried out among BD patients aged 18 and below show that the illness in this age group starts most often with a depressive episode. In the study by Goetz et al [11], the first episode was depression in 56% of children and adolescents. Furthermore, as much as 80% of young patients in this study were initially treated for other psychiatric conditions than BD, e.g., depression, acute psychosis, mixed/manic episode, adjustment disorders, obsessional thoughts and acts, ADHD, anorexia nervosa, anxiety disorders, conduct disorders or unspecified personality disorders.

BD in the population of children and adolescents is accompanied by a high rate of comorbid psychiatric conditions. Among them, the most frequent are as follows: ADHD, borderline personality, anxiety disorders, oppositional defiant disorder or conduct disorders. Furthermore, there may occur some specific disorders of school skills development, as well as psychoactive substance use [11]. Early onset of the illness is linked to the increased risk of psychoactive substance use, which, in turn, has an impact on the therapy of the patient and occurring complications. According to Goldstein et al. [23], as much as 32% of the studied young BD patients start to use psychoactive substances.

The most important clinical predictors of the development of bipolar spectrum disorder include anxiety and depressive symptoms, as well as affective lability. Alarming signals in young people include also sleep disturbances, energy shifts, cognitive dysfunctions, and also deterioration of functioning at school. An increased risk of illness is present in persons whose parents suffer from affective disorder. Children of BD parents earlier experience the first episode of mania as compared to children of non-BD parents. Traumatic events in early childhood also constitute a significant factor in BD development [24, 25].

It is important to define predictors of BD to provide medical service to persons susceptible to the illness as early as possible. However, it is also a very complicated task because the development and course of BD is characterized by a high degree of diversity and changeability. Moreover, the symptoms which often precede the development of BD may not be specific for this illness and occur equally often in the prodromal phases of other disorders, and therefore they may not be of help while diagnosing BD [26]. For instance, anxiety disorders – in retrospective studies up to 75% of BD patients reported trait anxiety in the prodromal phase of the illness, while anxiety did not prove to be a specific factor for the development of BD, since, in the prospective studies, anxiety disorders preceded also the development of other psychiatric conditions (not only BD) [27].

Most publications devoted to BD precursors fail to explain unambiguously whether they concentrate on prodromal symptoms (symptoms preceding illness onset, which can be accurately described only following occurrence of the condition), risk factors (i.e., features, variables or other factors that, if present in an individual, are associated with an increased risk of certain condition in comparison with general population, however, not every person with a risk factor will develop illness) or both [26]. Currently there are no fully described prodromal symptoms or risk factors for development of BD. Scott et al. [28] in their study have attempted to determine which adolescents with depressive symptoms are in the risk group of early onset of BD. Based on the obtained results they have concluded that presence of cyclothymia, subthreshold manic symptoms (even of low severity), atypical symptoms of depression, family history of BD, and the presence of considerably elevated mood as a reaction to antidepressants in young individuals significantly increased risk of bipolar disorder [28].

Diagnostic challenges in bipolar affective disorder in children and adolescents – ADHD and borderline personality

Diagnosing BD in the population of children and adolescents frequently presents a great challenge. BD symptoms should be differentiated between, e.g., the symptoms of various somatic diseases, behaviors caused by the use of psychoactive substances, the effect of taken drugs, schizophrenia (in particular, when the course of the illness is dominated by delusions, violent behavior or incoherent speech), schizoaffective disorders, conduct disorder, anxiety disorder, posttraumatic stress disorder, eating disorder, ADHD or the features of abnormally developing borderline personality.

The article focuses on difficulties resulting from differential diagnosis between two disorders: ADHD and abnormally developing borderline personality, which in the pediatric population are often wrongly diagnosed and confused with BD, and not infrequently coexist with mood disorders.

Table 1. **Symptoms of mania which may occur in children and adolescents with ADHD**

Diagnostic criteria for mania	Symptoms (+) which may occur in children and adolescents with ADHD (-) not occurring in children and adolescents with ADHD
1. Increased activity or physical anxiety	+
2. Increased talkativeness (pressure of speech)	+
3. Racing thoughts or a subjective feeing of acceleration	-
4. Loss of normal social inhibition leading to behavior not adjusted to circumstances	+
5. Decreased need for sleep	-
6. Increased self-esteem or the feeling of superiority	-
7. Easy distractibility or continuous changes of activities or plans	+
8. Off-hand and reckless behavior, underestimating risks	+
9. Increased sexual energy or sexual indelicacies	-

When it comes to BD and ADHD in individuals aged below 18, sometimes one disorder is confused with the other, and the other way round, because the symptoms of hypomania/mania overlap with some symptoms of hyperkinetic disorders (Table 1). ADHD is characterized by a triad of symptoms: inattention, difficulties with controlling impulsivity and hyperactivity. Therefore, both disorders may be manifested by such symptoms as: easy distractibility, excessive talkativeness or reduced social restraints. In the course of ADHD mood swings, which are characteristic for BD, are also present (24–50%). ADHD may also be difficult to differentiate from BD when the hyperkinetic disorders are accompanied by conduct disorders, because their manifestation (fits of anger, aggressive behavior) may overlap with the symptoms of mixed or manic states.

Differentiating between BD and ADHD is based on differences in their clinical symptoms, the course, comorbidity, psychiatric history in the family, and also a response to the applied therapy. It should also be remembered that these disorders may coexist. It is estimated that BD develops in approximately 30% of young individuals with ADHD, and the percentage of BD in adults suffering from hyperkinetic disorders is around 20%. On the other hand, it is estimated that ADHD occurs in 9.5% to 28% of BD patients. Contrary to ADHD, in BD the following symptoms are observed much more often: elevated mood, grandiose attitude, racing thoughts, as well as extremely rapid mood swings. In BD, somatic ailments typical for children in the course of a depressive episode are also frequently present [29].

In many cases, BD is manifested by chronic or intermittent periods of intensive hyperactivity or anxiety, frequently with increased impulsivity, as well as energy and aggression swings. The number of interests increases, insomnia, and grandiose attitude are sometimes present, which may facilitate the increase of activity and productivity. On the other hand, children with ADHD are hyperactive, anxious, fidgeting – in particular in situations which require concentration and prolonged intellectual effort. Their motor activity is high but stable. In BD, circadian rhythms are disturbed, while in ADHD –they are not. Both in BD and ADHD sleep problems are observed. However, in persons with hyperkinetic disorders decreased amount of daily sleep is not observed. Parasomnias, sleep time reduction, sleep fragmentation or bedwetting are more frequent in BD. A history of considerable irritability, dysphoria, periods of tearfulness, mood liability or fits of anger are described as the precursors of early-onset BD. By contrast, in children with ADHD, the symptoms of mood disorders are secondary to school or social challenges. In one fourth of young BD patients, suicidal behavior and tendencies were described. Psychotic symptoms may also occur, in particular grandiose delusions and various forms of aggression. Aggression may be present in the course of severe fits of anger or may be intentional, planned, sometimes also without remorse. On the other hand, in ADHD, aggression results from irritability, and property damage seems to be incidental, associated with inattention, impulsivity, lack of coordination or impaired spatial skills. In some children and adolescents suffering from BD stronger sexual behavior is described (provocative clothes, expressive make-up, violent, sexually provocative language, viewing pornography, masturbation). However, hypersexuality is not a part of the clinical picture of ADHD. Both disorders may cause learning problems. Children with ADHD find it difficult to finish a task or concentrate. On the other hand, children with BD manifest uneven performance at school, which is frequently correlated with the phase of the illness. Psychostimulants applied in the treatment of ADHD are ineffective in BD, they can also cause sleep problems or disturb circadian rhythms in BD patients [29].

Both BD and ADHD are characterized by high heritability. Both are inherited in a complex and polygenic manner. Based on available twin studies heredity of BD is estimated to be between 58 and 85%. In the case of ADHD it is considered to be between 60 and 80%. Current genetic and molecular studies show that there is a significant genetic correlation between ADHD and BD which consists in the presence of numerous common genes [30].

When it comes to BD and borderline personality disorder, these are two chronic disorders whose symptoms may overlap [31]. Individuals suffering from borderline personality disorder have unclear or disturbed self-image, goals, inner preferences, they are prone to engage in intense yet unstable relationships which frequently lead to emotional breakdowns, they strive to avoid the experience of being abandoned, experience inner emptiness and also present recurring auto-aggressive behavior.

Table 2. **Differentiation between bipolar disorder and borderline personality according to Dudek [32], with the author's consent**

Specification	BD	Borderline personality
Course	recurring, in phases, rarely chronic	chronic
Decreased mood	typical depressive episodes, depression criteria met	depressive affect: changeability in one day or even hours, high reactivity towards events and environmental stimuli, other typical symptoms rare, depression criteria often not met
Elevated mood	mania or hypomania with typical symptoms, lack of episode triggering or suppressing events	duration of the elevated mood rarely meets timeline criteria for diagnosing mania, however, it can meet the timeline criteria for hypomania or cyclothymia; precipitating events present
Family history of BD	+	-/+
Functioning	depending on the phase of the illness, often good in remission	Long-lasting periods of good functioning rare
The issues of inner world	diverse, depending on the phase/ state	fear of being abandoned

Differentiating between BD and borderline personality disorder is presented in Table 2, on the basis of the paper by Dudek [32], upon the author's consent. The differentiating elements include the course, the features of decreased and elevated mood, family history of BD, functioning and the issues associated with the environment. On the other hand, such symptoms as emotional instability, impulsivity, mood swings, increased risk of psychoactive substance use or auto-aggressive behavior are common both for BD and borderline patients. MacKinnon and Pies [33] found a relationship between affective lability characteristic for borderline personality and BD symptoms with rapid cycling. In some cases, such onset of BD may be inappropriately diagnosed as borderline personality.

Differentiating between BD and borderline personality disorder is based, for example, on the differences in their course, since the symptoms of borderline personality disorder persist over a long period of time as contrasted to BD symptoms which occur in the acute periods of the disorder but are absent during remission. Furthermore, persons with borderline personality disorder do not experience extremely elevated mood accompanied by, e.g., grandiose delusions or considerably reduced need of sleep. A positive family history of BD may also prove helpful in differentiating between these two disorders.

It should also be stressed that both disorders may coexist, and up to 20% of BD patients suffer from borderline personality disorder. In the longitudinal study carried out by Yen et al. [34], it was observed that the presence of borderline personality symptoms among young individuals with BD is linked with a more severe course of BD, and also a more frequent occurrence of auto-aggressive behavior. This is also confirmed by the latest study carried out by Riemann et al. [35] which shows that the characteristics of

borderline personality, affective instability, impulsivity and proneness to suicide or self-inflicted injury in particular, lead to a greater number of affective episodes in BD patients.

Some studies suggest that both BD and borderline personality disorder are linked with more frequent presence of family history of depression, antisocial personality as well as psychoactive substances use. Other studies present similar environmental risk factors in the development of these disorders. The factors include the following: early trauma, sexual abuse in childhood, emotional abuse in childhood, loss of parents in childhood, disturbed family background. Similarly to ADHD, recent genetic and molecular studies also point to a genetic correlation between BD and borderline personality which consists in the presence of numerous common genes [36].

Medications have limited efficacy in the treatment of borderline personality disorder, yet they may prove helpful in the treatment of accompanying impulsivity, affective lability as well as irritability and aggressive behavior [31].

Treatment of bipolar disorder in children and adolescents

In the treatment of BD in children and adolescents, it is recommended to apply psychopharmacotherapy in combination with psychosocial interventions. While controlling the pharmacological therapy of young individuals with BD, it should be remembered that the efficacy of the applied medications as well as their safety profile may differ from adults [37]. Similarly to adults, in the pharmacotherapy of pediatric BD population 1st and 2nd generation mood stabilizers are the basic pharmacological agents [38]. Lithium (1st generation mood stabilizer) as well as aripiprazole, quetiapine, risperidone, olanzapine, and asenapine (2nd generation mood stabilizers) were approved by the Food and Drug Administration (FDA) to treat manic or mixed episodes in adolescents suffering from BD, while atypical antipsychotics are not approved in the treatment of children aged below 10 (olanzapine — below 13 years old) and lithium — below 12 years of age [1, 39].

Recent studies show that atypical antipsychotics, i.e., risperidone, olanzapine, aripiprazole, and quetiapine may be more effective than 1st generation mood stabilizers in the treatment of manic and mixed episodes (improvement rate 66%) as compared to the rate of 38.5% for lithium. Regarding olanzapine, quetiapine and asenapine it was revealed in the placebo-controlled trials [40].

Findling et al. [41] carried out two major clinical studies to assess the efficacy of aripiprazole among children and adolescents with BD. In the first study which covered individuals aged between 10 and 17 with acute manic or mixed episode in the course of BD I, also with psychotic symptoms, ≥50% reduction on the Young Mania Rating Scale was obtained in the 4th week of treatment in 44.8% of individuals administered with 10 mg and in 63.6% of patients administered with 30 mg of aripiprazole against 26.1% in the placebo group [41]. In the second open study which included 96 children aged between 4 and 9 with BD with manic symptoms, such reduction was obtained in 62% of the patients [42].

Antipsychotics may also be applied to augment the treatment of manic symptoms, when monotherapy with lithium or anticonvulsants does not bring optimal results [37].

At the same time, it is stressed that atypical antipsychotics, despite high efficacy, lead to more metabolic disorders in young people than 1st generation mood stabilizers, and such differences were not observed in the studies among adults [39].

So far, valproates (1st generation mood stabilizers) have not been officially approved by the FDA in the treatment of manic and mixed episodes in children and adolescents, and its efficacy in this population is not documented as good as in adults. In a double-blind trial comparing valproates and quetiapine in the treatment of mania, quetiapine demonstrated better results. Although there is evidence for the efficacy of valproates in the treatment of acute episodes of mania in the pediatric population, the amount of available data and studies is still limited. Furthermore, carbamazepine, which also belongs to the group of 1st generation mood stabilizers, is not recommended by the FDA in the treatment of BD in children and adolescents; however, there are a few open studies which suggest potential benefits of carbamazepine treatment in the pediatric BD population [37].

Masi et al. [43] found that worse outcomes in the treatment of manic or mixed states in the pediatric population are linked with comorbidity of ADHD and conduct disorders and also with a higher initial severity of these disorders.

To treat depression in the course of BD, the FDA recommends combination of olanzapine and fluoxetine [37]. In a recently published study, an improvement was observed in children aged 10–17 regarding symptoms of depression after 6 weeks upon administration of lurasidone as compared to placebo [44]. On the other hand, the conducted studies did not reveal the efficacy of quetiapine in the treatment of depressive episode in BD in young individuals [45, 46]. Generally speaking, it is not recommended to apply antidepressants in monotherapy of depressive symptoms due to the risk of manic episode development. Antidepressants should rather be added to mood stabilizers [37, 39].

What proved to be effective in preventing relapses of affective episodes in the treatment of children and adolescents with BD was lithium, valproates, aripiprazole, ziprasidone, asenapine, and lamotrigine; however, further studies are still required in this respect [37]. In an 18-month double-blind trial of individuals with BD aged 5 to 17 (whose mental state had previously been stabilized with valproate in combination with lithium), it was found that valproates are less effective than lithium in the maintenance treatment among the patients who continued lithium or valproate monotherapy [47].

No evidence of oxcarbazepine efficacy was observed in the treatment of BD in children and adolescents [48]. However, recent publications provide preliminary positive information regarding therapy with ziprasidone (although a prolongation of the adjusted QT interval was observed) [49] and lamotrigine [50]. To assess the therapeutic efficacy of topiramate in the pediatric BD population further research is necessary [37]. A few papers point to potential benefits of administration of omega-3 fatty acids to treat manic and depressive symptoms and to improve the overall functioning or externalizing and internalizing behavior assessed by parents [51–53].

Various methods of psychotherapy are believed to be helpful in combination with medications in the treatment of BD in children and adolescents; however, the position of none of them is well-grounded in the treatment of this condition [1]. Family-fo-

cused therapy for adolescents and multifamily psychoeducational psychotherapy are believed to be "probably effective" in BD [54]. The therapy for adolescents focused on family consists of 21 50-minute sessions and lasts for 9 months. This therapy aims at psychoeducation (e.g., providing information about etiology, symptoms, course of the illness, risk factors, and pharmacotherapy), observing pharmacotherapy, preventing relapses, strengthening problem-solving and communication skills [1, 39]. In a two-year randomized trial carried out by Miklowitz et al. [55] which compared two groups of adolescents with BD treated pharmacologically in combination with a family-focused therapy or in combination with increased care, it was found that the family-focused therapy combined with medications is effective regarding alleviation of depressive symptoms. Furthermore, the subsequent study documented that this therapy may facilitate a remission of symptoms of mood disorders and may help to maintain improvement among adolescents with a high risk of BD development [56].

Multifamily psychoeducational psychotherapy is a group therapy for children with depression or bipolar spectrum disorder and their parents. This form of psychotherapy is aimed at psychoeducation, receiving the support of the group and the therapist and also developing social skills. In the study carried out by Fristad et al. [57] among children with mood disorders aged 8 to 12 years, a short, supportive, psychoeducational group psychotherapy in combination with pharmacotherapy resulted in better prognosis in the patients.

The cognitive-behavioral therapy focused on the child and family, as well as individual family psychoeducational psychotherapy are believed to be "possibly effective" [54]. The cognitive-behavioral therapy focused on the child and family consists in building the following skills: communication, problem-solving or regulating emotions [1, 39]. In the study of Pavuluri et al. [58] carried out among young BD patients treated with pharmacotherapy in combination with cognitive-behavioral therapy focused on the child and family, a high level of treatment integrity, compliance with recommendations and satisfaction of the studied patients were obtained. Individual family psychoeducational psychotherapy is aimed at improving the atmosphere in families of individuals suffering from mood disorders [54].

The dialectical-behavior therapy and interpersonal and social rhythm therapy are believed to be experimental forms of psychotherapy [54]. The dialectical-behavior therapy is offered to adolescents with BD, including their parents. It focuses on psychoeducation, emotional regulation, mindfulness, distress tolerance and interpersonal effectiveness [59]. On the other hand, the interpersonal and social rhythm therapy is also adolescent-oriented therapy including their parents, aimed at disturbances in the daily rhythm, interpersonal stress, and support for pharmacotherapy [60].

Despite promising outcomes of various forms of psychotherapy in the treatment of BD, further studies are necessary to determine the most effective therapeutic interventions [1, 39].

Final remarks

Despite the dynamic growth in the number of studies focused on BD in the population aged below 18 years in the last decades, the state of knowledge on this subject still needs to be broadened. We are now experiencing considerable increase in the number of diagnoses of this disorder in the pediatric population. We also gain access to data suggesting the onset of the illness in the childhood-adolescence period in a considerable percentage of the patients. The picture and the course of the illness frequently differ in children and adolescents as compared to adults. Therefore it poses significant diagnostic challenges and is confused with other disorders. As a consequence, BD diagnosis in children and adolescents is often delayed, and for this reason it is treated inappropriately or too late, which affects the quality of their lives and functioning. Also, further research is needed to determine the effective treatment of BD in the pediatric population.

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