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Chapter

Comorbidity in Children and Adolescents with ADHD

Marija Burgić Radmanović and Sanela-Sanja Burgić

Abstract

Attention Deficit Hyperactivity Disorder with or without hyperactivity disorder is a neurobiological disorder that involves the interaction of the neuroanatomical and neurotransmitter systems. It is a developmental disorder of psychomotor skills that is manifested by impaired attention, motor hyperactivity and impulsivity. This disorder is characterized by early onset, the association of hyperactive and poorly coordinated behavior with marked inattention and lack of perseverance in performing tasks; and this behavior occurs in all situations and persists over time. This disorder is inappropriate for the child's developmental age and maladaptive. Disorders of neurotransmitter metabolism in the brain with discrete neurological changes can lead to behavioral difficulties and other psychological problems. Most children and adolescents with Attention Deficit Hyperactivity Disorder have comorbidities, often multiple comorbid conditions in the same person. Comorbidity was observed in both clinical and epidemiological samples. It is estimated that about two-thirds of children with this disorder have at least one other psychiatric disorder diagnosed. Symptoms persist and lead to significant difficulties in the daily functioning of the child, such as school success, social interactions, family and social functioning, etc. Recent studies indicate the presence of various neuroophthalmological disorders in children and adolescents with ADHD. The most common comorbidities in children and adolescents with ADHD that will be covered in this chapter are autism spectrum disorder, mood disorder, anxiety, learning disabilities, conduct disorders, tics disorder and epilepsy.

Keywords: child, adolescent, ADHD, comorbidity, development

1. Introduction

ADHD is a neurobiological disorder that encompasses the specifics of neurotransmitter metabolism brain, and the interaction of the neuroanatomical and neurotransmitter systems. It is a developmental disorder of psychomotor skills that is manifested by impaired attention, motor hyperactivity and impulsivity [1]. Disorders of neurotransmitter metabolism in the brain with discrete neurological changes can lead to behavioral difficulties and other psychological problems. Behavioral disorders, secondary psychological problems, and interaction disorders with mild neurological symptoms may occur with this disorder [2]. To make a diagnosis, the symptoms must be frequent and severe than in children of comparable developmental level, and they must cause significant difficulties in the child's daily functioning [3]. It is a behavioral disorder that makes it difficult for a child to focus on daily requirements and routines. These children and adolescents usually have

difficulty organizing, focusing, making realistic plans, and thinking before they do something. The group of authors considers that ADHD is a developmental disorder of lack of behavioral inhibition, which manifests itself as a developmentally inappropriate degree of inattention, excessive activity and impulsivity, and complicates self-regulation and organization of behavior in relation to the future [4]. The main symptoms of ADHD are developmentally inappropriate for the age of the child and these are developmentally inappropriate levels of poor attention, hyperactivity and impulsivity. The degree of intensity of symptoms can vary according to the age of the child. Symptoms are manifested in the form of inattention of the child, the child does not perform its tasks, cannot organize, easily distracted, loses school and other things, "forgetful", avoids prolonged exertion.

The clinical picture in boys and girls differs in some aspects of the symptoms. Boys are more motor hyperactive and girls are more inattentive, as if "dreaming"; and their hyperactivity manifests itself as emotional and verbal (in the form of chatter, crying, etc.).

Data on the frequency of this disorder in developmental age differ depending on the applied methodology, age of the respondents, urban or rural region, number of persons providing data on the child's behavior (only parents, only teachers or both parents and teachers and others). Symptoms of hyperactivity are manifested in such a way that the child fidgets, gets up and leaves the bench, cannot play or do a task in peace, talks a lot, runs and climbs excessively, is always ready to "go" and others. Symptoms of impulsivity in a child are manifested by the child not being able to wait his turn, interrupting others when they speak, giving hasty answers, behaving intrusively and the like. Due to the symptoms, these children achieve poorer success in school, they have difficulties in mastering the school program, although they are most often of normal intellectual potential. Most adolescents who had ADHD as children still have difficulties in schooling, social interactions, and often emotional problems. Some adolescents may show irritability, poor school performance, disorganized learning, and poor communication with peers. ADHD always appears in early development, usually in the preschool period, and is most often noticed when a child starts school. This disorder usually lasts during schooling, and in some it continues into adulthood. Many people may experience improved activity and attention. Children with ADHD are often careless and impulsive so they are prone to accidents and injuries. These children often break the agreed rules and often have disciplinary difficulties. In relationships with adults, children with ADHD are often socially disinhibited, without caution and reserve, reckless behavior. Other children often avoid them, and are considered unpopular among peers, so they are often isolated.

The prevalence of ADHD is between 5 and 7% for children and between 3 and 5% for adults [5]. According to systematic review and meta-analysis, prevalence of ADHD among school-aged children and adolescent vary from 2.2% to 17.8% worldwide [6]. According to epidemiological studies, ADHD in children is thought to continue in 50–80% of cases in adolescence and adulthood. This high prevalence is of concern because this disorder negatively affects all neurodevelopmental areas and the psychosocial interactions of affected individuals. The risk may increase if symptoms such as aggression and irritability or comorbidities, such as behavioral disorders, are present.

In researching this problem, there are certain challenges in estimating the incidence of ADHD, such as are ways to assess ADHD, diagnostic methods, source of information about the disorder, agreement among respondents assessing ADHD symptoms, conducting assessments in one or more settings, age range of respondents, geographical location and characteristics of the community from which respondents originate [5].

Many studies indicate that ADHD is more common in boys [7]. The prevalence in boys and girls varies in different studies, and generally is more likely to be diagnosed and treated in boys than in girls [8]. The ratios from the clinical samples are higher than the ratios from the population samples. Research in this area of developmental psychiatry is extensive with a steady increase in the number of authors and professional literature dealing with this issue.

2. Comorbidity

The term "comorbidity" was introduced into medicine by Feinstein in 1970 to denote those cases in which a particular clinical entity exists simultaneously in a patient during the clinical course of his underlying disease [9]. Psychiatric disorders may coexist with somatic disorders and/or other psychiatric disorders when referring to "psychiatric comorbidity".

Different causes can lead to comorbidities, which can be accidental or the result of a combination of different risk factors; or two disorders may have the same or overlapping risk factors when one disorder causes the other; or there may be a multiform manifestation of one of the two basic disorders when the third - independent – occurs disorder. Due to insufficient knowledge of the etiopathogenesis of psychiatric disorders, modern classification systems (DSM and MKB) apply a descriptive, categorical system that classifies psychiatric symptoms and behaviors into a large number of different diagnoses.

The disadvantage of classification systems is that they poorly recognize the specifics and needs of child and adolescent psychiatry. The diagnostic process in developmental psychiatry is based on descriptive facts that determine the type of disorder, with the use of comorbidities to correct the shortcomings of this diagnostic process and to bring the diagnostic categories closer to the real clinical situation. These specifics are: symptomatic, developmental, environmental and prognostic. In developmental psychiatry, there are specific limitations in the external manifestation of symptoms, as well as in the possibility of insight into the existence of dependent symptoms. In child and adolescent psychiatry, there is the possibility of uneven development of basic developmental lines such as cognitive, emotional and social, especially during early childhood. In childhood, there is a clear dependence on past and current environmental conditions. Their interaction largely determines the manifestation of mental disorder at this age.

ADHD is one of the most common neurodevelopmental disorders in child and adolescent psychiatry and one of the most researched disorders in child psychiatry. Previous research indicates the existence of high comorbidity between ADHD and other psychiatric disorders in childhood. The presence of comorbidities largely depends on: case definition, assessment methodology, and control group. Studies have shown a high comorbidity between ADHD and behavioral disorders in the form of opposition and defiance, depression and anxiety. Some mechanisms for comorbidity include shared risk factors, distinct subtypes and weak causal relationships [10].

A 2015 study by Masi et al. showed more than 2/3 of patients with ADHD have a psychiatric disorder associated. The most common comorbid diagnoses with ADHD during early childhood are oppositional defiant disorder, enuresis and language disorder, and anxiety and tics in the mid-school years. In adolescence are observed mood disorder and substance use disorder. Many children with ADHD have a specific learning disorder [11]. The same study estimates that oppositional defiant disorder is concomitant with ADHD in 25–75% of the cases, conduct disorder about one third of cases, 6–30% of ADHD children have major depression,

more than 20% of bipolar disorder co-occur with ADHD; 87% of disruptive mood dysregulation disorder children had ADHD concomitantly; the prevalence of PTSD in children with ADHD is 5.2%; chronic tics disorder with ADHD is 55%; 85% of children with autistic spectrum disorder show a clinical picture of ADHD [11].

Barkley states that 67–80% of children diagnosed with ADHD who have been referred for clinical treatment have at least one more diagnosis, and almost half of them have two diagnoses [5]. Two-thirds of children with ADHD have at least one other psychiatric disorder diagnosed [12].

Some conditions occur more often than others. These are most often the following conditions:

- learning difficulties
- oppositional-defiant behavior
- conductive disorders
- behavioral disorders
- speech-language difficulties
- epilepsy
- mood disorders
- anxiety disorders
- sleep disorders
- tics/Tourette's syndrome
- obsessive–compulsive disorder
- eating disorders

The presence of comorbidities is significant because it complicates the diagnostic process, affects the course, prognosis and therapeutic process. Assessment and support in comorbid disorders are often as important as the assessment and treatment of ADHD symptoms [12].

2.1 Comorbidity with behavioral disorders

Behavioral disorders in developmental age are characterized by persistent and repetitive patterns of dissocial, aggressive, or defiant behavior. These behaviors in their most pronounced form can have criminogenic characteristics and deviate significantly from the socially expected ones according to the age of the child. These disorders are often accompanied by an unfavorable psychosocial environment, unsatisfactory family relationships and school failure. They are more commonly observed in boys than in girls.

Opposition-defiant behavior usually occurs in younger children, who exhibit extremely defiant, provocative, and disobedient behavior, and some children also exhibit aggressive behaviors. Most authors believe that 45–84% of children and adolescents with ADHD also exhibit oppositional-defiant behavior [5]. The

Multimodal Treatment Study of ADHD found that about 62% of preschool children with ADHD and 59% of school children in the sample had oppositional-defiant behavior [5]. It is hypothesized that emotional dysregulation that occurs in children with ADHD may affect the occurrence of comorbidities for oppositional-defiant behavior, anxiety, depression, bipolar disorder, and other conditions, and it has also been observed that these children often have more psychopathology and social problems in the family [5]. These children are also at higher risk of taking various psychoactive substances, rejection from peers, poorer school achievement, rejection and the development of anxiety and depression in adolescence.

Many children with oppositional-defiant behavior also have conductive disorder, which is manifested by recurrent antisocial, aggressive, or defiant behavior. Study by Pliszka included 1035 children and adolescents at a psychiatric clinic and reported that 167 children and adolescents with ADHD were also diagnosed with oppositional defiant or conductive disorder [13]. Research demonstrated that 30–50% children with ADHD fulfill criteria for conduct disorder or oppositional defiant disorder [14]. These children are also at higher risk of substance abuse, antisocial activities, rejection from peers, school failure, anxiety and depression. The families of these children show more psychopathology and social problems.

2.2 Comorbidity with specific learning difficulties

These specific developmental disorders of school abilities include a group of disorders that are characterized by significant difficulties and impairments in mastering school skills, such as reading and arithmetic. These learning disabilities are not a direct result of other disorders such as mental retardation, neurological diseases, uncorrected vision or hearing disorders, or emotional disorders; although they may co-exist with them. Developmental disorders of school ability often exist in comorbidity with ADHD.

These disorders are thought to have arisen from abnormalities in cognitive processing that are mainly the result of some biological dysfunction; and are more common in boys than in girls. These children experience academic failure, often irregular schooling, difficulties in social adjustment and this is more pronounced in the later years of primary school or secondary school.

Specific learning difficulties are more common in people with ADHD than in the general population [15]. A meta-analysis of previous research has concluded that the prevalence is 45% [16]. These children have greater learning difficulties than children who have only specific learning difficulties.

Children with ADHD and specific learning difficulties have a problem processing perceived information, difficulty reproducing words, sentences and letters, auditory discrimination, difficulty reproducing drawings (visual-motor discrimination), stringing letters, decoding letters or words [2]. Children with this comorbidity will have lower academic achievement, poorer grades in school, will drop out of high school more often, and will continue their education after high school less often than their peers without ADHD [5].

2.3 Comorbidity with mood disorders

The main disorder in mood disorders is a change in mood or affect, in the sense of the presence of low mood or excessively good mood. A change in mood is usually accompanied by a change in the overall level of functioning. Most of these disorders show a tendency to recur. The onset of individual episodes is often associated with certain stressful events.

Children and adolescents diagnosed with ADHD often have mood disorders at the same time, most commonly having major depressive disorder, depressive episodes, and bipolar disorder. Arnold et al. conducted a Longitudinal Assessment of Manic Symptoms and concluded that 60% of the sample met the criteria for ADHD, 6.3% met the criteria for bipolar disorder, 16.5% had both ADHD and bipolar disorder. 17.5% do not have either of these two disorders [17]. Otherwise, the results of research in this area are uneven, so in population samples the prevalence is 0–2%, while in clinical samples it is 11–30% [18]. A special problem is the diagnosis, differential diagnosis and treatment in children who have ADHD and mania. ADHD is more common in children, especially in boys, compared with bipolar disorder, which occurs in 1.8% of children and adolescents, and is somewhat more common in boys [19]. Comparing the symptoms of mania and ADHD, a high percentage of grandiosity is noticeable in mania (85%), while in ADHD it is only 6.7%. Elevated mood and bold behaviors occur in a high percentage in mania (87% and 79%, respectively), and in a very low in children with ADHD. Results from regression analyses suggest cognitive predictors of executive functioning impairment in ADHD and mood predictors for inhibition in pediatric bipolar disorder [20].

Comparing the symptoms between these two diseases in childhood, it is noticed that irritability is very pronounced in mania, and occasionally exists in ADHD; euphoria is excessive in mania, and situational in ADHD; children with ADHD have low self-esteem, while mania has a pronounced grandiosity; manic children have a reduced need for sleep, while children with ADHD resist going to bed but then sleep well; children with mania have a rapid flow of thought, while ADHD does not. In comorbidity, treatment preference is given to symptoms of high mood and therapy is primarily focused on mania (mood stabilizers or antipsychotics); while ADHD symptoms are treated secondarily, after mood stabilization.

One of the mood disorders that occurs in child psychiatry is depression. Studies in this area indicate that the prevalence of depression in children with ADHD is 18%, and another 15% had both comorbid anxiety and depressive disorder [21]. The presence of depression worsens the symptoms and functioning of children with ADHD, and also significantly worsens the prognosis and therapeutic process in these children.

Adolescents who have a comorbidity of ADHD and depression have more pronounced difficulties in social functioning, get depression at an earlier age, have a higher rate of suicidal behavior, more frequent recurrence of depressive episodes compared to adolescents who suffer only from depression. Also, these adolescents have more frequent family dysfunction, more frequent conflicts in family relations, they have experienced more negative life events and traumatic experiences compared to adolescents who have only ADHD.

2.4 Comorbidity with anxiety disorders

The prevalence of anxiety disorders in the general pediatric population is between 4% and 20%, while the prevalence of anxiety disorders in children with ADHD is 25% [22]. Clinical and epidemiological studies have shown that one-third of children with ADHD have some of the anxiety disorders at the same time. While some authors believe that there is no statistically significant difference between girls and boys in ADHD comorbidity and anxiety disorder, other authors state that 17.6% of girls and 17.9% of boys have comorbid ADHD disease with anxiety or depressive disorder [8]. Children suffering from anxiety disorder have higher rates of ADHD [5].

2.5 Comorbidity with the autism spectrum disorder (ASD)

Autism spectrum disorder refers to serious developmental disorders with specific patterns of communication and social interactions. These disorders have differences in the specificity and severity of symptoms, age of onset, level of functioning, and forms of social interactions.

Autistic children often have attention problems and information processing problems that lead to social deficits. In clinical samples, it is estimated that about 10% of children tested for ADHD have some comorbid disorder from the autism spectrum disorder [9] characterized by more pronounced hyperactivity and impulsivity. ADHD is diagnosed in the autism spectrum disorder when the symptoms are very pronounced and permanent with the prior exclusion of medical and other psychiatric conditions that may mimic the symptoms of ADHD. In the treatment of ADHD comorbidities with autism spectrum disorder, the symptoms of both disorders must be treated.

2.6 Comorbidity with specific developmental speech and language disorders

In specific developmental disorders of speech and language, there is damage to the normal patterns of speech acquisition from the early stages of development. These disorders are often accompanied by associated problems such as reading difficulties and interpersonal relationships, emotional problems, and behavioral problems.

Some children who have ADHD also have language difficulties, which are present in both receptive and expressive language. There are also difficulties in other language skills. The results of research on the frequency of these comorbid diseases are different. Recent study estimated 50% of children with ADHD have a comorbid language deficit, while 20 to 60% of children with ADHD have one or more learning disabilities or language problems [23]. Study from 2016 identified language impairments in the majority within the ADHD and reading disorder in >40% in children with ADHD [24]. A group of authors concluded in a 2013 study that children with ADHD exhibit various difficulties in pragmatic language [25].

2.7 Comorbidity with epilepsy

Epilepsy is a chronic brain disease characterized by recurrent epileptic seizures, accompanied by various clinical manifestations and laboratory abnormalities. Important features of epilepsy are chronicity and recurrence of excessive paroxysmal discharge of brain neurons that manifest as epileptic seizures.

Studies in children with ADHD have shown a significant risk of developing epilepsy and other seizures in these children. A study by a group of Norwegian authors in 2013 found that children with ADHD had 2.3% risk of epilepsy, which is four times higher than the general prevalence in children of 0.5% [26]. Previous research has also found a significant association between childhood ADHD and the risk of epilepsy. Epilepsy and ADHD are strongly associated although the underlying factors contributing to their co-occurrence remain unclear [27]. The same study suggests that epilepsy and ADHD share less genetic risk factors as compared with other neurodevelopmental disorders.

Children with ADHD often have irregularities in EEG findings, and an increase in frontal-central theta-wave activity is most common [28].

2.8 Comorbidity with sleep disorders

Inorganic sleep disorders can also occur in children of any age. The most common sleep disorder in children is a sleep–wake cycle disorder, i.e. waking up during the night. This is also the most common reason that worries parents and why they seek professional help. The next most common disorder is when the child delays going to bed, cannot fall asleep when put to bed or when constantly asking for parental attention. Other sleep disorders are less common in children.

Children with ADHD often have difficulty sleeping in the form of frequent waking at night, resistance to going to sleep, they need to fall asleep for a long time. Sleep disorders are more likely to occur if children with ADHD also have some anxiety disorder compared to children who have only ADHD [29]. In observational study in a population of children with ADHD, 63% had moderate or severe sleep problems [30].

Parents of children with ADHD also report that children have difficulty sleeping, resist going to bed, sleep shorter, and often wake up at night. Parents describe these children as tired after waking up compared to children without ADHD [31]. Studies investigating event–related potential (ERP) suggest impaired ability in children with ADHD to conserve the brain oscillations phase associated with stimulus processing [32]. Children with ADHD presented more sleep disturbances when compared to children without the diagnosis. These disorders were diverse, yet inconsistent among the surveys [33].

2.9 Comorbidity with tic

Tic is a sudden, fast, involuntary, aimless and repetitive muscle movement, limited to a certain muscle group or accompanied by vocalization, which worsens in stressful situations and disappears during sleep. Tic disorders are divided into transient and chronic motor or vocal and Tourette's syndrome. There is an irresistible need to repeat the action, and its prevention causes tension. Tick disorders are associated with poor self-esteem, problems in the family environment, difficulties at school. Children and adolescents with tics have a number of other problems such as speech or behavior problems, impulsivity, hyperactivity, obsessive compulsive symptoms. The prevalence of transient and simple tics is 20% in the pediatric population, and chronic motor tics and Tourette's syndrome about 3% [34]. Children with ADHD were 4.1 times more likely to have chronic tic disorder at age 7, and 5.9 times more likely at age 10 [35]. Children with ADHD and chronic tic disorder experienced higher rates of peer problems, and poorer quality of life than those with ADHD alone. Episodes of anger and aggression have been reported in children with tic disorders and are likely to contribute to psychosocial stress and low quality of life. It is assumed that aggressive behavior in children with tic disorders is associated with comorbid attention-deficit hyperactivity disorder [36].

2.10 Comorbidity with neuroophthalmological disorders

Ophthalmological examination of children and adolescents with ADHD is part of their evaluation as it is important to rule out underlaying ocular and neurological conditions that may cause behavioral aberrations. Some children with visual impairment may be misdiagnosed as ADHD. These children are not able to see adequately and in result are not able to keep their attention being focused on object of observation. To our knowledge, there are small number of studies investigating the relationship between ADHD and ocular disorders such as amblyopia, hypermetropia, astigmatism, and heterotropia. Children with amblyopia have greater risk

of developing ADHD than their counterparts without amblyopia (1,8 times; hazard ratio 1.81; 95% confidence interval 1.59–2.06) with the greatest risk in amblyopic children with deprivation type, followed by strabismic type and refractive type (hazard ratio 2.14; 95% confidence interval 1.56–2.92; hazard ratio 2.09; 95% confidence interval 1.15–3.79; hazard ratio 1.76; 95% confidence interval 1.54–2.02 respectively). Also, amblyopic children with ADHD tend to be diagnosed at younger age than those without amblyopia (median 8.14 vs. 8.45 years; P = 0.0096) [37].

Large cross-sectional study on 75,171 children without any intellectual impairment reported greater prevalence of ADHD among children with vision problems ($p < 0.0001$). Children with vision problems were more likely to have been diagnosed with ADHD than those without vision problems (15.6% vs. 8.3%; $p < 0.001$). Children with vision problems were also more likely to have ever been diagnosed with ADHD (18.6% vs. 10.4%; $p < 0.001$) [38].

Another large-scale cross-sectional study on 116,308 children with ADHD reported significant higher prevalence of ocular disorder in children with ADHD compared to children without ADHD: amblyopia (1.6% vs. 0.9%, $p < 0.001$), hypermetropia (2.4% vs. 1.3%, $p < 0.001$), astigmatism (0.2% vs. 0.1%, $p < 0.001$), and heterotropia (1.1% vs. 0.5%, $p < 0.001$) respectively [39].

Recent studies investigated relationship between ADHD and convergence insufficiency as symptoms of convergence insufficiency may overlap with those of ADHD. Within population of children with convergence insufficiency, three-fold greater incidence of ADHD is reported compared to ADHD incidence in general population. Also ADHD population had three-fold greater incidence of convergence insufficiency [40]. Children with ADHD had significant low near point convergence as well [41].

2.11 Treatment of comorbidities

Comorbid diseases often occur in children and adolescents with ADHD. It is estimated that about 66% of ADHD patients have at least one comorbid disorder, and the most common are learning disorders, sleep disorders, oppositional defiant disorder and anxiety disorders [42]. Treating children and adolescents with ADHD who have comorbid conditions is a challenge for clinicians [43].

When it is necessary to include medications in children with ADHD, existing guidelines suggest starting with a stimulant (methylphenidate MPH or amphetamine AMP). If the stimulant does not achieve an effect then an alternative stimulant is used. If stimulants are not effective or cause more severe side effects, we include nonstimulants (atomoxetine, alpha-2 agonists, and antidepressants) [44]. Stimulants have been approved by the Food and Drug Administration (FDA) in the treatment of ADHD, including methylphenidate and dextroamphetamine and amphetamine mixed salts, and these drugs act by blocking the reuptake of dopamine and norepinephrine into neurons. Side effects including insomnia, headache, changes in appetite, weight loss/gain, irritability and tics should be monitored during treatment with stimulants. Stimulants are the first line in treatment. Non-stimulants (atomoxetine, alpha-2 agonists, and antidepressants) are less effective than stimulants. Children with complicated epilepsy may be at greater risk for ADHD, and some antiepileptic medications may contribute to ADHD symptoms. Tricyclic antidepressants have been used in children with ADHD but can lower seizure threshold and should be avoided in patients with epilepsy. Methylphenidate is effective in treating the symptoms of ADHD in children and adolescents with epilepsy, but the effectiveness is less than that seen in children with ADHD without epilepsy [44].

The comorbidity of ADHD with bipolar disorder (BD) may be associated with more severe symptoms, poorer course, and poor outcome of both conditions, and

treatment is further complicated if there is substance abuse [45]. The use of stimulants may be contraindicated in the presence of comorbid drug abuse. Atomoxetine may be effective in treating the symptoms of ADHD in patients with bipolar disorder when used in conjunction with mood stabilizers.

In children with ADHD comorbidities and sleep problems, sleep hygiene and cognitive-behavioral psychotherapy are important, and consideration should be given to changing the dosage and formulation of the stimulant. The use of atomoxetine and melatonin are therapeutic alternatives for children with ADHD and more severe sleep problems [46].

Psychopharmacology is the primary treatment for ADHD, and behavioral treatment is used in combination with medication or in children with minimal impairment or when medication is not possible due to contraindications or parents 'refusal to accept medication. Most guidelines recommend a stepwise approach to treatment, beginning with non-drug interventions and then moving to pharmacological treatment in those most severely affected [47]. In large birth cohort study, where a great majority of children with ADHD used medication, only child characteristics were significantly associated with the use of medication [48]. In this study the authors concluded that the small differences between medicated and unmedicated children, might be due to strong established clinical practices where medication is offered as a treatment option, particularly for hyperkinetic conduct disorder in an egalitarian high-income society.

In a large meta-analysis that included 38 individual studies with 5111 participants aged 3 to 18 years, the authors concluded that methylphenidate may improve teacher-reported ADHD symptoms, teacher-reported general behavior, and parent-reported quality of life among children and adolescents diagnosed with ADHD [49].

Treatment of comorbid diseases in children with ADHD should be multimodal, including pharmacological and nonpharmacological interventions. It is important to recognize the presence of comorbid disease in these children because comorbid diseases complicate the diagnostic and therapeutic process, as well as the outcome of the disease.

3. Conclusion

Attention Deficit Hyperactivity Disorder is a neurobiological disorder that involves the interaction of the neuroanatomical and neurotransmitter systems. This disorder is characterized by early onset, the association of hyperactive and poorly coordinated behavior with marked inattention and lack of perseverance in performing tasks; and this behavior occurs in all situations and persists over time. Most children and adolescents with Attention Deficit Hyperactivity Disorder have comorbidities, often multiple comorbid conditions in the same person. It is estimated that about two-thirds of children with this disorder have at least one other psychiatric disorder diagnosed. Symptoms persist and lead to significant difficulties in the daily functioning of the child, such as school success, social interactions, family and social functioning. The presence of comorbidities is significant because it complicates the diagnostic process, affects the course, prognosis and therapeutic process. Assessment and support in comorbid disorders are often as important as the assessment and treatment of ADHD symptoms.

Conflict of interest

The authors declare no conflict of interest.

DOI: http://dx.doi.org/10.5772/intechopen.94527

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