

Current view on treatment of attention deficit hyperactivity disorder in adolescents

Cholewa K.^{1, A, B,C,D,F}, Wysokińska O.^{1,A,B,C,D}, Zaremba B.^{1,B,C,D}, Siwek M.^{1,D,F}, Jańczyk M.^{1, E}, Łopuszańska U.^{2,E}

1. Students' Scientific Club Department of Applied Psychology, Medical Univeristy of Lublin, Poland
2. Department of Applied Psychology, Medical University of Lublin, Poland

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ABSTRACT

Diagnosis of attention deficit hyperactivity disorder (ADHD) in adolescent patients may be problematic, because of the broad spectrum of symptoms. Population research display heritable character. The function of dopaminergic, adrenergic, and serotonergic systems is disordered in different ways in patients, who suffer from this disease. **Purpose:** The aim of this article is to show the actual view on the treatment of attention deficit hyperactivity disorder in teenage patients. **Results:** In the treatment of ADHD the most important thing is pedagogical therapy as well as cooperation of parents and medical crew. In some particular cases pharmacologic treatment should also be included in therapeutic process, which is described in this review. Methylphenidate is the most frequent drug

used in the treatment and that is why we focused on the complex description of the substance. **Conclusions:** Teachers and the school responsible for teaching these children must adapt didactic methods to the severity of the disorder. It is valuable to conduct the drug in the therapy of teenagers whose parents ready to cooperate, always with psychiatric supervision. In the process of pharmacotherapy, it is crucial to include breaks, for example during vacations. Psychostimulants are highly addictive substances, which is why many researchers are uncertain about the routine prescription of methylphenidate. **Keywords:** ADHD, methylphenidate, adolescents, psychotherapy, pedagogical therapy

DOI:

***Corresponding author:**

Krystian Cholewa
Krańcowa 110/51
20-320 Lublin, Poland
Tel. 698661781, e-mail: krystiancholewa1@wp.pl

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INTRODUCTION

Attention deficit hyperactivity disorder (ADHD), is a neurobiological disorder with unknown, multi-aspect ethology. The diagnostic criteria contained in ICD-10 and DSM-5 are currently mainly used to diagnose ADHD. The determinants in both classifications differ from each other (in ICD-10 they are more stringent) and each of them distinguishes other subtypes of the disease [1,2]. Diagnosis is based on the information about the patient's symptoms obtained from parents, caregivers or the patient himself, using appropriate questionnaires, as well as patient observations. Recommendations require the occurrence of symptoms up to the age of 12. Many times diagnostic process is more difficult in case of older patients [1]. Therefore, in adults, the most common is diagnosed with ADHD, when a patient comes to consult with a child diagnosed with a disorder, he or she reports to a specialist because of another illness or a coincidence [1]. Pharmacological, psychotherapeutic and pedagogical interactions are common used to treat ADHD. Each of the methods has its own indications and limitations. Choosing the right treatment is difficult without a proper interview and without additional tests. It is necessary to thoroughly understand the etiopathogenesis and characteristics of therapeutic methods.

ETHIOPATHOGENESIS AND EPIDEMIOLOGY OF ADHD

The etiopathogenesis of ADHD is still under investigation and is not fully understood [1]. The reason of doubts is the problem with subtyping characteristics symptoms, which allow to distinguish ADHD from other mental and somatic disorders [1]. It is familial disease with high rate of heritability (76%) [2,3]. It was demonstrated that there are connections between disorders in dopaminergic, adrenergic and serotonergic systems and ADHD [4]. Abnormalities are associated with genes, which code receptors for dopamine: DRD4, DRD5, DAT1 and receptors for serotonin: 5HTT, HTR1B [5]. Moreover it seems that there is an impact of mutation in gene SNAP-25 on development of disorder. That gene codes protein which takes part in discharging and stores up catecholamines and growth of axons [4]. It was established that are associations between illness and changes in chromosomes 5p13, 6q, 7p, 9q, 11q, 12q and 17p [1].

Abnormalities in pregnancy and in early child's development may have an impact on occurring of ADHD symptoms. Reports indicate on following pre- and postnatal risk factors: low birth weight, preterm birth, smoking cigarettes and drinking alcohol by mother [3]. Moreover the other

risk factors are poor nutrition of mother during pregnancy and breast-feeding perinatal complications like hypoxia and ischaemia of the child brain [6,7]. Symptoms of the disability can intensify as results of poor nutrition with deficit of ingredients, which are necessary to proper development of child nervous system: folic acid, omega-3 fatty acid, magnesium, zinc [1,6].

In patients with diagnosed ADHD were observed morphological changes in the striate body, basal nucleus, cerebellum (especially in the vermis of the cerebellum), and probably in the hippocampus and amygdaloidal body [1,2]. In addition, the decrease of the volume of grey matter in frontal, temporal, and occipital areas was detected as well as lower metabolic activity in frontal and prefrontal areas, caused by diminished uptake of glucose [2]. The aforementioned changes in the functioning of the brain result in cognitive and emotional dysfunctions such as attention deficit, interferences in non-verbal memory, difficulties in interpreting experiences from the past, problems with emotion regulation and motivations, emotional inadequacy, impulsivity in taking decisions, lack of planning skills or speech disabilities [2,7,8]. Disturbances in the development of the kinesthetic sphere can be also observed, for example, inability to stay in immobility for short time and increased associated movements.

The clinical picture of ADHD changes with age. Younger patients have greater impulsivity and overactivity, while older people have more severe problems with attention deficit [2]. Research shows that in one third of patients entering adulthood, ADHD symptoms are completely alleviated, in another 1/3 partially alleviated, and in the remaining group the symptoms disappear completely [2].

ADHD is associated with a deterioration of the quality of life, both in professional and private life. However these problems do not mainly result from the lack of intellectual skills, but from the inability to use them. It has been proven that patients with ADHD are more likely to enter the criminal path, they are less likely to marry, and usually become addicted to intoxicants [2]. There are also many cases of co-morbidities, including somatic diseases related to inappropriate lifestyles, such as coronary heart disease or primary hypertension, and mental disorders, including depression (more often in women) or anxiety disorders [1,2].

Studies also suggest partial overlap of ADHD symptoms with other neurodevelopmental disorders like autism spectrum disorders (ASD) and personality disorders such as borderline, histrionic and narcissistic [1,2,3]. Among this group of patients frequency of suicide attempts is higher than in general population. Differentiation of ADHD

from other diseases or personality disorders can be a serious issue [1,2].

In addition, it has been shown that regardless of pharmacological treatment or social status, ADHD is a growing risk factor for overweight (by 50% higher than in healthy people) and obesity (by 40% higher) [9,10]. It is estimated that the prevalence of ADHD in school-age children is 3-10%, while in adults 4.4% [2,11] 2/3 of all patients are expected to remain undiagnosed.

PHARMACOTHERAPY OF ADHD

Pharmacotherapy in the treatment of ADHD is used when psychotherapy does not bring expected effects or there are persistent. Adding drugs to for example behavioral therapy may be advised if the target behaviors are not improved by the psychotherapy and the child's functioning continues to be impaired. At least 80 percent of ADHD children will answer to psychostimulants pharmacotherapy [12]. However, it is still not clear whether psychostimulants have long-term positive effects on the child's concentration skills, school scores, behavior, or emotional aspects.

According to National Consultant before starting pharmacotherapy, patient as well as his family, carers and teachers must take part in the psychoeducation. Before ADHD treatment various available methods of psychotherapy must be considered. If the patient suffers from hyperkinetic disorders and severe functional disorders, pharmacotherapy should be started immediately. The following drugs are used in the therapy of this disease: psychostimulants; selective norepinephrine reuptake inhibitors (atomoxetine), tricyclic antidepressants (e.g. imipramine, amitriptyline, desipramine, clomipramine), alpha-mimetics (clonidine), bupropion, other typical antidepressants (moclobemide, venlafaxine), neuroleptics (risperidone) [13]. To make the right choice of the drug, a number of factors should be considered, for example: the patient's state of health (both somatic and mental), comorbidities, severity of symptoms and their impact on patient's functioning, the occurrence of other disorders related to ADHD (epilepsy, tic disorders), duration of action of the substance, possible side effects, the ability to ensure regular intake of specific doses, assessment of the risk of using the drug for non-medical purposes, preferences of children and parents [14]. The goal of ADHD pharmacotherapy is to achieve stabilization and improve the functioning of the patient, but the completely cure is not always affordable. Pharmacotherapy should be under doctor's constant control. The effectiveness of treatment should be assessed as well as the patient should be examined for side effects. In the treatment of ADHD in children and adolescents there is no need to apply a combination of drugs,

monotherapy is highly recommended. It is necessary to change the drug, if the expected improvement is not achieved in the expected time or serious side effects occur. The first choice in ADHD therapy from all of the considered drugs are psychostimulant drugs. The effect of psychostimulants is to increase the release of dopamine and inhibit the re-uptake of serotonin and catecholamines. As a result, the coordination of incoming impulses in the prefrontal cortex improves, which for the patient means better concentration, easier focusing as well as reduction of excessive mobility and impulsiveness. The characteristic feature of psychostimulant drugs is that their action starts in a short period of time from the patient's intake, while in case of withdrawal they stop working quickly. It is proven that the effectiveness of this group of drugs in the treatment of ADHD reaches 80 percent and is significantly depended on dose [12].

Before starting treatment, the patient's circulatory system especially blood pressure and heart rate must be checked. It is also necessary to obtain information about the medicines taken by the patient, accompanying physical and mental disorders as well as cases of sudden cardiac death (SCD) in the patient's relatives. The interview should contain detailed measurements of height and weight taken before the beginning of treatment and these data must be applied on centile charts. The absolute contraindications to the use of Medikinet include hypersensitivity to the active substance, glaucoma, pheochromocytoma, use of non-selective and irreversible MAOI - monoamine oxidase inhibitors, hyperthyroid, thyrotoxicosis, persistent disorders of the cardiovascular system and cerebrovascular vessels, mental disorders such as severe depression, schizophrenia, psychosis. It is important to continuously monitor mental state, condition of circulatory system as well as patient's height and weight. After each dose modification blood pressure and heart rate score should be noticed on the a percentile grid. Once the a dose has been determined, measurements should be made at least every 6 months, as well as the assessment of height, weight and-level of appetite. Patient should be also observed in case of occurrence previously absent mental disorders or deterioration of patient's condition. It is also necessary to check patient for the risk of skipping doses or for abuse of methylphenidate for other than therapeutic purposes [15].

Studies showed that ADHD diagnosed patients have an increased number of dopamine active transporter (DAT). The mechanism of action of methylphenidate is based on the blockade of noradrenaline DAT, which are responsible for reuptake of these neurotransmitters from the synaptic gap, as well as increasing the release of monoamines by presynaptic neurons. As a result,

cerebral cortex structures of the brain are stimulated and what is more reticular formation is also activated. An increased influence of the drug on the psyche was observed, compared to physical activity [16,17]. The use of Methylphenidate in children and adolescents allow to reduce an excessive mobility and impulsiveness and what is important it improves concentration skills, which result in better patient's behaviour both at home and school. Such treatment also prevents the appearance of behavioural disorders that often co-occur with ADHD.

The characteristic fact about Methylphenidate is that this drug is highly and rapidly absorbed from the tablets. Because of extensive first-pass metabolism, the absolute bioavailability attains only 30 percent. Ingestion with food causes an increase in the extent of absorption. Peak plasma concentrations of the active substance are reached approximately 1-2 hours after the oral administration of a 10 milligrams dose of the drug. Levels of maximum plasma concentrations are characterized by significant inter-individual variability, but this probably does not affect therapeutic efficacy. Methylphenidate is eliminated from the plasma with a half-life of 2 hours. As a result, it is possible to adjust the time of administration to the patient's activity during a day. It is recommended to take the drug just before the start of school activities, to improve the child's functioning and concentration skills while it is the most desirable [15].

Methylphenidate and its metabolites are not significantly bound to plasma proteins. Biotransformation of the drug is rapid and intense. Cytochrome P450 is not clinically significant involved in the metabolism, therefore it is assumed that Methylphenidate does not significantly affect the metabolism of other drugs taken in the same time by the patient. About 78-97 percent of the dose is excreted with the urine during 48-96 hours, the rest is removed with the faeces. Studies has shown that there is limited renal excretion of methylphenidate metabolites in patients with impaired renal function. There were no apparent differences in the pharmacokinetics of methylphenidate between hyperactive disorder children and healthy adults [15].

Methylphenidate treatment should begin with the recommended dose of 5 mg once or twice per 24 hours and may be taken for example during the a breakfast and a lunch. If necessary the dose may be increased every week by 5-10 mg per 24 hours. The daily dose needed to achieve the desired symptoms control should be as low as possible. To avoid problems with falling asleep a 4-hours sleep-time interval should be kept. It is important to not to exceed the maximum daily dose of 60 mg.

The pharmacotherapy with methylphenidate is usually continued until patient reaches

puberty. In case of continuing therapy in children and adolescence for more than 12 months, it is necessary to periodically verify the advisability of pharmacotherapy, as well as to evaluate functioning during the withdrawal attempt. It is recommended to adjourn methylphenidate during the holiday period to evaluate patient's health and eventually make decision to end the pharmacotherapy [15].

However, if after proper dose adjustment no reduction in disease symptoms is observed during one month the treatment should be terminate. In case of worsening patient's condition and intensifying symptoms of the disease or severe side effects, a dose reduction or suspending therapy is recommended. The most common side effects of Methylphenidate are:

- nausea and lack of appetite which can lead to inhibiting weight gaining (or even decrease);
- slowdown of growth (average 0,1-0,2 cm/year);
- sleep disorders (mainly problems with falling asleep);
- nervousness,

Table 1 – Examples of situations in which the drug may be justified for preschool children are headaches and dizziness; increase of blood pressure (both systolic and diastolic blood pressure observed in the studies was over 10 mmHg) [15] and heart rate; drop of the convulsive threshold; the appearance of tics; occurrence of rebound effect – irritability after significant dose reduction or suspending of the drug.

PSYCHOTHERAPY AND PSYCHOSOCIAL ASPECT OF TRETMENT OF ADHD

The occurrence of ADHD in childhood can have a significant impact on academic achievements, well-being and social interactions among children. Therefore, behavioural treatments are usually recommended for pre-schoolers.

It is recommended to use cognitive - behavioural therapy alone, in pre-school children who are not in the risk group described in table 1.

Provided that parents cooperate closely with the child's doctor and therapist, because care for a child with attention deficit must be coordinated properly.

Cognitive-behavioural therapy is indicated for the acquisition of organizational and planning skills. It also relieve coexisting psychiatric problems in adolescents with ADHD and is recommended during pharmacotherapy [18].

Psychotherapeutic interventions are helpful in coping with co-morbidities or skills deficits. Play-based interventions improve social skills in children with ADHD [19].

Table 1. Examples of situations in which the drug may be justified for preschool children are [20]

● Expulsion (or threat of expulsion) from kindergarten
● A significant risk of injury to other children or child carers
● A high prevalence of ADHD in family ancestors
● Suspected or confirmed damage to the central nervous system (eg Prenatal exposure to alcohol or cocaine)
● ADHD symptoms interfere with other therapy needed

Treatment strategies for children with ADHD depend on age. In addition, research results indicate that the effectiveness of treatment of children is closely related to the school conditions in which they attend. Profits achieved due to psychotherapeutic interventions are usually not higher than environmental impacts in the classroom or at home.

It is very important to give parents and the child clear therapeutic goals, and then monitor the course of the therapeutic process. If the chosen management strategy does not achieve the target result, the original diagnosis, co-existing conditions and compliance with the management plan should be re-evaluated [20,21]. Symptom management techniques are presented in Table 2.

Table 2. Behavioural therapy and environmental changes can be used by parents or teachers to master the behaviour of children with ADHD [24]

● Keeping the daily schedule
● Limiting the interruptions to minimum
● Providing children with specific and logical places to keep school supplies, toys and clothes
● Setting small, achievable goals
● Rewarding positive behaviours (e.g. with "symbolic economics")
● Identification of unintentional reinforcement of negative behaviours
● Using charts and checklists to help your child stay "on the task"
● Limiting choices
● Finding activities in which a child can succeed (e.g. Hobby, sport)
● Using quiet discipline (e.g. Time limit of entertainment)

The research results show that one-third of children with ADHD have one or more coexisting conditions: learning disabilities, oppositional and rebellious attitudes, behavioural disorders, anxiety disorder, mood disorders, tics, sleep disorders [22].

Generally, psychotherapeutic interventions are not suggested in children with ADHD, unless they have coexisting states requiring psychotherapeutic interventions, e.g. depression, anxiety, social deficits. In randomized studies and systematic reviews, psychotherapeutic interventions did not prove beneficial for the basic symptoms of ADHD in children [23].

The research results show that modern guidelines for the treatment of children with attention deficits are effective. Children were examined using the KIDSCREEN-52 quality assessment questionnaire (version for children).

Currently in the treatment of the disease families simultaneously use alternative therapeutic methods, which include massage, support groups and biofeedback.

Supplementary and alternative therapies (CAMs) that have been tried in ADHD include eye training and special diets (e.g. avoiding sugar and

allergens, preservatives and dyes), megavitamins, herbal and mineral supplements.

However, the studies did not confirm the benefits of these treatments, and the risk was not well understood. An important concern is the failure of treatment that will cause a child's sense of failure. Another risk includes high costs; CAM therapies are not covered by health insurance.

Elimination diets for children with ADHD are not proposed, but decisions on dietary intervention for disease must be made on a case-by-case basis. Some experts suggest that short (no more than five weeks) use may be justified for some children (e.g. those whose carers are concerned about the use and potential side effects of pharmacological agents and are motivated to comply with the diet) [24,25]. If a decision is made to apply an elimination diet, it should be overseen by the child's health care and dietetics to ensure adequate intake. If the behaviour improves during its use, limited food can be added back once a week, one item, to identify problem foods that should be excluded from the less restrictive menu.

The impact of nutrition on attention, hyperactivity and behaviour is controversial.

According to studies, dietary factors, e.g. food additives, food allergy or intolerance, etc.; in general, they do not affect the behaviour advantageously in the majority of ADHD cases. However, a small percentage of children may exhibit mild adverse behavioural effects in response to specific nutrients and an improvement of behaviour after elimination of these products is observed [26].

CONCLUSIONS

The choice of treatment method must be preceded by an analysis of all patient's problems. Treatment must be carried out in accordance with the latest international standards that are constantly evolving.

Individual psychotherapy is not recommended as a basic form of helping children with attention deficit hyperactivity disorder. However, it is crucial to involve the child's family in the treatment process because they are the key link in therapy. Teaching children with ADHD should include didactic methods applied to the severity of the disorder.

Some people have an increased number of transporters for dopamine in the brain, this is an explored biological difference in this group of patients. Therefore, drugs should be used in children with attention deficit hyperactivity disorder, but this therapy must be strictly supervised by a psychiatrist. Not every child with this disorder requires pharmacotherapy. However, for many patients, this is the only option that will allow them to use their intellectual potential.

The fact of the occurrence of biological diversity in some children raises the question - in what another way than clinical observation, decide on the introduction of pharmacotherapy?

Is the use of functional tests a way to accurately diagnose?

In addition, the familial occurrence of the disorder is observed and the role of genetic factors is increasingly emphasized. These connections are not routinely tested and the treatment is not personalized. Clinicians operate on therapeutic standards established from above, and in them, there is a lack of important issues regarding the examination of the patient's biological structures.

As you know, psychostimulants are highly addictive substances, which is why many researchers are uncertain about the routine prescription of methylphenidate

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Conflicts of interest

The authors declare no potential conflicts of interest.

ORCID

Cholewa Krystian: 0000-0002-1310-1615

Wysokińska Olga: 0000-0002-9679-9958

Zaremba Bartłomiej: 0000-0002-3255-2745

Siwek Michał: 0000-0002-0930-9333

Jańczyk Magdalena: 0000- 0001-6517-7577

Łopuszańska Urszula: 0000- 0002-4948-9463

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