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Adherence: Its Role in Achieving Asthma Control in Children

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The article is devoted to the actual problem of modern pediatrics and neurology — a comprehensive diagnosis and correction of sleep disorders in children. The features of clinical manifestations of sleep disorders in childhood (insomnia and parasomnia) are reviewed in detail, great attention is paid to sleep the apnea syndrome as a risk factor for somatic and psychopathological disorders in children. The current capabilities of complex instrumental diagnosis of sleep disorders with the use of highly effective methods of polysomnography and pulse oximetry are highlighted, as well as the actual dimensions of non-drug and drug treatment of sleep disorders in children, taking into account the pathogenetic features of their occurrence. From the standpoint of evidence-based medicine we have demonstrated efficient methods of herbal medicine, developed on the basis of traditional Chinese recipes, as well as modern nootropics and magnesium preparations. It is shown that sleep disorders in children not only lead to a deterioration of the emotional mood, cognitive function, health and school performance, but also are associated with increasing risk of somatic disorders, which determines the need for timely diagnosis and comprehensive differentiated medical and psychological data correction of pathological conditions, taking into account the neurophysiological and biochemical mechanisms of their development, as well as polymorphism of clinical manifestations, in order to increase the effectiveness of treatment and quality of life of patients.
Key words*: sleep, children, polysomnography, insomnia, parasomnia, sleep apnea, melatonin, phytotherapy, infants.*
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RELEVANCE

Allergic diseases present one of the most important medical and social problems. They rank fourth in the world among the major chronic diseases (according to the World Health Organization); they cause a serious burden for the public health budget [1, 2]. Adversely affecting the physical and psychological state, social life and school performance, they reduce the quality of life of both the patients and their families [1 - 7]. The widely used term "atopic march" confirms the evolving nature of the allergy course: having started in childhood, this pathology accompanies the patient throughout their lives.
In recent years there has been an increasing tendency in the number of patients suffering from respiratory allergies – bronchial asthma and allergic rhinitis [2, 5, 8, 9], which is caused by many

factors, including the changing microenvironment, influence of unfavorable eco-environmental factors and impaired immune response to external and internal antigens.

BRONCHIAL ASTHMA

Bronchial asthma (BA) - heterogeneous in nature and variable in its course - is characterized by chronic inflammation and is associated with transient and changing airway obstruction and bronchial hyperreactivity. It is manifested by recurrent episodes of hissing respiration, coughing, shortness of breath and chest tightness [2 3 5, 10].

The basic goal of asthma therapy for patients of any age is to achieve control over symptoms and to minimize the future risk (of developing both exacerbations and adverse effects) [2, 35, 10].

At the present stage, the most preferred and common dynamic asthma criterion is the control level [3, 5, 10]. Control means locking the disease symptoms using adequate basic anti-inflammatory therapy. In clinical practice the achievement of control - the main goal of asthma treatment - consists of such components as the degree of control over existing symptoms and risk assessment of disease progression.

The degree of control over existing symptoms (assessment of current clinical manifestations) includes [3, 5, 10]:

- severity of daytime and nighttime symptoms;
- the need for short-acting β2-agonists (SRBA);
- limitation of physical activity.

Assessment of future risks consists of determining both the potential risks of exacerbations and progressive disorders of the pulmonary function up to fixed pulmonary obstruction, as well as the side effects of therapy. It should be remembered that the future risk not always depends on the current symptom control, but poor control increases the risk of exacerbation [10].

Risk factors of BA exacerbations:

- intubation in anamnesis;
- uncontrolled symptoms;
- presence of ≥ 1 exacerbation during the past 12 months;
- reduction of forced expiratory volume by 1 s (when determining the parameters of respiratory function at the beginning of therapy; to achieve best results - every 3-6 months, and periodically thereafter);
- improper inhalation technique and / or poor adherence;
- smoking, obesity, eosinophilia.

Risk factors of a persistent decrease in respiratory function indicators:

- absence of treatment with inhaled glucocorticoids (IGCC);
- smoking;
- eosinophilia.

Risk factors of adverse effects:

- frequent oral glucocorticoids courses;
- high dose / powerful IGCC;
- P450 inhibitors.

A simplistic asthma control estimation algorithm is shown in the table. [3, 5, 10].

Treatment adherence

An integrated approach to treatment in case of a confirmed “bronchial asthma” diagnosis includes a number of components [3, 5, 10]:

- medicamental therapy;
- impact on risk factors;
- training (information on asthma, inhaler technique and regime, written plan of actions, constant monitoring, regular clinical examination);
- exclusion of trigger factors;
- specific immunotherapy;
- non-drug methods.

Each element plays an important role in achieving success.

Most patients suffering from asthma respond well to conventional therapy; on condition of optimal adherence and compliance with the correct inhalation technique they achieve and maintain control over the disease. Unfortunately, in spite of the significant progress in understanding the various aspects of children's asthma and the efforts to establish guidelines for its treatment, many patients still cannot control their asthma [5, 11, 12].
Results of the study [13], which included 298 patients with bronchial asthma aged over 12 years (48.7% of which are patients with uncontrolled BA according to the AST test during IGCC basic therapy; the period of observation in general - 581.6 patient-years), showed that up to 25% of severe exacerbations are caused by low therapy adherence, wherein 24.4% of exacerbations could be avoided if the appointments were followed. It is shown that the degree to which prescribed recommendations are implemented is dynamic in time and changes before and after BA exacerbations. A high level of adherence is needed to prevent asthma exacerbations.
There are strong evidences in daily practice that the main reason for a lack of therapy efficacy is the patients' disregard for basic the therapy on a daily basis [14-16]. Increasing adherence in children with bronchial asthma is the most effective method of achieving control over the disease [17].

Table. ***Assessment of asthma control***

Area	**Component**	**The level of control**		
		Full	**Fractional**	**Absent**
Current clinical manifestations	Symptoms: Day	No	1-2 weeks	Constantly
	Symptoms: night / wake	No	1-2 months	Weekly
	The need for reserve therapy	No	1-2 weeks	Daily
	Limiting activity	No	Some	Uttermost
Risk	Exacerbations (per year)	0	1-2	> 2
	Side effects of treatment	No	Different	Different

It is especially usual for children not to follow the regime of using IGCC. According to observations, in which adherence was measured with electronic devices, its average level was 30-70% to the general amount of prescribed IGCC doses [18]. Other studies show that 75% IGCC adherence gives children and adults a full or partial control over asthma [18, 19]. Thus, low IGCC adherence significantly reduced the treatment efficiency, led to uncontrolled asthma and increased the expenditure of budgetary funds [20].
A study of an alternative asthma treatment strategy for mild course BA in children with the use of montelukast in the form of oral tablets for a single application (originally Singulair was used) showed a significantly higher degree of adherence to the prescribed treatment. A multicenter open 6-month observation [21] of efficacy, safety and satisfaction of the montelukast therapy versus inhaled beclomethasone included 124 children with asthma aged 6 - 11 years old. Indicators of overall effectiveness and safety were similar and had no significant differences. However, it was noted that patients taking the drug in the form of oral tablets, were more responsible towards the doctor's prescriptions: the average percentage of days during which the children implemented recommendations fully was 98% in the montelukast group and 83% - in the group of beclomethasone. Differences between the groups reached 15% and were statistically significant ($p < 0, 001$). Adherence in montelukast group was almost two times higher than in children receiving inhaled corticosteroids (82 and 45%, respectively). In satisfaction degree of prescribed therapy a higher level was observed in the group of montelukast, which the patients and parents have noted as more convenient ($p < 0.001$) in use and less complicated ($p = 0.005$); this drug was applied in accordance with the instructions over a longer period of time ($p = 0.0\ 06$) as compared to beclomethasone.

The problem of adherence to daily treatment in children with severe uncontrolled asthma is studied particularly closely. Failure to comply with prescriptions is a common cause of symptoms persistency in this group of patients [5, 10]. Research on adherence and mild and moderate asthma control showed that the main cause of wheezing, breathlessness, nocturnal cough and persistent mild symptoms that can be provoked by physical exercises, is also a failure to comply with the prescribed recommendations [14, 19].

In case of an insufficiency or absence of asthma control in children, an important question must be answered: what is really prescribed to the patient – therapy volume enlargement or adherence increasing? During the decision-making process it is critically important to identify non-adherent patients, which can be extremely problematic [14].

In one of the prospective studies [22], the implementation of prescriptions in 24 children with asthma aged 8 - 12 years was evaluated specifically. These children needed to inhale glucocorticoids and β 2-agonists in order to control the disease, and were believed to correctly implement the doctor's prescriptions. According to patients' diaries, the frequency of doctor's prescriptions implementation reached 95,4% (i.e., 95,4% of taken doses). But the electronic meters installed on aerosol metered-dose inhalers showed that less than 60% of the prescribed doses were used. Moreover, only 31,8% of the prescribed doses were taken in time. Overall, 92% of patients exaggerated the use of the prescribed therapy. The researchers concluded that the reason for this was not only a deliberate child failure to comply with prescriptions, but also misperception of the taken dose by children and their parents.

Thus, neither the information provided by parents, nor the patients' self-report, nor their diaries, nor personal anonymous questionnaires can reliably reflect the real picture of adherence to treatment [18, 23 - 25]. Patients and their parents tend to overestimate the implementation of daily therapy recommendations, which is often based on the memories and generalization of time periods instead of describing particular events - using the drug [25]. In addition, the desire of the patients and their parents to "please" the doctor plays an important role. To please the doctor, they need to report implementing all of the prescriptions even if they did not really implement all of them [18, 25].

A sufficiently accurate way to assess the adherence can be the counting of metered-dose aerosol inhalers used or using an inhaler with an automatic dose counter. However, this does not eliminate the risk of emptying the device before a visit to the doctor in order to simulate high adherence [26].

A reliable method of assessing adherence is using electronic control devices, which record the exact time and date when the drug is taken, but they have a very limited application and are used usually in clinical trials [27].

True adherence includes both observance of the medication dispensing regime and correct inhalation technique [28]. However, the adherence monitoring methods do not provide a full guarantee that even during the drug taking, the inhalation technique will not suffer. Studies have shown that repeated instruction for the procedure implementation and demonstration of the device to the patient are key factors that determine the correct inhalation technique in children with asthma [14].

Only a complete parental and patient awareness of the risk factors of not complying with the recommendations can improve adherence to treatment.

The reasons causing absence of adherence may be the following [14, 29]:

1) unintentional: bad recommendation from a doctor or a lack of awareness among parents and the patient;

2) intentional: typical for patients who consciously decided not to follow the recommendations;

3) unplanned (unintended), caused by difficulties in strict regime observance: occur in patients of low social level, with limits and lack of support from family members, and lack of motivation.

Overall, unintentional non-compliance with the recommendations is a relatively rare phenomenon [30-32]. Awareness of the disease and understanding of the drug therapy purpose by patients and parents is an important factor of following the recommendations [14].

It happens that the patients and their parents make up their own opinion about the causes and manifestations of asthma, based on the information from very unreliable sources - friends, neighbors, the mass-media, the Internet [33]. Asthma is often seen as an episodic condition, and

parents do not have awareness of the need for daily therapy taking [14, 33]. This behavior indicates the willful default on recommendations. At the same time some parents openly "resist" giving drugs to their child on a regular basis, arguing that there is no need to "stuff" with drugs if the child feels good anyway [34]. Such motivation can be supported with steroid phobia - fear of adverse side effects development in the patients who are assigned to IGCC [35, 36].
Even when the parents and the child have decided to comply with all the prescriptions and follow the doctor's recommendations, there may be obstacles that could cause unpremeditated nonadherence. Recent studies have shown the complexity and diversity of such unexpected barriers [14].
An important factor contributing to poor adherence in adolescents is the absence of a daily routine. Problems with remembering and lack of time caused by competing interests (socializing with friends, gadget-addiction) may also cause failure to comply with prescriptions. Moreover, for a group of adolescent patients, family and social difficulties, difficulties in communicating with their peers, as well as causes related to education of the child, may be an obstacle for adherence [14]. This is where a crucial role can be played by excessive responsibility entrusted to the child at a relatively young age by parents, responsibility to take daily medication on their own, without parental control and reminders [37]. A frequent obstacle for compliance with the recommendations is a financial problem, especially without providing the patient with drugs at the expense of health insurance [31].
Of course, adherence consists of complex behavioral processes caused by a number of interacting factors. There is no doubt that the most important links in this chain are the motivation and interpersonal relations between the doctor and the patient [14]. Herewith, the direct use of drugs is only a small particle of the patient behavioral model; self-control, or monitoring, - self-government, - becomes a more broad concept. The use of drugs for the purpose is one of the self-control skills, which is quite easy to learn. Thus, the commitment is not a constant characteristic of a patient and can vary depending on various reasons and situations [14]:

- getting familiarized with information;
- taking medications;
- symptoms control;
- psychological condition control;
- changing the lifestyle;
- using social support;
- efficient communication (interaction, communication with doctor).

These are seven basic skills for patients with such chronic disease as asthma. In this context, "skill" means a form of activity formed in the process of learning. That is why adherence is not a feature of human personality: in accordance with the surrounding circumstances, the patient can change their lifestyle [14]. It is important to understand that the achievement of 100% adherence to the prescribed therapy is a difficult but doable task for each doctor. Here are some effective methods for the achieving of this goal [1 4]

- offer parents to come up with a system of rewards;
- help the patient to associate drugs receiving with conventional routine daily activities (e.g., teeth brushing, eating, etc.);
- help the patient to establish a reminder system on the cell phone;
- set reasonable, specific goals with the patient and his/her parents;
- invoke positive emotions in the patient;
- teach parents to praise children for adherence and not to pay attention to minor offenses;
- help parents to come up with a visual reminder at home.

It should be understood that such a large number of patients with poor adherence is caused both by the complexity of recognition of such patients, and a variety of reasons causing non-compliance with the recommendations. A number of studies also indicate the opposite reality: achieving a good level of asthma control and a high level of adherence. There is no doubt that having a comprehensive approach will be particularly effective in addressing this issue [2, 3, 5, 10, 14].

A high adherence level can be reached by using remote monitoring using Internet-technology, as well as the active cooperation of the ill child, their parent and a doctor; this method can be especially actual for adolescent patients [38-40]. Herewith, the professionals' belief in the possibility of achieving the intended treatment goal will be a reliable incentive for compliance to the assigned regime and recommendations by the patient [35].

One of the main success factors in the treatment of such chronic disease as asthma, is clear step-by-step recommendations - an individual plan [2, 3, 5, 10, 17]. At the same time, studies show that doctors often do not inform parents and patients about the possible prospects [41, 42]: only in 9% of the cases specialists made up an individual action plan during consultations [41]. Self-control and principles of therapy education, the discussion of possible prospects as well as fears, doubts and apprehensions, joint goal setting and decision-making contribute to the development of a trusting partnership between the doctor and the patient's parents [10]. Studies have demonstrated that it is joint decision-making that associates with a higher adherence level and improving of achieved treatment results in both adults and children [43, 44]. It has been shown that specialists' training of this patient-centered approach helps to improve the control of asthma in children [14, 45, 46].

It should be noted that the absence of asthma control in pediatric patients could be caused by non-compliance with the principles of conducting children with asthma in accordance with clinical guidelines. According to the observations, such discrepancies and errors are found particularly much in primary care and among general practitioners [14]. Some international studies testify prescribing high doses of IGCC to children without a persistent asthma diagnosis. For example, patients who have not had a single episode of bronchial obstruction and hissing respiration during the past 2 years took inhaled glucocorticoids protractedly [47-49], and the strategy of treatment has not been revised. There are cases when a long course of a combined therapy (IGCC + β2-s long-acting agonists) without prior IGCC monotherapy was prescribed to children [50]. Studies all over the world testify to such non-compliance with the basic principles of asthma conduction [51, 52]. There are many cases when IGCC is used in short courses only when symptoms appear. In addition, IGCC is prescribed to children with nonspecific respiratory symptoms, who do not have a diagnosis of BA. Research analyzing the organization of asthma schools, showed unsystematic and irregular event management and their low attendance by patients [47]. Problems identified at the primary public health link, are common to many countries.

In order to provide for a higher asthma control level and better adherence, an interdisciplinary approach is also required. It means bringing together the paramedical practitioners and specialists of allied health professions into the treatment process, which increases the degree of self-control and the level of the patient and parents education in matters of the disease [10, 14, 53]. One of the links in the interdisciplinary approach is the work of a psychologist together with the family of a sick child [2]. Often, children with asthma suffer from alexithymia - the inability to express their emotions and feelings. A psychologist's work allows to harmonize the perception of the disease and the treatment process by the child, to correct the improper inner image of the disease; to form an active, constructive position towards treatment and health; to change the stereotype of intrafamily relations; to develop communication skills and to uncover the personality; to impart a proper direction to the line of parental conduct with a sick child and to help him cope with the disease.

While assessing children with an asthma condition, a professional must [10]:

1) determine the degree of control over the disease:
- symptoms control over the last 4 weeks;
- risk factors ;
- external respiratory function indications;

2) control the therapy, and in particular:
- the inhalation technique and the adherence level;
- adverse events;
- individual written treatment plan;
- patient and his parents attitude to asthma; formulate the treatment goals together;

3) exclude the impact of comorbidity, which can worsen asthma and cause exacerbations and reduction of life quality:
- rhinosinusitis, gastroesophageal reflux disease, obesity, obstructive sleep apnea, depression, anxious disorders.

The conventional approach of stepped asthma therapy in pediatric practice is implemented with the complete exclusion of an alternative diagnosis taking into account the commitment degree and compliance with the trigger elimination requirements [2, 3, 5, 10]. The ability to move to the next or previous stage of therapy is estimated at regular time intervals depending on the severity of asthma. Careful monitoring and timely drugs dosages or therapeutic strategies in general adjustment are needed.

It should be remembered that individual response to the drug may be different, suggesting a role of some flexibility in the choice of treatment options and the possibility to choose a different strategy if the first one happens to be a failure [3, 5].

CONCLUSION

Drug therapy is the selection of an optimal preparation for maximum symptoms control and reducing the total poor prognosis risk. One must take into consideration the possible phenotypic characteristics of asthmatic patients, the preferences of the patient and his parents, consider the possible goals, as well as the doubts and concerns on treatment issues. Drug therapy should also answer the practical questions of adherence to prescribed assignments (medication multiplicity can sometimes be decisive, especially for the adolescent age group) [2, 3, 5]. In this context, the cost of the drug is also important, resulting in availability and respectively adherence to the prescribed treatment [14].

Effective interaction of the doctor and the parents of a child with asthma, particularly the approach that focuses on the patient and shared decision-making, will improve the commitment and elevate the chance of reaching and maintaining disease control. Initial training by a specialist needs to be complemented by other educational activities such as training in an asthma-school. One of the most promising alternatives both for educational purposes and for maintaining the adherence is the use of educational computer programs and internet resources [54, 55]. Various informational and technological solutions are used to comply with using daily basic therapy drugs, early detection and relief of exacerbations in accordance with a personalized work plan (for example, a reminder for a timely drug dose or self-control measures), as well as unplanned doctor attending in synchronous and asynchronous modes.

CONFLICT OF INTEREST

The authors have indicated they have no financial support / conflict of interest relevant to this article to disclose.

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