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Psychopathologies as asthma-related comorbidities

Key words: *bronchial asthma, comorbidities, psychopathologies.*

Significant progress has been seen in understanding the pathogenesis and development of effective methods for the bronchial asthma (BA) treatment recent years. International consensus (GINA, PRACTALL, ICON, Global Atlas of Asthma), and national protocols based on them allow to improve the quality of life for most patients with asthma. But there remain a number of patients who fail to achieve control of the disease, despite the use of the most modern and effective asthma medications. The study of this problem by the leading scientific schools showed that one of the causes of poor asthma control are asthma-related comorbidities [1, 2, 3]. Subsequent progress of medical assistance to those the most severe patients with asthma who do not respond to standard therapy, is associated with the identification, diagnosis and development of treatment of comorbid conditions. Many comorbid conditions have been well studied and effective therapy is developed, including in Ukraine. The examples are allergic rhinitis and atopic dermatitis. But there is not enough attention for discussion about psychopathy as asthma-related comorbidities at the national level. Therefore, the aim of the article is an overview of contemporary foreign literature on the subject.

It is well known that mental disorders play a negative role for many chronic diseases, including asthma. Luban-Plotstsa B., 1997 defined asthma as «somatic final destination» for various mental factors [3]. At the same time it is recognized that asthma is heterogeneous disease. Thus, consideration of the impact of mental disorders, the so-called psychopathy, on the formation, course and prognosis of asthma is important. Among of psychopathy, influencing to the course of asthma there are considered following:

- depression;
- anxiety disorder and panic attacks;
- psychological stress;
- attention difficulty syndrome and hyper reactivity [4].

Depression, anxiety disorder, panic attacks are more common in patients with asthma compared to the general population [5, 6]. They have a significant impact on the level of BA control and catamnesis by reducing the treatment procedures (medications, adherence, etc.). Depression, anxiety disorders and panic attacks occur together often in the same patient [7, 8, 9]. According to the WHO, depression is common disease throughout the world. It affects about 350 million people. It gives severe suffering to people, reduces productivity at work, at school, breaks the relationship in the family and it can be a cause of serious chronic diseases, especially in protracted and severe forms. In the worst cases it leads to suicide, and 1 million cases of suicides caused by depression take place in the world every year, according to WHO experts, [10].

According to the National Institute of Mental Health United States, depression is a disorder of mental activity with a variety of reasons, including genetic, environmental, psychological, and biochemical. Depression starts between 15 and 30 years usually and it is more common for women.

Symptoms of depression include:

- Lack of pleasure in usual activities;
- Fatigue;
- Headache without clear localization;
- Bad mood, irritability for a long time;
- Sleep disturbance — increase or decrease its duration;
- Change in appetite, usually leads to an increase in body weight;

- Lack of interest or pleasure in everyday activity;
- Feelings of guilt, worthlessness, self-loathing;
- Hopelessness, pessimism;
- Difficulty of concentrating;
- Slowness of movement or restlessness;
- Recurrent thoughts of suicide [11].

According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), diagnosis of depression is based on complaints and medical history. Any specific laboratory or instrumental studies to confirm the diagnosis do not exist. If the patient has symptoms of depression over past two weeks depression can be diagnosed [12].

Depression is a common complication of any chronic diseases, and every third of such patients suffer from it. And asthma is not an exception. Sorgen C., 2008, showed that approximately 20 % of patients with asthma suffer from depression. And patients with daily limits as a result of uncontrolled asthma are more susceptible [13].

Patients with asthma and depression are less likely to receive prescription medications and perform of individual programs to control of the disease. This neglect of treatment interventions can lead to decreasing of asthma control, which in turn leads to a worsening of depression and creates a vicious circle.

In the meta-analysis Lu Y., 2012, it was found that the common prevalence of depression and anxiety in adolescents with asthma was significantly higher versus adolescents without asthma. It is found no effect of gender and severity of asthma on the development of this psychopathy [14]. The risk of death is higher in adolescents with asthma and it is not related directly to their disease of the respiratory system. Kuo CJ, 2010, conducted a population-based study involving 162 766 adolescents aged from 11 to 16 years. It was shown that risk of suicide was twice as higher in patients with asthma versus healthy children (11 and 4.3 suicide attempts per 100,000 per year, respectively). This study shows that young people, especially those with severe asthma require careful medical supervision [15].

School-age children with asthma are also prone to depression. Absence in school, inability to play with other children, hospitalizations in case of asthma attacks can cause a feeling of helplessness, depression, self-worthlessness. The researchers found that patients with asthma have lower levels of self-esteem, feeling guilty for their attacks. Often, these patients do not seek to succeed in the fight against the disease, which affects the level of asthma control and leads to depression [14].

In children, symptoms of depression are the same, however, the smaller the child, the more difficult diagnosis of depression, because a small child can not express his feelings in words, and he is not aware of feelings of sadness, grief, depression. Thus, in toddlers, pre-preschool and school age children symptoms of depression can be detected by a change in the child's behavior. Apathy, isolation, retardation or regression of a child without organic causes will be observed. For the diagnosis of depression in children of this age the clinician must examine the anamnesis of the parents, family relationships thoroughly and consult a child by a psychiatrist.

It is very important the psychological condition of the caregiver. The presence of depression in caregiver has a nega-

tive impact on the it's ability to care for the child's and has negative impact to the behavior and mental development of children, increase the number of medical consultations. Mothers of patients with asthma have higher levels of depression compared with mothers of healthy children (Szabó A., 2010; $p < 0.01$). There were no correlation between the level of education of mothers and their present of depression. Symptoms of depression have been reported in one third of fathers in children with asthma, and the gender differences have been identified [16]. To improve the quality of care for children with asthma, a doctor should screen mothers and other caregivers for depression periodically [17]. According to WHO, a mild form of depression can be confidently diagnosed and treated by primary health care doctor without drugs, but patients with moderate or severe depression require medication and psychotherapy [18].

Algorithm for the prevention and treatment of depression in patients with asthma:

- Maintain relationships with family and friends. Psychological support of loved ones is very important. Communicating with them supports your activity and independence, helps to cope with the daily chores, other things, support you in the implementation of therapeutic interventions.

- Stay active – pay attention to the earlier activities with interest to you.

- Be informed. Learn information as much as possible about asthma and depression. Knowledge can influence the level of self-control and will help to choose the most effective treatment. Ask your doctor to provide you all necessary information.

- Attend a support group or asthma-school to communicate with people with the same disease as you have. Educational programs about asthma can significantly improve your physical and mental condition. Asthma can be controlled fully with the proper using of medications and lifestyle changes, and you can lead normal lifestyle with minimal restrictions.

- Build a solid team of physicians. You must have a physician, nurse and other health care providers that you trust and with whom you feel comfortable.

- Study the instructions for your medication against asthma. Some bronchodilators can cause depression. If it occurs, ask your doctor to choose the best alternative medicine.

- Explore alternative therapies – acupuncture, exercises, art therapy, and others. They are often effective in maintaining of a good mood.

- Do not be afraid to ask for help. People experiencing depression should get help to save their sanity as soon as possible.

- Take medications for depression, if they are prescribed by a doctor [14].

Anxiety disorders, panic attacks

Anxiety disorders are also common in patients with asthma. They are combined with poor control of the disease, an increased amount of u bronchodilators using, poor quality of life for patients, but do not affect the frequency of hospital admissions and referrals for emergency care. These data were obtained in the survey 794 adult patients with the use of sta-

tistical analysis, excluding the impact of age, gender, smoking and the severity of asthma (Lavoie KL, 2011) [19]. Similar results were obtained by Urrutia I., 2012. It was found that anxiety disorder and depression reduce the degree of asthma control and degrade the quality of life of patients [20].

Feldman JM, 2013, examined the effects of anxiety disorder in 97 children aged 7-11 years with asthma and their mothers on the respiratory function, self-esteem of the function and frequency of medications using. It was found that the symptoms of anxiety in children with asthma combined with low self-esteem of the respiratory function and the increased number of drugs for the relief of acute asthma. Symptoms of depression in children combined with an increased risk of medication use and did not affect the self-esteem of respiratory function. Children, whose mothers had symptoms of anxiety or depression, had reduced lung function compared to children of mothers without psychopathy [21].

Psychological stress

Psychological stress is frequent asthma-related comorbidity. Its formation promotes awareness of the impossibility of complete control of asthma. On the other hand, the psychological and biological mechanisms which are underlying stress, modulate inflammation in asthma and thus heavier over its [22].

Yonas A.M. 2012 found that psychological stress on the individual, family and social levels increases the incidence of asthma in children, and this effect persists throughout life [23].

Interest large population-based study was made in Denmark and Sweden by Liu X., 2013. Hypothesis of the study suggested that psychological stress in early childhood influenced on the formation and the frequency of asthma exacerbations. The 5,202,576 children were involved in the study. The observations were made from birth to the date of first hospitalization for asthma, emigration, death, or the age of majority – depending on which event occurred first. All children were referred to the group without mental stress until they have lost a close relative (mother, father, siblings), and then included in the group with psychological stress. It was found that the risk of hospitalization for asthma increased in children who had lost close relatives aged 14-17 ($p \leq 0,05$), but not in younger children. Also, this risk did not change through out the time after the loss of close relatives. It was suggested two hypotheses to explain the effects of psychological stress on the course of BA.

Firstly, older children may perceive the death of a loved one due to a hard-formed personal scale of values.

Secondly, asthma has different phenotypes depending on the age and «late asthma», is not atopic form usually characterized the more severe course with neurological and psychiatric disorders.

It is also found that children, who have lost of a loved one, were less likely to implement the doctor's appointments, and it increases possible risk of hospitalization due to asthma as the result of inadequate treatment. It was established that caregivers experience stress due to the death of a loved one and feel unable to conduct activities to asthma control, which leads to a deterioration of the disease.

Psychological stress leads to an increase in frequency of somatic and infectious diseases by modulating the function of immune cells by exposing them through the nervous and endocrine systems [24]. Chronic psychological stress can lead to resistance of corticosteroid therapies, perhaps through effects on the expression or function of glucocorticoid receptor cells.

Ohno I. 2010, found that psychological stress leads to an increase in the frequency and severity of asthma exacerbations by increasing airway inflammation with predominance of Th2-cytokine profile in experiments on mice. Thus, the binding of opioid peptides and their receptors (μ -, δ - and κ -) plays a key role in changing the homeostasis in response to psychological stress. Hypothalamic-pituitary-adrenal system is activated in stressful conditions when the compound of opioid peptides with μ -receptors, resulting in the release of cortisol, which inhibits the expression of Th1-cytokines and shifts the immune response toward a Th2-type. Additionally, it was found that inhibition of negative emotions, so-called «good temper» also causes psychological stress and simultaneously compounding allergen-induced airway inflammation and expression by Th2-cytokine through μ -opioid receptors in the CNS [25, 26].

It was noted in the works of many researchers the fact of relationship between the various psychopathy, when the presence of a psychiatric disorder triggers another, and together they lead to somatic realization of psychological problems [10, 15, 22].

In the study Murdock KK, 2010, with the participation of 23 girls and 22 boys aged from 7 to 12 years with moderate to severe asthma from Boston (USA), it was found association between asthma-associated psychological stress and anxiety [26].

Slavich GM, Irwin MR, 2014, put forward a multi-level hypothesis of depression as a result of the impact of psychological stress by neural, physiological and genetic mechanisms. The key point of this theory is the activation of psychological stress components of the immune system involved in inflammation. Proinflammatory cytokines «responsible» not only on inflammation, but also can cause sadness, anhedonia (indifference to the pleasures of life), fatigue, psychomotor retardation, social and behavioral isolation. This adaptive biological response is essential to the survival of the organism under the threat of life, physical injuries, but it can also be activated under the influence of modern social conventions or imagined threats, leading to the formation of pro-inflammatory phenotype of the immune response, which plays a key role in the formation of the BA and depression [26].

Attention difficulty and hyperactivity disorder (ADHD) is a chronic disorder, characterized by the difficulty concentrating, and behavioral disorders such as hyperactivity, anxiety, impulsivity and poorly managed [4, 27]. Also, ADHD is neurological-behavioral developmental disorder that begins in childhood.

The prevalence of ADHD is 2-12 % in children, and 3-5 % in adults. Many children with ADHD symptoms persist into adulthood, causing difficulties in education, employment and social integration. ADHD is often combined with other psychopathy - depression and mood disorder [28, 29, 30, 31].

Chen MH, 2013, held in Taiwan nationwide population-based prospective cohort, case-control study on the comorbidity of ADHD and AD 2294 with the participation of a child with asthma and 9176 children without asthma at the age of 0-3 years. When the statistical processing results, after eliminating the influence of age, gender, urbanization accompanying atopic diseases (rhinitis and dermatitis), it was found that children with asthma had a significantly higher risk of developing ADHD compared with peers without asthma (7 % and 4 and 6 %, respectively, $p < 0.001$) [32].

Tsai JD, 2013 studied a common database of insurance claims from 2002 to 2009. It was selected 4692 children with ADHD and 18,768 randomly selected children (control group). It was found that children with ADHD had significantly higher incidence of atopic diseases (allergic rhinitis, conjunctivitis, asthma and eczema). Using logistic regression analysis it was revealed that children from large cities had a higher risk of developing ADHD. The risk of developing ADHD increased with the number of atopic disease and the patient's age [33].

Fasmer O., 2011 on the basis of the Norwegian database drug prescriptions in 2006 studied how often the same patients were prescribed medications for the treatment of asthma and ADHD. It was shown the increase risk for 65 % of the subsequent appointment of a medicament for the treatment of ADHD, if the patient is receiving treatment for asthma, especially in females. The strongest correlations were found in women aged 20-49 and men aged 30-49 [34]. Thus, psychopathies are frequent comorbid conditions asthma and aggravate its course and prognosis. Conducting cognitive-behavioral therapy improves the quality of life of patients with asthma [35], but its mechanisms, especially in children, are still poorly understood, and its effects - variable [36, 37].

The management of patients with asthma should be considered a high probability of psychopathies. The words of the great therapist Mudrov M.J., 1825, for clinical practice do not lost their relevance: «I'm going to tell you a new truth that many people do not believe it, and that perhaps not all of you come upon ... Healing is not in the treatment of disease ... Healing is the treatment of the patient.»

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ПСИХОПАТІЇ ЯК КОМОРБІДНІ СТАНИ БРОНХІАЛЬНОЇ АСТМИ

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Резюме

Проведено аналіз сучасної англійської літератури, яка присвячена дослідженням взаємозв'язку бронхіальної астми (БА) та таких психопатій, як депресія, тривожні розлади, панічні атаки, психологічний стрес, синдром дефіциту уваги та гіперактивності. Наведено результати досліджень щодо поширеності психопатій серед хворих на БА, механізми їх впливу на перебіг захворювання, заходи щодо діагностики та лікування психопатій.

Ключові слова: бронхіальна астма, коморбідні стани, психопатії.

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PSYCHOPATHOLOGIES AS ASTHMA-RELATED COMORBIDITIES

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Summary

The analysis of modern English literature is made. The literature is deal with comorbidity of bronchial asthma and psychopathologies as depression, anxiety, panic attacks, psychological stress, attention difficulty syndrome and hyperreactivity. It was shown the results of investigations of psychopathologies prevalence among patients with bronchial asthma, mechanisms of their influence on asthma, methods for diagnostic and treatment of psychopathologies in patients with asthma.

Key words: bronchial asthma, comorbidities, psychopathologies.

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