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The effect of auto-cpap therapy on parameters of sleep disordered breathing in patients with bronchial asthma combined with obstructive sleep apnea-hypopnea syndrome

Key words: *asthma, obstructive sleep apnea-hypopnea syndrome, polysomnography, CPAP therapy, comprehensive treatment.*

Bronchial asthma (BA) – actual problem of medical and social importance, covering about 300 million people worldwide. According to epidemiological studies – 15 % of the world population suffer from asthma. This disease affects all age groups in the population and inefficient control leads to significant deterioration in quality of life, disability, and in some cases – to the death of patients [7]. Severe asthma that responds poorly to treatment, and in which you can not achieve a controlled flow reaches 10–15 % of all cases [9, 16].

The aim goal of asthma treatment – to achieve and maintain control of the clinical manifestations of the disease for a long time considering the safety of treatment, potential side effects, cost of treatment required [5]. Grade control should include not only control the clinical manifestations (symptoms, nocturnal awakenings due to asthma, the number of used bronchodilators of short action as «first aid», limiting daily activity, lung function) but also control future risks to the patient, such as sharpening, increasing speed deterioration of lung function and adverse effects of therapy. Overall, achieving a full asthma control leads to a risk reduction of exacerbations. However, a certain percentage of patients may not achieve adequate control [2]. The reasons are different: symptoms of asthma are difficult to treat by standard schemes, and the comorbidities are presence.

One of the most common symptoms in patients with uncontrolled asthma is sleep disorders.

Many asthma patients is associated with a decrease in the subjective assessment of sleep quality and increased daytime sleepiness. Sleep disorders in patients with asthma adversely affect the levels of hormones that are synthesized during sleep. Thus, violation of the synthesis of melatonin, which is characterized

by a natural « sleeping pill » action may adversely affect the tone of the muscles of the bronchi and the flow of inflammatory processes in the mucous membranes [21, 23].

Some authors have noted a relationship between asthma symptoms and sleep disturbances. Proved that difficulty falling asleep, sleep fragmentation (diagnosed by polysomnography), early morning awakening and daytime sleepiness in patients with asthma are more common than in healthy individuals [18]. Over 40 % of children with asthma complain of clinically significant daytime sleepiness [21]. Up to 50 % of adult patients with asthma noted daytime sleepiness. The reasons for this are: sleep disturbances associated with irregular therapy, patients abnormal sleep mode and insomnia caused by medication used in the treatment of asthma [22], the presence of concomitant syndrome apnea-hypopnea obstructive sleep (SOAHS) [23].

Despite the fact that women, compared to men, more clearly comply with therapy and take more inhaled corticosteroids, the number of complaints of insomnia is not reduced [10]. Sleep disorders can also be caused by the use of theophylline, beta agonists and long-acting oral corticosteroids in high doses. In addressing the above problems can help optimize the process of receiving inhaled corticosteroids [8, 22]. Analysis of character «morning downs» in terms of volume peak expiratory flow helps to identify the severity of asthma and to choose the most effective drugs [17].

Common cause of severe asthma and lack of control over the disease is late detection and inadequate treatment of comorbidities diseases, including SOAHS [23]. SOAHS much more common among patients with severe asthma, especially with obesity. Symptoms of sleep apnea related to the severity

of asthma and don't depend on allergization or allergenic stimulation, the presence of infections, smoking, and others [11, 17, 14].

«Gold» standard SOAHS treatment is CPAP therapy – support continuous positive airway pressure (continuous positive airway pressure) [2]. CPAP therapy provides air frame for upper airway, preventing periodic collaps of soft tissues and episodes of apnea. In conducting CPAP therapy also is the elimination of pathological changes in the lower airways, resulting from bronchial obstruction – namely, reducing lung hyperinflation, improvement of respiratory mechanics, opening collapsed alveoli. Methods CPAP therapy provides therapeutic pressure titration in polysomnography laboratory [8, 12]. The aim titration is selection of the pressure level at which will be eliminated episodes of apnea and hypopnea, snoring and desaturation during all stages of sleep [19].

Creating a device for automatic CPAP therapy (auto-CPAP) significantly improved the treatment. Auto-CPAP is the technology which minimizes the average night the pressure required to treat SOAHS. The device records the sensor signals from the flow and snore, changes the level of treatment pressure in response to changes in airway resistance that can change overnight, depending on the stage of sleep and body position. If the usual CPAP therapy in the patient's airway is supplied sufficiently high pressure continuously during the night, then the auto-CPAP therapy pressure medium is at a low level [15, 20], which is the main advantage of this method.

Thus, an integrated approach to the assessment of patients with asthma in combination with SOAHS use and adequate treatment of asthma as well as comorbidity help improve control symptoms, improve quality of life, reduce the risk of complications like asthma and SOAHS.

The aim of this study was – to investigate the effect of auto-CPAP therapy on the parameters of respiratory disorders during sleep in patients with bronchial asthma (BA) in combination with the syndrome of obstructive sleep-hypopnea sleep (SOAHS).

The work carried out by the state budget.

Object of study

The influence of auto-CPAP therapy on polysomnography indices was studied in 20 patients with asthma in combination with SOAHS (13 men and 7 women, mean age $(56,7 \pm 2,2)$ years, FEV1 $(68,0 \pm 3,3)$ %, the increase in FEV1 with bronchodilators in the sample $(11,7 \pm 1,4)$ %.

Note that all patients with asthma treated with basic therapy of asthma according to severity of the disease according to current standards of treatment, which was held for 4 weeks before inclusion in the study.

Methods of study

Selection of patients with asthma was conducted according to the criteria of the Order № 868 of Ministry of Health of Ukraine of 08.10.2013 p. «On approval and introduction of medical and technical documents on standardization of care in asthma» [4].

All patients conducted: surveys (using questionnaires and questionnaires Epvort, ACQ), research and clinical symptoms of asthma SOAHS, research indicators of lung function and

polysomnographic research on machine «SomnoStar Pro» company «Cardinal Health» (Germany).

To assess the symptoms of asthma and definition controllable disease patients with asthma were asked to complete a questionnaire ACQ [14], and for research to fill the diary of introspection.

To determine the presence of daytime sleepiness patients were asked to fill Epvorta sleepiness scale [13]. Sleepiness Score on a scale Epvorta carried out as follows: 0 –5 points – the norm; 6 –8 points – the initial stage of sleepiness, 9 –12 points – moderate, 13–18 – points – marked 19 and more – extreme degree of sleepiness.

When using hardware research methods (spirometry and polysomnography) were taken into account reference values entered in the software equipment that was used.

In order to establish the diagnosis, determine the degree of bronchial and lung ventilation function study all patients with the analysis carried spirometry curve «flow-volume» forced expiratory pletzmozografiya and total body kit on to study respiratory system «Master Screen Pneumo» unit and «Master Screen PFT» firm «Cardinal Health»(Germany). The study was conducted in the morning, after a 12–14 hour break in taking medicine. We took into account and recorded to the individual patient card values of lung function that were obtained in 15–30 minutes after 2 inhaled β_2 -agonists short action. All figures are measured in the ratio to standard values developed by G. F. Clement et al. [3].

SOAHS diagnosis was confirmed by polysomnography. Polysomnography (PSG) study (electroencephalogram – EEG elektrookulohrama – EOG, electromyogram – EMG, electrocardiogram – ECG, electromyogram, which is registered with limb patient – EMGK, abdominal breathing gain – CHDP, breast breathing strengthening – ODS, air breathing flow – pulsoksymetriya) conducted on the machine «SomnoStar Pro» company «Cardinal Health» (Germany).

Analyzed the following signs: the index of apnea-hypopnea (IAH) – (number of episodes of apnea + hypopnea per hour), the index desaturations (number of episodes desaturations per hour), average SpO2 per night %, minimum SpO2 per night %, the total duration of sleep (TST), duration of REM sleep phase (% of total sleep time), duration of 1, 2, 3, 4 stages of NREM sleep phase (% of total sleep time), REM latency phase, min., sleep efficiency, %.

All the data accumulated in the developed database, which became the basis package «Excel».

When performing calculations commonly used statistical and mathematical function program Excel, which made it possible to consider the results of using the methods of variation and correlation analysis.

Since we were dealing with small groups of patients to assess the reliability of differences of average values of samples used in the t-Student test (for independent observations and a series of related cases), and Fisher's criterion (for distributed far from normal and the number of observations < 30) and Mann – Uytneya criterion (when comparing quality indicators).

Methods of treatment. When treating patients with asthma in combination with SOAHS conducted an open, randomized study.

For the treatment of patients studied was recommended two modes of therapy conducted sequentially. The first mode of therapy patients followed the first 10 days of observation. It called for the continuation of basic treatment of asthma in daily doses according to current standards of treatment that patients received within 4 weeks before inclusion in the study. Then same patients administered second mode of therapy. It provided the basic combination of drugs therapy at daily doses in accordance with the applicable standards of treatment of auto-CPAP therapy (while sleeping). For the auto-CPAP therapy device used for the treatment of snoring and sleep apnea with humidifier SOMNOsmart 2 which SOMNOclick Smart PAP (auto-CPAP). The duration of combination therapy was 10 days. Then again, patients switched to the first mode of therapy in which surveillance is conducted within 10 days.

Design study of patients with asthma in combination with SOAHS consisted of five visits. Patients were examined in «National Institute of Phthysiology and Pulmonology. F. G. Yanovsky AMS of Ukraine» to the beginning of the study – visit 1, after 10 days of observation for the basic treatment of asthma – visit 2, of the first night of therapeutic auto-CPAP – visit 3, after 10 days from the start of complex therapy – visit 4, 10 days after end of complex therapy – visit 5.

Results and discussion

Prior to treatment in the studied patients had uncontrolled asthma, as evidenced by the data in terms of the questionnaire ACQ – $(1,8 \pm 0,1)$ points. Patients noted the waking at night due to asthma symptoms several times a day, morning moderate symptoms limit daily activities due to asthma, shortness of breath, wheezing in the chest – from a small to moderate amount of time. Thus there was a high level of daytime sleepiness on a scale Epvorta – $(15,2 \pm 0,8)$ points (Table. 1).

All patients noted the excessive daytime sleepiness, short of falling asleep at monotonous work, increased daytime fatigue, loud night snore and stop breathing during sleep, which complained of people: restless sleep with frequent awakenings, engine response during sleep (restless limb movements, twisting in his sleep), night awakening due to claims to urinate, morning headaches. Some patients have noted nocturnal heartburn, dry mouth and throat upon awakening, changes in blood pressure and cardiac abnormalities, changes or other sexual potency disorders.

Against the background of the basic treatment of asthma (1 to 2 visits) dynamics of clinical symptoms of asthma and

SOAHS not observed. The level of disease control for the ACQ questionnaire did not change and amounted to $-(1,7 \pm 0,1)$ points. The level of daytime sleepiness on a scale Epvorta also remained unchanged – $(15,1 \pm 1,0)$ points.

Extra using CPAP therapy after 10 days contributed to improving asthma control questionnaire according to ACQ $(1,1 \pm 0,1)$ points out statistical ($p < 0,05$) and clinical (more than 0.5 points) significance difference sings. After 10 days after the complex treatment (visit 5) Asthma control was the best – $(0,9 \pm 0,1)$ points compared to visit 4 – $(1,1 \pm 0,1)$ scores ($p < 0.05$). Night, morning, day significantly reduced symptoms, were recorded very rare and were weak. Although both of sings ACQ for 4 and 5 visits related to the «gray zone» within 0,75 – 1,25 points when asthma control is regarded as adequate border control, as compared to patients before beginning CPAP therapy was observed convincing clinical dynamics.

Extra -using 10-day auto- CPAP therapy helped reduce the degree of sleepiness on a scale of Epvorta $(15,1 \pm 1,0)$ points to $(8,1 \pm 0,8)$ points, ($p < 0,05$), followed by a decrease in sleepiness to $(6,5 \pm 0,7)$ 5 points at the time of the visit (Table. 1).

All patients with asthma in combination with SOAHS were examined by polisomnography (Table. 2).

Analysis of the data showed that the baseline for patients on a background of severe clinical symptoms of asthma and SOAHS determined significant violations PSG parameters, namely: a high index of apnea – hypopnea (IAH) – $(33,6 \pm 5,6)$ / h, indicating the presence of the majority of patients II – III severity SOAHS. Was marked significantly increased desaturation index (number of episodes per hour desaturation) – to $(47,3 \pm 5,8)$ / h. Prolonged suspension of pulmonary ventilation and prolonged partial upper airway decrease led to a decrease compared with the norm for the average level of SpO2 night – to $(87,9 \pm 1,6)$ % and the minimum SpO2 per night – to $(72,8 \pm 2,7)$ %.

After 10 days of observation for the basic treatment of asthma (2 visit) statistically significant dynamics of PSG study was not found. After the first night of therapy using auto- CPAP therapy in combination with basic treatment of asthma (visit 3) marked improvement in PSG – namely, the reduction of respiratory disorders during sleep, with IAH $(27,6 \pm 4,6)$ / h to $(6,9 \pm 2,5)$ / hr ($p < 0,05$), reducing desaturation index of $(48,7 \pm 6,2)$ / h to $(17,8 \pm 4,2)$ / hr ($p < 0,05$) increase in the mean level for SpO2 night of $(87,3 \pm 2,0)$ % to $(91,4 \pm 1,3)$ % ($p < 0,05$), increasing the minimum SpO2 per night $(72,5 \pm 3,3)$ % to $(82,4 \pm 2,3)$ % ($p < 0,05$).

Analysis of the questionnaire patients with asthma in combination with SOAHS during treatment (M ± m)				
Indexes	Visit 1 (the beginning of the study)	Visit 2 (10 days observation at the basic treatment of asthma)	Visit 4 (10 days from the start of coplex therapy)	Visit 5 (10 days after the complex therapy)
The questionnaire ACQ, points	1,8 ± 0,1	1,7 ± 0,1	1,1 ± 0,1 ^{*2-4}	0,9 ± 0,1 ^{*4-5}
Scale Epvorta, points	15,2 ± 0,8	15,1 ± 1,0	8,1 ± 0,8 ^{*2-4}	6,5 ± 0,7 ^{*4-5}

Notes: ²⁻⁴ statistically significant difference rate between 2 and 4 visits ($p < 0,05$). ⁴⁻⁵ statistically significant difference rate between 4 and 5 visits ($p < 0,05$).

Indicators PSG in patients with asthma in combination with SOAHS during treatment (M ± m)

Table 2

Signs	Visit 1 (the beginning of the study)	Visit 2 (10 days observation at the basic treatment of asthma)	Visit 3 (the first night of therapeutic auto- CPAP)	Visit 4 (10 days from the start of complex therapy)
IAH, / h	33,6 ± 5,6	27,6 ± 4,6	6,9 ± 2,5 ^{*2-3}	6,6 ± 2,2 ^{*2-4}
Index desaturation, / h	47,3 ± 5,8	48,7 ± 6,2	17,8 ± 4,2 ^{*2-3}	14,9 ± 4,5 ^{*2-4}
Mean rate per night SpO ₂ %	87,9 ± 1,6	87,3 ± 2,0	91,4 ± 1,3 ^{*2-3}	92,1 ± 0,8 ^{*2-4}
The minimum level for night SpO ₂ %	72,8 ± 2,7	72,5 ± 3,3	82,4 ± 2,3 ^{*2-3}	83,9 ± 1,9 ^{*2-4}

Notes: ^{2,3*} statistically significant difference between index 2 and 3 visits (p < 0,05). ^{2,4*} statistically significant difference rate between 2 and 4 visits (p < 0,05).

After 10 days from the start of complex therapy (visit 4) There was a further improvement in performance compared to the 2 PSG visit: IAH happened reduction of (27,6 ± 4,6) / h before (6,6 ± 2,2) / h (p < 0,05) reduction index desaturation of (48,7 ± 6,2) / h to (14,9 ± 4,5) / hr (p < 0,05), increase in the mean level of SpO₂ per night (87,3 ± 2,0) % to (92,1 ± 0,8) % (p < 0,05), increasing the minimum level for SpO₂ night of (72,5 ± 3,3) % to (83,9 ± 1,9) % (p < 0,05). This performance PSG was not significantly differed by 3 (the first night of therapeutic auto-CPAP) and 4 visits is possible due to the short duration of treatment.

Thus, the additional purpose of auto-CPAP therapy to standard basic treatment of asthma resulted in improvement of clinical symptoms of asthma, SOAHS and signs PSG – occurred a significant decrease in respiratory disorders during sleep: IAH, index desaturation and a significant increase in the mean and minimum levels of SpO₂ per night, indicating improving sleep, gas exchange and control of disease.

Conclusion.

Found that in patients with asthma in combination with SOAHS clinical symptoms of asthma are not exposed to the full control during the application of the basic drug therapy at daily doses according to current standards of treatment.

Typical breathing disorders during sleep in patients with asthma in combination with SOAHS according PSG are: apnea-hypopnea index (AHI) during sleep increasing up to II – III degree, high desaturation index, reducing the average and minimum SpO₂ per night.

Additional appointments of auto-CPAP therapy to the inhalation basic treatment improves the clinical course of both asthma symptoms and SOAHS, as evidenced by a significant decrease in ACQ questionnaire from (1,7 ± 0,1) points to (1,1 ± 0,1) points (p < 0,05) improvement of asthma symptoms, according to the patient's diaries, reduction of daytime sleepiness on a Epworth Sleep Scale from (15,2 ± 0,8) points to (8,1 ± 0,8) points, (p < 0,05).

Combined treatment with the use of auto-CPAP therapy positively affects the basic parameters of respiratory disorders during sleep according to night polysomnography – a decrease of AHI from (27,6 ± 4,6) / h before to (6,9 ± 2,5) / h after therapy, (p < 0,05), reducing desaturation index from (48,7 ± 6,2) / h to (17,8 ± 4,2) / h (p < 0,05), increase in the average level of SpO₂ per night from (87,3 ± 2,0) % to (91,4 ± 1,3) % (p < 0,05), increasing the minimal night level of SpO₂ from (72,5 ± 3,3) % to (82,4 ± 2,3) % (p < 0,05), that indicate the improvement of sleep, gas exchange and control of disease.

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