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Y. I. Feschenko, L. O. Iashyna, V. I. Ignatieva, O. V. Potochniak, I. V. Zvol, S. M. Moskalenko, L. O. Savelieva, N. I. Yuhno
SI «National institute phthisiology and pulmonology n.a. F.G. Yanovsky NAMS of Ukraine», Kiev

Antidepressant agomelatine use in treatment of patients with chronic obstructive pulmonary disease combined with depressive episode

Key words: *chronic obstructive pulmonary disease, depressive episode, agomelatine, comprehensive treatment.*

Chronic obstructive pulmonary disease (COPD) – a disease that can be prevented and treated, characterized by persistent airway restriction, which is usually progressive and associated with increased chronic inflammatory response of the respiratory tract and lungs to noxious particles and gases. Exacerbations and comorbidities further worsen the overall severity in individual patients [6, 7].

Next to the lung, COPD leads to significant extrapulmonary (systemic) effects, comorbidities, which burden the course of COPD [4, 6].

Literary sourses indicate that despite the practical implementation of modern principles of diagnosis and treatment of COPD, can not to achieve full control of the disease. In most cases, this is connected with the presence of comorbidities in COPD, which is not always diagnosed in a timely manner, resulting in patients not receiving adequate medical care. There is insufficient attention to psychosomatic disorders, especially depressive syndrome. Remain poorly known parameters of quality of life in patients with COPD based on emotional and mental state of patients in connection with which methods of correction are not developed properly [8, 18].

Risk factors for depression in COPD are: young age, female gender, smoking, low FEV1, cough, poor quality of life related to health, cardiovascular disease history [16]

Depression that occurs in COPD is most often manifested as a depressive episode (DE). DE – affective disorder characterized by emotional, cognitive and somatic disorders (depressed mood, loss of interest and pleasure, reduced vigor and increased fatigue). Among the symptoms are also present additional reduced ability to focus and attention, reduced self-esteem and self-confidence, self-blame secondary ideas, gloomy and pessimistic vision, ideas or actions aimed at self-harm or suicide, disturbed sleep, decreased appetite [3].

Depression affects the quality of life and the course of the underlying disease. DE affects the quality of sleep, reduces physical endurance, and significantly reduces the effectiveness of rehabilitation programs. Patients with depression often seek outpatient care, they have higher frequency of exacerbations and hospitalizations, lower compliance to therapy and higher mortality rates [8]. Therefore timely detection and treatment of depression in patients with COPD is of current interest.

It should be emphasized that depression in COPD occurs secondarily. The main pathogenic factor in the development of depressive episodes in patients with COPD is a physical illness – COPD. That's way, specific therapy of depression in this case primarily involves pulmonary rehabilitation using adequate basic treatment of the disease, which is the appointment of several alternative modes depending on the patient's clinical groups: inhaled β2-agonists short and long-acting, inhaled short or long holinolitics combination, bronchodilator drugs with different mechanisms of action and duration (β_2-agonists and holinolitics), theophylline, inhaled and oral corticosteroids [16]. Only with no effect on the applied basic treatment can be prescribed antidepressants.

Treatment of depression in patients with COPD should be conducted in accordance with the Order of the Ministry of Health of Ukraine of 27.06.2013 № 555 «Unified clinical protocols of primary, secondary (specialized), tertiary (higly specialized) medical care and rehabilitation». Chronic obstructive pulmonary disease [4], which is recommended with concomitant depression to the basic treatment of COPD prescribe antidepressants.

In the treatment of depression, according to the literature, the most commonly used, tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs) and norepinephrine (CI33CiN) [3].

There antidepressants groups TCAs, CI33C and CI33CiH for clinical effect requiring prolonged their use, besides as SSRIs and TCAs often be combined with taking hypnotic drugs that have the ability to increase airway resistance and decrease respiratory drive. This affects gas exchange, which may worsen the course of COPD in patients with comorbidity. In addition, the range of undesirable side effects of tricyclic antidepressants, SSRIs and CI33CiN quite wide. Adverse properties of TCAs include: dry mucous membranes, diplopia, constipation, increased weight, orthostatic hypotension, cardiotoxic effect (the ability to extend the interval QT), dizziness and requirements of individual dose selection. Nausea and gastrointestinal disorders are the most common cause of discontinuation of SSRIs and CI33CiN, especially in the first weeks of treatment [11, 12, 17, 24].

Also, be aware that patients with COPD combined with DE in the basic treatment of the main disease receiving inhaled and oral drugs of different pharmacological groups that may adversely interact with the abovementioned drugs.

So today, in the absence of effective standard treatment regimens COPD in combination with DE, especially important is the study of the efficacy and safety of new psychotropic action drugs – antidepressants, which would be above mentioned characteristics for use in general practice and would not have the negative effects as means already used [3].

An interesting drug in this sense is Agomelatine, which recently appeared on the Ukrainian market.

Agomelatine – new generation antidepressant, is agonist of melatonin MT1 and MT 2 receptors and 5-HT2c antagonist of serotonin receptors, so it provides a pronounced antidepressant effect, primarily due to the restoration of circadian rhythms (violation of which is one of the main factors of neuropsychiatric disorders), which significantly affected in patients with depression and has anxiolytic effect. This is achieved without increasing the level of amines in plasma, which leads to the well-known serotonergic and noradrenalinergic adverse events associated with the use of CI33C and CI33CiN. As agomelatine does not affect serotonin levels, it is not typical for many other antidepressants side effects – gastrointestinal, sexual and metabolic, including weight gain, sexual function disorder, psychomotor excitation, etc. [1, 10, 15, 17].

The stability of a therapeutically effective dosage of 25 mg/day once before bedtime, mostly eliminates the issue of the need for individual selection of treatment. Lack of pharmacologically active metabolites and minimal interaction with cytochrome enzymes of the liver form the most important difference of agomelatine from other antidepressants – virtual absence of drug interactions [3]. This property makes it possible to use agomelatine in the treatment of COPD patients taking multiple drugs in the basic treatment of the main disease.

The purpose of this study was to examine the effectiveness of complex therapy with antidepressant agomelatine in COPD patients with ED.

The work carried out by the state budget.

Object of research

The observation was located 30 patients with COPD combined with DE (20 men and 10 women, mean age (61,7 ± 1,9) years, duration of COPD (14, 8 ± 1,1) years and duration of smoking (14,6 ± 2,7) pack-years), after tests with bronchodilators FEV1 was (55,3 ± 3,6) %, FEV1/FVC – (53,9 ± 3,7) %. All patients with COPD treated with basic therapy according to the severity of the disease according to current standards of treatment [4], which was carried out for 4 weeks prior to inclusion in the study and had a stable course of COPD (exacerbations in the past 4 weeks wasn't observed).

Materials and methods

For the treatment of patients studied successively conducted two modes of therapy. On 1 visit was prescribed basic therapy of COPD, in daily doses according to current standards of care, which patients received within 4 weeks before enrollment. After 12 weeks patients were re-examinated and evaluated the effectiveness of basic therapy. After that, in addition to the basic treatment prescribed antidepressant agomelatine 25 mg 1 time per day (1 hour before bedtime) for 3 months.

Study design consisted of 6 patient's visits. Patients undergoing examinations in SI «National Institute of Phthisiology and Pulmonology. n.a. F. G. Yanovsky NAMS of Ukraine» to the beginning of the study – visit 1, after 12 weeks of observation for the basic treatment of COPD and complex treatment with agomelatine – visit 2, 2 weeks after complex treatment – visit 3, 4 weeks after – visit 4, 8 weeks after – visit 5 and 12 weeks after initiation of complex treatment – visit 6.

To determine the severity of the disease and assessing the quality of life in patients with COPD during treatment, proposed to fill: dyspnea scale of the Medical Research Council (Modified Medical Research Council (mMRC) Dyspnea Scale) test of COPD evaluation (COPD Assessement Test (CAT)) [16], the quality of life questionnaire of St. George hospital [19].

Scale mMRC reflects one symptom – shortness of breath, correlates well with other instruments to measure health status and foresee the risk of future mortality. CAT test more fully reflects the impact of the disease on the patient's daily activities and his health, consists of 8 points that measure the worsening of health status in COPD. Total score from 0 to 40; closely correlated with health status, measured by questionnaire hospital of St. George, is a reliable and sensitive [7].

To assess the quality of life in addition to hospital of St. George questionnaire were also asked to complete a compact health questionnaire EuroQoL-5D (EQ-5D), which provides answers to five questions: the ability to travel, personal care, daily activities, presence pain or discomfort, anxiety or depression. Response was assessed by three ball scale: 1 – no violation, 2 – there are some violations, 3 – pronounced changes [23].

All patients were conducted lung ventilation function tests according to the analysis spirogram curve «flow-volume» forced expiratory volume and total body plethysmografy on the «Master Screen PFT» firm «Cardinal Health» (Germany). Were studied: vital capacity (VC), forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), maximal expiratory volume velocity at 25, 50, 75 %, lung capacity (MEF25 %, MEF50 %, MEF75 %), peak expiratory volume (PEF), total bronchial resistance (Rtot), total lung capacity (TLC), residual lung capacity (RV), expiratory reserve volume (ERV), inspiratory capacity (IC). The study was conducted in the morning, after a 12–14 hour break in taking treatment. For detection and assessment of bronchial obstruction reversibility studies of lung function was carried out before and after 15–30 minutes after 2 inhalations (200 mcg) β_2-agonist short-acting (salbutamol).

To assess the dynamics of the symptoms of a depressive episode during the treatment offered to fill the depression scale: PHQ-9, Montgomery-Asberg (MADRS), Spielberger, Epworth, Lincolnshire, Bergen and SDCS–16. Before initiation of therapy and during treatment conducted consultation psychiatrist, who finally determined the presence or absence of DE.

As a result of the questionnaire PHQ-9 showed depressive episode and assessed the degree of its severity [20]. With the value of PHQ-9 < 5 points –considered absent of DE, 5–9 points – easy, 10–14 – intermediate, 9–15 – moderate, and a value of 20–27 points – severe. Montgomery-Asberg Scale (MADRS) used for fast and accurate assessment of the severity of depression and its dynamics during therapy [21]. Filling the scale is not based on responses to direct questions, and the evaluation of the patient during the clinical examination. The scale consists of 10 questions, each assessed on a scale from 0 to 6. The doctor decide whether a given symptom severity scores (0, 2, 4, 6) or in between (1, 3, 5). If the value MADRS < 15 –considered absent of DE, when set MADRS 16–25 – easy, a value MADRS 26–30 – moderate, and a value of 30 and > – severe ED.

Spielberger self scale is an informative method of self-esteem level of anxiety at the moment (reactive anxiety (RA)) and the level of anxiety as stable characteristics of the person (personal anxiety (PA)) [5]. The scale consists of self-esteem of 2 parts separately assessed RA (number of statements from 1 to 20) and PA (number of statements from 21 to 40). For each of the statements should be given one of four possible answers: 1 – almost never, 2 – sometimes 3 – often 4 – almost always. Indexes RA and PA calculated by the formula: RA = A – B + 35, where A – the sum of the digits crossed in form scale on items 3, 4, 6, 7, 9, 12, 13, 14, 17, 18; B – the amount of other digits crossed by paragraphs 1, 2, 5, 8, 10, 11, 15, 1b, 19, 20. PA = C – D + 35, where C – the amount of digits crossed in form scale on items 22, 23 24, 25, 28, 29, 31, 32, 34, 35, 37, 38, 40; D – the sum of the other digits in paragraphs 21, 26, 27, 30, 33, 36, 39. When interpreting the results evaluated as follows: 30 points – low anxiety; 31–45 – moderate anxiety, 46 points or more – high anxiety.

To determine the presence of daytime sleepiness patients were asked to fill in Epworth sleepiness scale [13]. Evaluation of sleepiness on a scale Epworth held as follows: 0–5 points – the norm; 6–8 points – the initial degree of sleepiness, 9–12 points – moderate, 13–18 – points – severe, 19 or more – an extreme degree of sleepiness.

To estimate the severity of dysfunctional beliefs about sleep, patients were asked to complete the scale of dysfunctional convictions concerning sleep – SDCS-16 [22]. The scale contains 16 statements. The patient is evaluated on a 10-point scale the extent to which he agreed, and which neither with each statement.

Also, patients were asked to complete the Bergen insomnia scale [9]. This questionnaire contains 6 questions concerning sleep and fatigue. The patient is asked to circle the number (number of days per week), which is most consistent with his answers, where «0» means that the problem was not even once a week, «7» means that the problem was every day for a week.

The criteria for stabilization of clinical depression symptoms considered significant decrease in the severity of illness or absence of DE on the results of questionnaires: PHQ-9, MADRS, Spielberger, Epworth, Bergen, SDCS-16 and the conclusion of a psychiatrist.

To determine the effect of agomelatine to biochemical blood parameters was performed biochemical examination of patients before and after complex treatment. Measurements were carried out on an automated biochemical analyzer «Vitalab Selectra E», № 8-7008, 2007, the actual value of the measurement error ± 0,5 %. The results were compared with the reference values of blood biochemical substances.

Treatment was considered effective if: assessed positively by doctor and patient, there was a positive dynamics of clinical symptoms of COPD and DE on selected research methods, was improving quality of life.

The accumulation of data and mathematical processing carried out with the help of licensed software included in the package Microsoft Office Professional 2000 license Russian Academic OPEN No Level № 17016297. Statistical analysis was performed using mathematical and statistical capabilities of MS Excel and included the identification of fraction (percent) and their average error followed by comparison, to determine the authenticity of the differences particles using Students t-test. Correlation analysis was performed by the method of parametric Pearson correlation followed authenticated result by using the Students t-test [2].

Results and discussion

Prior to treatment evaluation of symptoms in COPD patients studied by a scale mMRC (2,3 ± 0,2) points and CAT – (20,1 ± 1,5) points, corresponding to the presence of significant symptoms and predicted high risk of complications.

According to the results of the statistical analysis it was found that for a period of 12 weeks of observation from 1 to 2 visit, when patients received only basic therapy, changes in clinical symptoms of COPD on scales mMRC and CAT test doesn't occurred.

However, during the combined treatment using Agomelatine all patients had positive dynamics relevant indicators. The severity of dyspnea on a scale mMRC at baseline (visit 2) was (2,4 ± 0,2) points, and 12 weeks after initiation of combined treatment (visit 6) was noted a statistically significant reduction in severity of dyspnea to (1,9 ± 0,2) points ($p < 0,05$). CAT score before the combined treatment was (20,8 ± 1,3) points, and after 12 weeks observed a statistically significant reduction in the deficit to (11,9 ± 1,4) points ($p < 0,0001$). The results of the study are presented in Table 1.

During the 12 weeks of observation (1 to 2 visit) when patients were only on base treatment of COPD, improving the quality of life according to the questionnaire SGRQ was not observed. Additional appointments to the basic treatment of COPD agomelatine led to improved quality of life according to hospital of St. George questionnaire. The 2 visit St. George (SGRQ) score was (71,6 ± 3,2) points, and after 12 weeks of complex treatment (visit 6) was noted clinically significant difference of – (61,9 ± 4.5) points. Statistically significantly reduced restriction of activity (57,7 ± 3,4) points to (43,4 ± 3,5) points ($p < 0,05$). Limitations of activity and score of St. George questionary at 12 weeks after initiation of combined treatment unchanged (Tab. 2).

Improving the quality of life according to the health questionnaire EQ-5D after 12 weeks of observation for basic treatment (1 to 2 visit) also wasn't noted (Tab. 3).

But additional use of agomelatine to basic treatment after 12 weeks of treatment resulted in improved quality of life,

Table 1

Dynamics of the results on a scale mMRC (points) and CAT test in patientswith COPD combined with DE, (M ± m)

Scales	Visits					
	Visit 1 (start of study)	Visit 2 (start of complex treatment)	Visit 3 (after 2 weeks)	Visit 4 (after 4 weeks)	Visit 5 (after 8 weeks)	Visit 6 (after 12 weeks)
mMRC, points	2,3 ± 0,2	2,4 ± 0,2	2,1 ± 0,1	2,1 ± 0,1	2,0 ± 0,1	1,9 ± 0,2*
CAT, points	20,1 ± 1,5	20,8 ± 1,3	17,7 ± 1,1	16,2 ± 1,2	14,0 ± 1,5	11,9 ± 1,4#

Notes: * – statistically significant difference between the indices 2 and 6 visits ($p < 0,05$); # – a statistically significant difference between the indices 2 and 6 visits ($p < 0,0001$).

Table 2

Dynamics of quality of life score hospital of St. George questionnaire in patients with COPD combined with DE, (M ± m)

Indicators of quality of life questionnaire hospital of St. George (SGRQ)	Patients with COPD combined with DE (n = 30)		
	Visit 1 (start of study)	Visit 2 (start of complex treatment)	Visit 6 (after 12 weeks)
Calculation symptom, score	73,6 ± 4,1	71,6 ± 3,2	61,9 ± 4,5 *
Activity limitation, score	57,2 ± 3,9	57,7 ± 3,4	43,4 ± 3,5 **
Restriction of activities, score	46,4 ± 3,5	46,0 ± 3,8	44,5 ± 4,7
Total score	56,6 ± 3,0	53,0 ± 3,3	50,4 ± 4,0

Notes: * – clinically significant difference between the indices 2 and 6 visits; ** – statistically significant difference between the indices 2 and 6 visits ($p < 0,05$).

Table 3

Dynamics of health questionnaire EQ-5D in patients with COPD combined with DE, (M ± m)

Scale of health	Visits					
	Visit 1 (start of study)	Visit 2 (start of complex treatment)	Visit 3 (after 2 weeks)	Visit 4 (after 4 weeks)	Visit 5 (after 8 weeks)	Visit 6 (after 12 weeks)
EQ–5D, score	8,5 ± 0,4	10,1 ± 1,5	10,1 ± 2,2	9,8 ± 2,2	7,0 ± 0,3	6,5 ± 0,4*

Note: * – statistically significant difference between the indices 2 and 6 visits ($p < 0,05$).

according to health status questionnaire EQ-5D. In the beginning of complex treatment (visit 2) score for health questionnaire EQ-5D was (10,1 ± 1,5) points, and after 12 weeks (visit 6) was observed statistically significant reduction in the score to (6,5 ± 0,4) points ($p < 0,05$).

Basic therapy of COPD did not affect the course of the clinical symptoms of COPD and DE. But during combined treatment using agomelatine was recorded positive dynamics of clinical symptoms of COPD as well as DE. Prior to the combined treatment (visit 2) in all patients data of: PHQ-9 questionnaire and MADRS, scales: self-esteem Spielberger, dysfunctional beliefs regarding sleep – SDCS-16 and insomnia Bergen, were raised and met moderate severity DE, that confirmed the final diagnosis which was set psychiatrist (Tab. 4).

After 12 weeks from initiation of complex treatment (visit 6) in patients receiving agomelatine statistically significant reduction in depression according to the PHQ-9 questionnaire of (16,8 ± 0,3) points to (5,9 ± 0,6) points ($p < 0,0001$), which corresponded to mild severity of depression. Scale MADRS – of (25,5 ± 0,8) points to (10,3 ± 1,1) points ($p < 0,0001$), which corresponded to the absence of symptoms of depression. Prior to the complex treatment of daytime sleepiness Epworth index was in the normal range and was (5,2 ± 0,6) points, and after treatment decreased to (2,7 ± 0,5) points ($p < 0,001$). After 12 weeks of agomelatine patients experienced a statistically significant increase in subjective sleep quality, according to the scale SDCS-16. Thus, the indicies of scale SDCS-16 decreased from (82,0 ± 4,6) points to (58,2 ± 4,8) points ($p < 0,01$), indicating a decrease of dysfunctional beliefs about sleep. Also observed a statistically significant improvement of sleep and reduce fatigue according to the scale dynamics of insomnia Bergen – before treatment (70,8 ± 6,8) points after treatment – (53,3 ± 5,8) points ($p < 0,05$) .

Admission of agomelatine helped reduce anxiety, as evidenced dynamics of self-rating Spielberger scale. Thus, in the studied patients was significantly decreased rate of PA, which Spielberger scale before treatment was (38,0 ± 3,1) points, and after combined treatment – (32,4 ± 2,2) points ($p < 0,01$). Statistically significant changes in RA were noted. Thus, in patients with COPD combined with DE agomelatine showed mild anxiolytic effect, namely, reduced anxiety symptoms (PA) within depressive disorder (Tab. 5).

In the study of lung function parameters revealed the following. Indicators of lung function over 12 weeks of observation (1 to 2 visit) when patients received only basic therapy of COPD was not significantly changed.

Table 4

Dynamics of PHQ-9 questionnaire, MADRS, the scale of Epworth, SDCS -16 and scale Bergen insomnia in patients with COPD combined with DE, (M ± m)

Index of depression	Visits					
	Visit 1 (start of study)	Visit 2 (start of complex treatment)	Visit 3 (after 2 weeks)	Visit 4 (after 4 weeks)	Visit 5 (after 8 weeks)	Visit 6 (after 12 weeks)
PHQ-9, score	15,68 ± 0,3	16,8 ± 0,3	12,9 ± 0,8	10,5 ± 0,5	7,2 ± 0,8	5,9 ± 0,6*
MADRS, score	–	25,5 ± 0,8	19,5 ± 0,9	16,7 ± 0,9	13,0 ± 1,2	10,3 ± 1,1*
Epworth scale, score	–	5,2 ± 0,6	4,9 ± 0,6	4,4 ± 0,6	3,9 ± 0,5	2,7 ± 0,5*
SDCS –16, score	–	82,0 ± 4,6	75,0 ± 5,0	72,7 ± 4,8	62,2 ± 5,0	58,2 ± 4,8[&]
Scale Bergen insomnia, score	–	70,8 ± 6,8	64,0 ± 6,6	61,1 ± 6,5	57,1 ± 5,8	53,3 ± 5,8[#]

Notes: * – statistically significant difference between the indices 2 and 6 visits ($p < 0,0001$); [&] – a statistically significant difference between the indices 2 and 6 visits ($p < 0,01$); [#] – a statistically significant difference between the indices 2 and 6 visits ($p < 0,05$).

Table 5

Dynamics of self-rating Spielberger scale in patients with COPD combined with DE, (M ± m)

Indicies self-rating Spielberger scale	Patients with COPD combined with DE (n = 30)	
	Visit 2 (start of complex treatment)	Visit 6 (after 12 weeks)
RA	33,6 ± 1,1	31,1 ± 1,6
PA	38,0 ± 3,1	32,4 ± 2,2*

Note: * – Statistically significant difference between the indices 2 and 6 visits ($p < 0,01$).

Table 6

Dinamics of respiratory function indicies in patients with COPD combined with DE, (M ± m)

Indicies	Patients with COPD combined with DE (n = 30)				
	Visit 1 (start of study)	Visit 2 (start of complex treatment)	Visit 4 (after 4 weeks)	Visit 5 (after 8 weeks)	Visit 6 (after 12 weeks)
R tot, %	229,5 ± 50,8	249,1 ± 37,8	226,8 ± 27,6	195,7 ± 22,6	188,5 ± 11,1
VC MAX, %	79,2 ± 3,2	76,1 ± 2,8	76,7 ± 3,1	77,0 ± 3,4	78,3 ± 2,9
IC, %	79,2 ± 3,2	84,4 ± 4,4	85,2 ± 4,0	86,9 ± 5,1	87,0 ± 4,1
RV, %	162,3 ± 12,0	160,5 ± 15,5	158,3 ± 14,2	153,2 ± 13,1	151,1 ± 11,4
ITGV, %	140,2 ± 9,2	149,0 ± 16,1	133,3 ± 9,2	132,7 ± 10,1	131,4 ± 9,2
TLC, %	111,8 ± 5,0	114,1 ± 5,5	116,2 ± 5,0	115,4 ± 7,0	115,0 ± 5,5
FEV_1, %	55,3 ± 3,6	53,1 ± 2,8	55,4 ± 3,0	56,8 ± 3,2	59,6 ± 5,0 *
FVC, %	79,6 ± 3,3	75,8 ± 2,8	79,0 ± 2,9	81,9 ± 3,6	83,6 ± 2,8 *
FEV_1/FVC_{MAX},	53,9 ± 3,7	57,1 ± 2,0	56,9 ± 2,3	56,7 ± 2,5	68,2 ± 2,2 *
MEF_{75}, %	35,4 ± 5,6	31,9 ± 3,0	32,3 ± 2,9	35,7 ± 3,6	41,4 ± 0,3
MEF_{50}, %	29,0 ± 3,3	25,6 ± 2,2	27,0 ± 2,3	28,4 ± 2,3	30,9 ± 2,6
MEF_{25}, %	26,8 ± 3,1	25,5 ± 2,1	25,9 ± 1,8	26,1 ± 1,3	28,2 ± 2,0
PEF, %	56,4 ± 4,5	51,7 ± 3,7	53,9 ± 3,7	59,9 ± 3,6	63,8 ± 4,2

Note: * – Statistically significant difference between the indices 2 and 6 visits ($p < 0,05$).

However, additional appointments to the basic treatment of COPD agomelatine resulted in improvement of respiratory function in patients studied.

Thus, before the complex treatment period was FEV1 (53,1 ± 2,8) %, and after 12 weeks of complex therapy – (59,6 ± 5,0) %, $p < 0,05$; FVC of (75,8 ± 2,8) % increased to (83,6 ± 2,8) %, $p < 0,05$, and, respectively, and increased index FEV1 / FVC of (57,1 ± 2,0) to (68,2 ± 2,2) %, $p < 0,05$ (Tab. 6).

In 26 (86,7) % of patients treatment was considered effective – estimated positively by doctor and patient, while there was a positive dynamics of clinical symptoms of COPD and DE and indicators of lung function testing.

In the process of conducting a complex treatment contraventions of compliance is not found. The tolerability of the treatment was evaluated positively both patient and doctor. In the analysis of biochemical parameters of blood, both before and after treatment, was found deviations from the reference values, indicating the absence of toxic action agomelatine.

Conclusions

As a result of studies found that antidepressant additional administration of agomelatine to the basic treatment of patients with COPD combined with DE conduce to positive dynamics of clinical symptoms of COPD as well as DE, improving the quality of life, to the improvement of respiratory function, resulting to the effeciency of treatment COPD combined with DE was 86,7 %.

Complex therapy using agomelatine well tolerated by patients with comorbidity and not commit negative effects on biochemical parameters of blood.

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ПРИМЕНЕНИЕ АНТИДЕПРЕССАНТА АГОМЕЛАТИНА В КОМПЛЕКСНОМ ЛЕЧЕНИИ БОЛЬНЫХ ХРОНИЧЕСКИМ ОБСТРУКТИВНЫМ ЗАБОЛЕВАНИЕМ ЛЕГКИХ В СОЧЕТАНИИ С ДЕПРЕССИВНЫМ ЭПИЗОДОМ

Ю. И. Фещенко, Л. А. Яшина, В. И. Игнатьева, А. В. Поточняк, И. В. Зволь, С. М. Москаленко, Л. А. Савельева, Н. И. Юхно

Резюме

На сегодня, при отсутствии стандартных эффективных схем лечения хронического обструктивного заболевания легких (ХОЗЛ) в сочетании с депрессивным эпизодом (ДЭ), особую актуальность приобретает вопрос изучения эффективности и безопасности новых препаратов психотропного действия – антидепрессантов, которые бы хорошо сочетались с базисной терапией основного заболевания, не оказывали негативных побочных эффектов и хорошо переносились больными.

Целью данного исследования было изучить эффективность комплексной терапии с применением антидепрессанта агомелатина у больных ХОЗЛ с ДЭ. Обследовано 30 больных ХОЗЛ в сочетании с ДЭ (20 мужчин и 10 женщин, средний возраст (61,7 ± 1,9) года, с длительностью ХОЗЛ (14, 8 ± 1,1) года и продолжительностью курения (14,6 ± 2,7) пачко-года), FEV_1 – (55,3 ± 3,6) %, FEV_1 / FVC – (53,9 ± 3,7). Для лечения исследуемых больных последовательно проводилось два режима терапии. На 1-м визите назначалась базисная терапия ХОЗЛ в суточных дозах, соответствующих действующим стандартам лечения, которую пациенты получали в течение 4 недель до включения в исследование. Через 12 недель проводилось повторное обследование и оценивалась эффективность базисной терапии. После этого к базисной терапии дополнительно назначали антидепрессант агомелатин в дозе 25 мг 1 раз в сутки (за 1 час до сна) в течение 3 месяцев.

В результате проведенных исследований установлено, что дополнительное назначение антидепрессанта агомелатина к базисной терапии больных ХОЗЛ в сочетании с ДЭ способствует положительной динамике клинических симптомов как ХОЗЛ, так и ДЭ, повышению качества жизни, улучшению показателей функции внешнего дыхания, в результате чего эффективность лечения больных ХОЗЛ в сочетании с ДЭ составила 86,7 %.

Комплексная терапия с применением агомелатина хорошо переносилась больными с сочетанной патологией и не оказывала негативного влияния на биохимические показатели крови.

Ключевые слова: *хроническое обструктивное заболевание легких, депрессивный эпизод, агомелатин, комплексное лечение.*

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Ю. И. Фещенко
академик, профессор,
ГУ «Национальный институт фтизиатрии и пульмонологии им. Ф. Г. Яновского НАМН Украины»
03680, Украина, г. Киев, ул. Амосова, 10
тел.: +38(044)275-04-02; +38(044)275-21-18
e-mail: admin@ifp.kiev.ua

ANTIDEPRESSANT AGOMELATINE USE IN TREATMENT OF PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE COMBINED WITH DEPRESSIVE EPISODE

Y. Feschenko, L. Iashyna, V. Ignatieva, A. Potochniak, I. Zvol, S. Moskalenko, L. Savelieva, N. Yuhno

Summary

Today, in the absence of effective standard treatment regimens in chronic obstructive pulmonary disease (COPD) in combination with depressive episode (DE), special importance is the question of the study of the efficacy and safety of new drugs psychotropic action – antidepressants, which is good combine with basic treatment of the underlying disease, have not negative side effects and well tolerated by patients.

Aim of the investigation – to examine the effectiveness of complex therapy with antidepressant agomelatine in COPD patients with DE.

The study involved 30 patients with COPD combined with DE (20 men and 10 women , mean age (61,7 ± 1,9) years, COPD duration (14,8 ± 1,1) years and duration of smoking (14,6 ± 2.7) pack-years), FEV_1 – (55,3 ± 3,6) %, FEV_1/FVC – (53,9 ± 3,7). For the treatment of patients studied successively conducted two modes of therapy. On 1 visit was intended basic therapy of COPD in daily doses according to current standards of care that patients receive within 4 weeks before enrollment. After 12 weeks repeat examination and evaluation the effectiveness of basic therapy were performed. After that, in addition to the basic treatment prescribed antidepressant agomelatine 25 mg 1 time per day (1 hour before bedtime) for 3 months.

As a result of studies found that additional antidepressant agomelatine prescription to the basic treatment of patients with COPD combined with DE promotes positive dynamics of clinical symptoms of COPD as well as DE, improving the quality of life and respiratory function, resulting in the effectiveness of treatment COPD combined with DE was 86,7 %.

Combined therapy using agomelatine well tolerated by patients with comorbidity and not commit negative effects on biochemical parameters of blood.

Key words: *chronic obstructive pulmonary disease, depressive episode, agomelatine, comprehensive treatment.*

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Y. I. Feschenko
academican, professor
SO «National Institute of phthisiology and pulmonology named after F. G. Yanovskii NAMS of Ukraine»
03680, Ukraine, Kyiv, M. Amosova str., 10
tel.: +38(044)275-04-02; +38(044)275-21-18
e-mail: admin@ifp.kiev.ua