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Original article

Positive Effect of Rabeprazole/Sulpiride Combination Therapy on Bronchial Asthma Combined with Gastroesophageal Reflux Disease

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Abstract:

Background: The pathology of the digestive system often accompanies lung diseases. From 30% to 90% of the population have the pathology of the gastrointestinal tract in the presence of bronchial asthma (BA). Currently, the correction of psychoemotional status changes in patients with gastroesophageal reflux disease (GERD) combined with BA is understudied;

Objective: The study of clinical response of various research methods for BA combined with GERD progression.

Methods: 110 patients with persistent BA combined with GERD, who were prescribed one of four treatment regimens, took part in the study.

Findings: We found that the use of rabeprazole/sulpiride combination therapy was reliably improving both the external respiratory function indicators and the state of psychoemotional status as well as was reducing the clinical and endoscopic aspects of GERD.

Conclusions: Obtained results showed the efficiency of the use of sulpiride with rabeprazole in GERD combined with BA therapy.

Keywords: Chronic kidney disease, Serum uric acid, Hemodialysis, Creatinine clearance

Introduction:

The pathology of the digestive system often accompanies lung diseases.[1,2,3,4,] It is known that the pathology of the esophagus and stomach is able to worsen the bronchial asthma (BA) progression having an effect on different mechanisms such pulmonary microaspiration [5] and the reflex effect of receptors of lower esophageal mucosa that is reproduced through n.vagus via effectors appears in the development of bronchial obstruction. According to some authors, this particular mechanism is the most significant in the formation of reflux-induced BA.[6,7,8]

In its turn, BA is able to influence the gastroesophageal reflux disease (GERD) progression in some cases.[1,9,10,11] As a result, there is a feedback between pathogenetic mechanisms of these diseases mutually reinforcing each other.

Pathogenesis of the upper gastro-intestinal tract lesions is a process where the ratio between damaging factors and protective properties of the esophageal and gastric

mucosa is broken.[12] However, neuropsychiatric features of patients also influence the mechanisms of inflammatory and erosive-ulcerative processes in the upper gastro-intestinal tract significantly.[9,11]

The purpose of this research is to study a clinical response of various methods for gastroesophageal reflux disease treatment of patients with bronchial asthma (steps 3 and 4) based on studying the clinical course, pH, the condition of mucous membrane of the lower third of the esophagus and external respiratory function.

Methods:

The research was conducted within the pulmonary and therapeutic department of State Budgetary Healthcare Institution of the Republic of Crimea "Simferopol Municipal Clinical Hospital No. 7" in 2017-2019. This research is approved by the Ethics Committee of Federal State Autonomous Educational Institution of Higher Education "V.I. Vernadsky's Crimean Federal University" (minutes No.3 dd. 10/03/2017).

110 patients aged between 17 and 55 were under medical supervision. 11 people (10%) were under 25 years old; 17 people (15.4%) were aged between 26 and 35; 31 people (28.2%) were aged between 36 and 45; 51 people (46.4%) were aged between 46 and 51. All patients were of working age.

Men accounted for 35 (31.8%), women for 75 people (68.2%).

BA severity was determined in accordance with Global Strategy for Asthma Management and Prevention [6], by results of anamnesis, the severity of clinical signs and degree of functional respiratory disorders using spirography (SPG).

When selecting patients, GERD was diagnosed based on the presence of one of the following gastroenterological criteria: complaints indicating the presence of GERD; the results of intraesophageal pH monitoring that confirm the presence of gastroesophageal reflux; the results of fiberoptic esophagogastroduodenoscopy (FEGDS).[13]

All examined patients were divided into four groups depending on the pathogenetic treatment of GERD with the purpose to study the impact of GERD on BA progression:

- 1st group − 30 people, who received complex therapy according to the standards of treatment of both diseases;[6,14]
- 2nd group – 25 people – sulpiride at the dose of 50 mg 3 times a day was added in addition to standard treatment regimens for BA and GERD treatment;
- 3rd group − 25 people – prokinetic domperidone was excluded from the standard GERD treatment for them. The treatment included the use of rabeprazole and sulpiride. BA was treated according to standards;
- 4th group − 30 people – both rabeprazole and domperidone were excluded from the standard GERD treatment for them. The treatment included the use of sulpiride only. BA was treated according to standards.

With the purpose of diagnosis verification, we conducted an endoscopic examination of the upper gastro-intestinal tract (esophagus and stomach), which is a method of choice in clinical examination of patients with GERD.[15]

The intraesophageal pH monitoring for esophageal and gastric acidity (pH) studies was conducted for all patients at presentation to the in-patient department and four months after the end of treatment.

We chose the pH monitoring indicators that gave a fair view of the processes in the studied area for the analysis of the therapy effectiveness.[15,13,16] We defined the GER quantity, the highest and the lowest pH in esophagus, the percentage of acid and alkaline refluxes. These indicators are the most informative and important in diagnostic and prognostic terms.

To identify disorders of the psychoemotional sphere,[11] we surveyed patients with their consent according to The St. George's Respiratory Questionnaire.[17]

We compared the obtained results, studied in dynamics, among each other and with reference ranges relevant to these functional and instrumental research methods. We used standard software package Statistica 10 for statistical data processing. Comparative statistical analysis of differences between cumulative features was carried out using Student's t-test. The connection between features was studied using methods of correlation and regression analysis. The results were considered reliable at $p<0.05$.

Results:

In patients with BA combined with GERD at presentation to the in-patient department demonstrated a sharp decrease in forced expiratory volume in 1 second, vital capacity and Tiffeneau index comparing with the reference range ($p<0.05$), which corresponded to moderate-to-severe obstructive ventilatory disturbances (Table 1).

Table 1. Dynamics of SPG indicators of patients with BA and concomitant GERD on standard treatment (1st group, n=30)

SPG indicators	Before treatment	One month after treatment	P_1	P_2	Four months after treatment	P_3
Vital capacity,%	78.2±1.1	86.0±1.7	>0.05	<0.05	83.3±1.3	**>0.1**
FEV1	40.0±1.1	54.1±1.0	<0.05	<0.05	44.7±1.5	**<0.01**
Tiffeneau index (FEV1/ Vital capacity),%	**52.1±1.5**	**62.9±1.2**	**<0.01**	**<0.05**	**41.0±1.3**	**<0.01**

Note: P_1 – in comparison with the reference range;

P_2 – in comparison with the indicators before treatment;

P_3 – in comparison with the indicators one month after start of treatment.

pH measurement showed very high (572±11.0) GER quantity with a wide range of acidity of each reflux (from 2.7±0.4 to 7.7±0.3), while the ratio of acid and alkaline refluxes estimated at 56.7% to 43.3% (Table 2).

Table 2. Dynamics of pH measurement indicators of patients with GERD combined with BA on standard treatment (1st group, n=30)

pH measurement indicators	Before treatment	Four months after treatment
GER quantity	572 ± 11.0	**152.2 ± 7.0***
Lowest pH	2.7 ± 0.4	**2.2 ± 0.2**
Highest pH	7.7 ± 0.3	**7.9 ± 0.4**
Reflux quality:		
Acid	17 (56.7%)	**11 (36.6%)**
Alkaline	**13 (43.3%)**	**19 (63.4%)**

Note: * – $p<0.05$ in comparison with the indicators at the presentation.

FEGDS conducted to all patients during this period showed that 50% had edema and hyperemia of gastric and the lower third of the esophagus mucosa, while 26.7% patients had erosions and ulcers (Table 3).

Table 3. Dynamics of FEGDS results of patients with GERD combined with BA on standard treatment (1st group, n=30).

Morphological changes of the esophagus	Before treatment		Four months after treatment	
	Abs	%	Abs	%
Esophagitis stage I	15	50.0	18	**60***
Esophagitis stage II	**8**	**26.7**	**6**	**20***

Note: * – p<0.05 in comparison with the indicators at the presentation.

However, four months after standard BA and GERD treatment, the study of the selected parameters showed that functional activity of the respiratory system had no tendency to normalization or decrease of ventilation disturbances, while Tiffeneau index was reliably (p<0.05) worse than six months ago (before treatment). GER quantity decreased by 3.5 times four months after treatment, however, acid and alkaline refluxes were still present. At the same time, there was a shift in the quality ratio when alkaline refluxes increased from 43.3% at the presentation (13 patients) to 63.4% (19 patients) four months after treatment (Table 2).

The morphological condition of esophageal mucosa also changed in six months (Table 3).

Thus, one month after standard treatment patients with BA combined with GERD (1st group of examined patients) showed stable improvement as the number of asthma attacks during the day and the night reduced (p<0.05), only 13.3% still had lung rales. The symptoms of the psychoemotional sphere still remained, but in fewer cases.

Thus, 16.7% had hypochondriac syndrome, 70% had asthenic syndrome, and 60% of patients had depressive syndrome. Before treatment dizziness worried 19 patients (63.3%), 5 (16.7%) still had it one month after start of treatment, 26 (86.6%) patients felt weak before treatment and 5 (16.7%) one month after start of treatment, 15 (50%) against 6 (20%) had performance decrement, 27 (90%) against 21 (70%) had irritability.

Table 4. Dynamics of BA combined with GERD clinical signs on standard treatment (1st group, n=30)

Symptom	Before treatment		One month after start of treatment			Four months after treatment		
	Abs	%	Abs	%	P_1	Abs	%	P_2
Quantity of asthma attacks:								
during the day	4.3±0.5	–	2.0±0.5	–	<0.05	5.5±0.3	–	**<0.05**
during the night	3.1±0.5	–	1.1±0.6	–	<0.05	5.0±0.2	–	**<0.05**
Sleep disturbance	27	90	16	53.3	<0.01	29	96.7	**>0.05**
Dyspnea in total:	30	100	19	63.3	<0.05	29	96.7	**>0.05**
light physical activity	19	63.3	1	3.3	<0.01	7	23.3	**<0.0**
moderate physical activity	11	36.7	18	60.0	<0.01	22	73.3	**<0.0**
Lung rales	**30**	**100**	**4**	**13.3**	**<0.01**	**30**	**100**	**>1.0**

Note: P_1 – in comparison with the indicators at the presentation to the in-patient department;

P_2 – in comparison with the indicators at the presentation to the in-patient department.

Conducted GERD therapy eliminated epigastric burning, chest pain, food and acid eructation in 100% cases, the patients were released from the hospital in satisfactory condition with moderate disorders of pulmonary ventilation (Table 5).

Table 5. Dynamics of GERD clinical signs of patients with BA on standard treatment (1st group, n=30)

Symptoms	Before treatment		One month after start of treatment			Four months after treatment			
	Abs	%	Abs	%	P_1	Abs	%	P_2	P_3
Epigastric burning	30	100.0	0	0	<0.001	24	80.0	<0.001	**>0.1**
Chest pain	24	80.0	0	0	<0.001	26	86.6	<0.001	**>0.05**
Eructation in total, incl.:	25	83.3	11	36.6	<0.05	24	80.0	<0.05	**>0.1**
acid	9	30.0	0	0	<0.001	9	30.0	<0.001	**>0.1**
gaseous	16	53.3	11	36.6	<0.05	17	56.6	<0.05	**>0.1**
food	18	60.0	0	0	<0.001	11	36.6	<0.001	**<0.05**
Feeling a lump in the throat	14	46.6	5	16.7	<0.05	13	43.3	<0.05	**>0.1**
Difficulty in swallowing	**11**	**36.6**	**6**	**20**	**<0.05**	**7**	**23.3**	**<0.05**	**<0.05**

Note: P_1 – in comparison with the indicators at the presentation;

P_2 – in comparison with the indicators at the release;

P_3 – in comparison with the indicators at the presentation.

However, four months after treatment all clinical signs returned, had the same severity and frequency. Despite the significant reduction of GER quantity four months after treatment, this indicator did not positively reflect spirography results (Table 1). We consider that reinforced obstruction, increased asthma and dyspnea attacks of patients with BA combined with GERD together with GERD complaints repeated four months after treatment are connected with a change in the ratio of acid and alkaline refluxes towards alkalization of the lower esophagus (57% at the presentation against 36.6% four months after treatment of acid and 43% at the presentation against 63.4% four months after treatment of alkaline).

Solid evidence of restoration of the nature and quality of patients' mental state complaints also showed the intensification of excitation in the central nervous system and pathological effect on obstruction degree and GER quantity. This should be taken into account during the observation of patients with BA combined with GERD and to additionally prescribe medicine that increases the activity of gastro-intestinal tract, normalizes the processes of excitation and inhibition in the cerebral cortex and regulates acidity by physiological effects.[18,19,20,21]

The disorders of the neuropsychic sphere, external respiratory function, esophageal and gastric pH, that were detected during our study, precipitated the use of sulpiride in multiple treatment of patients with GERD combined with BA.

We compared results of clinical, functional and instrumental studies with results of patients who did not take sulpiride (1st group) and also with each other (2nd, 3rd and 4th

groups). Prescription of sulpiride in addition to traditional treatment for patients with GERD combined with BA had a favorable therapeutic effect in all cases.

We found changes in the studied clinical indicators in all groups of patients with GERD combined with BA who were treated with sulpiride added to the therapy. Thus, starting from the 2nd group these changes were significantly better ($p<0.05$), while patients of the 3rd group, whose GERD was treated only with sulpiride and rabeprazole, had the most significant difference in indicators ($p<0.01$).

Thus, patients of the 2nd group at the release from the in-patient department did not demonstrate asthma stacks during the day, only 40% of patients (53.3% in the 1st (control) group) had sleep disturbance. No one had dyspnea during light physical activity and there were 20% less dyspnea during moderate physical activity than in the 1st group of patients. There were fewer patients who had sibilant lung rales ($p<0.01$).

Table 6. Dynamics of psychoemotional state symptoms of patients with BA combined with GERD on standard treatment with added sulpiride (2nd group, n=25)

Symptoms	1st group (n=30)			2nd group (n=25)		
	Before treatment	One month after treatment	Four months after treatment	Before treatment	One month after	Four months after treatment
Dizziness	19 (63.3%)	5 (16.7%)	18 (60.0%)	16 (64%)	0 (0%)	**16 (64%)**
Irritability	27 (90.0%)	21 (70.0%)	29 (96.7%)	22 (88%)	2 (8%)	**16 (64%)**
Asthenic syndrome	27 (90%)	21 (70%)	28 (93.3%)	22 (88%)	2 (8%)	**15 (60%)**
Weakness	26 (86.6%)	5 (16.7%)	25 (83.3%)	22 (88%)	0 (0%)	**21 (84%)**
Anxiety and fear	14 (46.7%)	5 (16.7%)	15 (50%)	12 (48%)	0 (0%)	**12 (48%)**
Hypochondriac syndrome	24 (80%)	5 (16.7%)	24 (80%)	21 (84%)	0 (0%)	**18 (72%)**
Sleep disturbance	26 (86.6%)	21 (70%)	28 (93.3%)	21 (84%)	2 (8%)	**15 (60%)**
Performance decrement	15 (50%)	6 (20%)	14 (46.7%)	14 (46.7%)	0 (0%)	**13 (52%)**
Depressive syndrome	**22 (73.3%)**	**18 (60%)**	**24 (80%)**	**19 (76%)**	**0 (0%)**	**15 (60%)**

Patients with BA combined with GERD of the 2nd group also had less severe mental symptoms. Patients of the 2nd group did not notice dizziness, weakness, performance decrement or anxiety and fear. At the same time, the patients of the first group had these symptoms with the frequency from 7 to 20% respectively (Table 6).

Table 7. Dynamics of symptoms of GERD that proceeds combined with BA on standard treatment with added sulpiride (2nd group, n=25)

Symptoms	1st group (n=30)			2nd group (n=25)				
	Before treatment	One month after treatment	Four months after treatment	Before treatment	One month after	Four months after treatment	P_1	P_2
Epigastric burning	30 (100%)	0	24 (80%)	25 (100%)	0	18 (72%)	<0.05	**<0.05**
Chest pain	24 (80%)	0	26 (86.6%)	20 (80%)	0	21 (84%)	>0.1	**>0.05**
Feeling a lump in the throat	14 (46.6%)	5 (16.7%)	13 (43.3%)	12 (48%)	3 (12%)	9 (36%)	<0.05	**<0.05**
Eructation in total:	25 (83.3%)	11 (36.6%)	24 (80%)	21 (84%)	5 (20%)	17 (68%)	<0.05	**<0.05**
Acid	9 (30%)	0	9 (30%)	8 (32%)	0	5 (20%)	<0.05	**<0.05**
Gaseous	16 (53.3%)	11 (36.6%)	17 (56.6%)	14 (56%)	5 (20%)	11 (44%)	<0.05	**>0.05**
Food	18 (60%)	0	11 (36.6%)	14 (56%)	0	7 (28%)	<0.05	**<0.01**
Difficulty in swallowing	**11 (36.6%)**	**6 (20%)**	**7 (23.3%)**	**9 (36%)**	**5 (20%)**	**5 (20%)**	**>0.1**	**<0.01**

Note: P_1 – in comparison with the 1st group;
P_2 – in comparison with the indicators before treatment.

Patients of the 2nd group also had less GERD symptoms than the patients of the 1st group. Epigastric burning disturbed nobody (disappeared in 100% of patients), only 20% of patients had gaseous eructation (significantly less than the patients of the first group ($p<0.05$)). 20% of patients had difficulty in swallowing at the release, which is also less compared with the 1st group.

Only 2nd group of patients was comparable for the presence of specific BA symptoms with the 1st group four months after the end of treatment. The clinical course has intensified for the patients of both groups regardless of the choice of treatment, and patients of the 2nd group had even a little bit more sibilant lung rales and asthma attacks four months after treatment. All mental symptoms of the patients in both groups restored in full four months after the end of treatment (Table 6). The patients of the 2nd group had less GERD clinical signs six months after the release. Thus, 72% of patients (80% of the patients of the 1st group) had epigastric burning, 20% had difficulty in swallowing, which is less than the patients of the 1st group ($p<0.05$) (Table 7).

Discussion:

The results of patients of the two groups that we received after clinical observation of the BA combined with the GERD course confirm the feasibility of sulpiride prescription even by adding it to the GERD standard treatment. However, analysis of the results of functional and instrumental studies, as well as comparison of the 3rd and the 4th groups among themselves and with control (1st) group showed that complaints of patients with GERD combined with BA along with the psychoemotional manifestations, that are inherent in this condition, are not always criteria for assessing the severity of the disease and do not characterize the state of external respiration and pathomorphological changes in the esophageal and gastric mucosa.

For example, basic pathognomonic indicators that characterize the external respiratory function improved after one-month treatment in patients of the 2nd group in comparison with the indicators of the patients of the 1st group ($p<0.05$). However, the studied indicators in the patients of both groups did not differ among themselves four months after the end of treatment ($p>0.05$). Therefore, the patients of the 2nd group had better spirography results only at the release from the in-patient department (Table 8).

Table 8. Dynamics of SPG indicators of patients with BA that proceeds combined with GERD (2nd group, n=25)

SPG indicators	Before treatment	One month after the start of treatment	P_1	P_2	Four months after treatment	P_3
Vital capacity	77.0±1.0	98.2±2.0	<0.05	<0.05	80.0±1.3*	**<0.05**
FEV1	39.5±1.0	65.5±1.5	<0.05	<0.05	39.6±1.0*	**<0.05**
Tiffeneau index (FEV1/ Vital capacity)	**43.2±0.9**	**67.6±1.7**	**<0.01**	**<0.05**	**46.0±1.9***	**<0.05**

Note: P_1 – in comparison with reference ranges;

P_2 – in comparison with the indicators before treatment;

P_3 – in comparison with the indicators one month after the start of treatment;

* – no significant differences in comparison with the indicators of the 1st group ($p>0.05$).

At the same time, pH measurement indicators show that the comprehensive treatment of the patients of the 2nd group with the use of sulpiride did not change the quality of refluxes four months after the end of treatment (Table 9).

Table 9. Dynamics of core indicators of pH monitoring in lower third of esophagus of the patients with BA combined with GERD (2nd group, n=25)

pH measurement indicators	Before treatment (n=55)	Four months after treatment	
		1st group n=30	2nd group n=25
GER quantity	565.0±10.0	152.2±7.0	**121.0±3.0**
Lowest pH	2.5±0.7	2.2±0.2	**2.5±0.5**
Highest pH	7.9±0.3	7.9±0.4	7.5±0.6
Acid	31 (56.4%)	11 (36.6%)	10 (40%)
Alkaline	24 (43.6%)	19 (63.4%)	15 (60%)

Prescribing sulpiride to the patients of the 2nd group, who did not stop taking domperidone and rabeprazole within their standard treatment regimen, we noticed only the reduction of GER quantity instead of positively increased gastric and intestinal motility and thereby reduction of GER quantity. At the same time, they had the same complaints as the patients of the 1st group 4 months after the treatment. In our opinion, sulpiride and domperidone should not be prescribed simultaneously as they have a similar effect on gastrointestinal motility, especially if there are mental health complaints in anamnesis.

Relying on the received results, we excluded domperidone from the standard GERD treatment regimen of the patients of the 3rd group and treated the patients of the 4th group only with sulpiride (BA was treated according to the standard regimen).

Clinical observations of the patients of the 3rd and the 4th group showed that reduction or disappearance of the analyzed BA, GERD and mental status symptoms completely depended on conducted GERD treatment. The patients of the 4th group showed the most stable indicators of clinical improvement for all systems. Considering that the patients of the 3rd group in comparison with the patients of the 2nd group showed almost all better clinical, functional and instrumental indicators reliably ($p<0.05$), we suggest analyzing the results of the study of the 4th group in comparison with the same indicator of the patients of the 3rd group(Table10).

Table 10. Dynamics of psychoemotional state symptoms of patients with GERD combined with BA on sulpiride treatment (4th group, n=30)

Symptoms	3rd group (n=25)			4th group (n=30)		
	Before treatment	One month after the start of treatment	Four months after treatment	Before treatment	One month after the start of treatment	Four months after treatment
Dizziness	17 (68.0%)	0	9 (36.0%)*	20 (66.7%)	0	**7 (23.0%)****
Irritability	22 (88.0%)	0	9 (36.0%)*	27 (90.0%)	0	**8 (26.0%)****
Asthenic syndrome	22 (88.0%)	0	9 (36.0%)*	26 (86.7%)	0	**8 (26.0%)****
Weakness	22 (88.0%)	0	13 (52.0%)*	26 (86.7%)	0	**8 (26.0%)****
Anxiety and fear	11 (44.0%)	0	8 (32.0%)*	13 (43.3%)	0	**7 (23.0%)****
Hypochondriac syndrome	20 (80.0%)	0	10 (40.0%)*	24 (80.0%)	0	**7 (23.0%)****
Sleep disturbance	22 (88.0%)	2 (8%)	11 (44.0%)*	27 (90.0%)	2 (6.6%)	**8 (26.0%)****
Performance decrement	15 (60.0%)	0	10 (40.0%)*	20 (66.7%)	0	**6 (20.0%)****
Depressive syndrome	**19 (76.0%)**	**0**	**10 (40.0%)***	**24 (80.0%)**	**0**	**7 (23.3%)****

Note: * – $P_1<0.05$, all indicators are reliably lower in comparison with the indicators of the 2nd group;** – $P_2<0.05$, all indicators are lower in comparison with the indicators of the 3rd group.

Comparative analysis showed that all BA clinical signs stabilized in the patients of the 4th group. The symptoms typical for BA (day and night asthma attacks, sleep disturbance, lung rales) were observed in the same percentage of cases after release from the hospital and six months after the release. Moreover, the patients with BA had reliably less complaints than patients of the 3rd group, where sulpride was used together with rabeprazole ($p<0.05$).

100% of patients of the 4th group had no most important mental symptoms one month after the start of treatment (excluding sleep disturbance: only 6.6% − 2 people − had this symptom). Psychoemotional condition of the patients of the 3rd and 4th groups one month after the end of treatment did not differ. However, there were differences in psychoemotional condition of patients of these two groups four months after the treatment. All patients of the 4th group complained less often ($p<0.05$) about change in psychoemotional state than the patients of the 3rd group (Table 13).

Dynamics of morphological changes of esophageal and gastric mucosa in patients of the 3rd group differed from the examination of other groups. 40% cases demonstrated edema and hyperemia with no erosions and ulcers. 60% of the patients of the 4th group had edema and hyperemia of mucosa, 6.7% of them had erosion and ulcers (Table 11).

Table 11. FEGDS dynamics of patients with BA combined with GERD on sulpiride treatment (n=30)

Morphological changes in the esophagus	Before treatment (n=55)	Four months after treatment			
		3rd group (n=25)	P_1	P_2	4th group (n=30)
I stage of esophagitis	27 (49.0%)	10 (40.0%)	<0.05	<0.01	**18 (60.0%)**
II stage of esophagitis	**14 (25.4%)**	**0**	**<0.01**	**<0.05**	**2 (6.7%)**

Note: P_1 − in comparison with the indicators of the 2nd group;
P_2 − in comparison with the indicators of the 4th group.

Conclusion:

The results of clinical and instrumental research methods clearly show the advantage of sulpiride and rabeprazole combination therapy against GERD combined with BA. Despite clinical evidence about the predominance of only sulpiride treatment effectiveness, instrumentation data show that the patients of the 3rd group experience better process of reparation and normalization of intraesophageal pH.

The conducted clinical observations allow us to conclude beneficial effects of sulpiride, used both in combination with other pathogenetic agents, and in the form of monotherapy. In the latter case, used as a means of accelerating the relief of the main clinical symptoms of GERD and BA when combined, but in a lesser degree than the combination of rabeprazole and sulpiride, improving mucosal reparation. This demonstrates an advantage of such therapy of patients with GERD combined with BA comparing to traditional. In our opinion, sulpiride might be also used in combination therapy of BA even without GERD to eliminate the symptoms of the psychoemotional sphere.

Results of our observation may be of some importance for the substantiation of the pathogenetic treatment of patients with BA

combined with GERD. Positive changes in patient's health according to their assessment after the treatment with sulpiride, the best external respiratory function indicators of all treatment options, acidity and morphological changes in the esophagus are a reliable criterion for confirming a positive result.

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