Wobenzym in the Complex Treatment of Pneumonia among Military Personnel Immunized with Pneumococcal Vaccine

I. M. Borisov, T. G. Shapovalova

ABSTRACT

The **purpose** of the work: to evaluate the clinical efficacy of preparation Wobenzym inclusion in the complex therapy of pneumonia in previously vaccinated with pneumococcal vaccine "Pneumo-23" and unvaccinated patients.

The method of research. The study included 157 patients with pneumonia, men, soldiers performing military service at the age of 18 to 22 years (19.2 ± 0.19), admitted to the pulmonology department of the military hospital in the period from 2007 to 2010. Depending on the treatment, all patients included in the study were divided into four groups randomly. The 1st main group (MG, n = 46) included patients previously vaccinated with pneumococcal vaccine and treated with standard therapy; in the 2-nd (MGSET) - vaccinated patients (n = 44), who were prescribed in addition Wobenzym; in the third group - the comparative (CG, n = 34) - patients previously non-vaccinated and treated with standard therapy, and the 4th (CGSET) - unvaccinated patients, but additionally treated with medication Wobenzym (n = 33).

Results. It is shown that the inclusion of the preparation Wobenzym in the complex therapy of pneumonia contributed to a more rapid regression of all clinical manifestations of pneumonia and reducing the probability of formation of residual radiological changes of lung tissue. It is found that the inclusion of systemic enzyme therapy drugs in the complex treatment of pneumonia is pathogenetically substantiated.

Keywords: pneumonia, systemic enzyme therapy, Wobenzym.

INTRODUCTION

The problem of diagnosis and treatment of pneumonia continues to be one of the most relevant in the modern health care. Despite the continuous improvement of diagnostic methods and the availability of modern high antibacterial drugs, pneumonia remains a leader in the structure of morbidity and mortality from infectious diseases in developed countries [2, 11]. Remains a high incidence of pneumonia in the Armed Forces of the Russian Federation among the soldiers performing military service [3, 5, 8], despite ongoing treatment and preventive measures, including vaccination of personnel autumn appeals pneumococcal vaccine [1, 10]. Promising to study the possibility of potentiation medication events in patients with pneumonia,

including those previously vaccinated with pneumococcal vaccine, through the use of systemic enzyme therapy. At present, a number of studies have shown that the presence of drugs in systemic enzyme therapy (SET) plant and animal enzymes with different substrate specificity allows for synergistic anti-microbial agents at various stages of treatment of infectious and inflammatory processes affecting the microcirculation disorders and immune disorders [4, 6].

Objective: to evaluate the clinical efficacy of inclusion in the complex therapy of pneumonia preparation Wobenzym in previously vaccinated with pneumococcal vaccine "Pneumo-23" and the non-vaccinated patients.

MATERIALS AND METHODS

The study included 157 patients with pneumonia, men, soldiers performing military service at the age of 18 to 22 years (19,2 ± 0,19), admitted to the pulmonology department of the military hospital in the period from 2007 to 2010. Depending on the treatment, all patients included in the study were divided into four groups randomly. In the 1st main group (MG, n = 46) included patients previously vaccinated with pneumococcal vaccine and treated with standard therapy in the 2 nd (MGSET) - vaccinated patients (n = 44), which was prescribed in addition Wobenzym, a the 3th group - the comparative (CG, n = 34) included patients previously non-vaccinated and treated with standard therapy, and the 4th (CGSET) - unvaccinated patients, but additionally treated with medication Wobenzym (n = 33). Pneumococcal vaccination vaccine "Pneumo-23» (Aventis Pasteur SA, France) soldiers conducted only once, in the first days after the arrival of a military unit, 0.5 ml intramuscularly concurrently with the administration of purified adsorbed tetanus-diphtheria toxoid. The preparation Wobenzym (Mucos Pharma GmbH & Co, Germany) was administered in groups and OGSET SGSET simultaneously with an antibiotic to 3 tablets 3 times a day for 7 days, 30 minutes before a meal. Side effects during treatment with the drug have been identified. All patients received empirical antibiotic treatment with amoxicillin or III generation cephalosporin (ceftriaxone, cefotaxime), or azithromycin, or cephalosporin combined with a macrolide. Select antimicrobial dose and route of administration (intravenous, intramuscular or oral) dependent on the probability of the proposed agent pneumonia and severity of disease. According to the testimony appointed detoxification infusion therapy, bromhexine 48 mg / day, range of physical therapy and physiotherapy. The control group consisted of 20 healthy individuals

The study used classification of pneumonia, proposed by the European Respiratory Society (ERS) in 1995, taking into account the conditions in which the disease has developed, especially infection of lung tissue, as well as state of immunological reactivity of the patient [9, 12].

Inclusion criteria were the presence in the patients of clinical and radiographic evidence of pneumonia. Exclusion criteria were patients with severe pneumonia requiring treatment in the intensive care unit and intensive care, and the presence of comorbidity.

The study used the following diagnostic methods:

- general clinic: general blood, urine, sputum, including Mycobacterium tuberculosis, bacteriological culture of sputum on the microflora and its sensitivity to antibiotics diskodiffuzionnym method;

- biochemical studies: determination of ALT, AST, fibrinogen, C-reactive protein seromucoid, serum glucose, serum total protein.

- instrumental: radiography or fluoroscopy of the chest in a straight line, the left and / or right lateral views in the dynamics of the disease, the study of respiratory function (ERF), an electrocardiogram.

Fluorography of the chest was performed with a scanning digital fluorograph "Proscan 2000". Standard X-ray examinations of the chest cavity - a digital installation DuoDiagnost vertical module Bucca company «Philips» at 100% of the patients on admission and on the 14th day of treatment. In the case of persistent infiltration of X-ray examinations of the chest were added every 10 days until complete resolution of infiltrative changes in the lung tissue. ERF study was carried out with the help of computer spirometer MedGraphics CPFS - D / USB 1, 8 and 14 day hospital treatment.

The analysis of the clinical efficacy of the drug was conducted in Wobenzym study groups on the following criteria: the duration and intensity of the temperature response on a 4-point standardized scale [7], the severity and duration of symptoms of intoxication, the dynamics of clinical symptoms of pneumonia - weakness, malaise, cough severity and number of sputum on a 4-point standardized scale [7], we supplemented with a detailed symptom severity of pleural pain syndrome, physical signs over the zone of destruction of lung tissue, the rate of complications. Consideration was also given laboratory (white blood cell count, erythrocyte sedimentation rate, C-reactive protein, fibrinogen, α2 - globulins) and instrumental data (radiographic infiltration of the lung tissue, lung function) and the duration of antibiotic therapy.

The obtained data were processed using the statistical software Micro-soft Office Excel 2007 and Statistica 6.0 (StatSoft, Inc. 2001). Universal statistical package Statistica 6.0 was used to test the hypothesis of equality of the means for the two different data from general populations using two-sample Student's t-test. For a comparison of the percentages used goodness $\chi^2$of fit

calculated using the package Statistica 6.0.

RESULTS AND DISCUSSION

The main clinical symptoms (cough, chest pain, fever, weakness) and objective signs of pneumonia (shortening of percussion tones over an area of damage to lung tissue and moist finely wheezing) were arrested in MGSET for 3 - 4 days earlier than in MG and in CGSET, and 5 - 6 days faster than in the CG. By the 3 rd day of febrile patients in MGSET was 91% lower in all the examined were cropped symptoms of intoxication, and by the 5th day - and all of the original pathological symptoms. Patients in this group normalization of body temperature occurred two times faster (at 4,2 ± 0,2 days) than in patients with CG ($p<0,05$). If the first third day in patients MGSET and MG statistically determined before the benefits of the vaccination pneumococcal vaccine, in the following 4 days of treatment - inclusion in the complex treatment of pneumonia preparation Wobenzym, and especially in vaccinated patients.

So, if in the 1st study day statistically significant difference between groups MGSET, MG, and CGSET, CG in the number of patients who had chills, chest pain, shortness of breath ($p<0,05$ / χ^2/) attracted attention, then on day 3 – there was a statistically significant difference in the above characteristics between CGSET and CG, MGSET and MG. Regression MGSET cough occurred in 2.4 times faster than MG ($p<0, 05$ / χ^2/). In CGSET since the third day from the beginning of application Wobenzym observed a decrease in cough and expectoration of sputum and their subsequent termination of an average of 8-day, and by the 7th day of treatment in this group was a statistically significant difference on the clinical symptom with ill CG ($p <0,05$ / χ^2/) and MG ($p <0,05$ / χ^2/) In the CG character of the cough within the first 5 days of treatment is not significantly changed, and completely arrested only 14 - the 15th day of treatment.

Duration periods of fever and toxicity were shorter in 1.5 and 1.2 times shorter than MGSET than in MG, 1.8 and 1.3 to CGSET times than CG, 0.9 times and 1.1 MGSET times shorter than CGSET, respectively (Table 1). The decrease in body temperature to the 3rd day of treatment was observed in 91% of patients MGSET and only 79.4% of patients CG. By 4rd day all patients MGSET body temperature to normal one, while the CG to 5-day body temperature dropped from 91.1%, and only on the 7th day - all patients. Low scores were higher in patients CG and CGSET is 1.8 times higher than in MGSET and MG. Patients MG normalized temperature at the 6th day, CGSET - 5-th day and CG - to 7-day treatment. In MGSET temperature normalization occurred two times faster than CG, wherein the average baseline score was higher than the temperature of CGSET and CG. In the course of treatment was observed alignment scoring indicators of temperature reaction between groups MGSET and CGSET. The worst results were

noted in CG: on the 6th day of fever corresponded to 0, 3 points. Normalization auscultation pictures over the affected lung segments in patients MGSET occurred on the average for the 5th, in patients CGSET - to 7-th, and in patients MG and CG - to only 8 - 9 day of treatment, there was a 1, 4 times slower than MGSET.

Length antibacterial therapy did not exceed MGSET 5 - 6 days, dose rate - 10.2 g, while in these MG were 6 - 7 days. and 13.8 g of CGSET - 6 - 8 days. and 15.6 g of CG - 8 - 9 days. 17.9 g and thus the effectiveness of antibiotic therapy in MGSET was the highest, and the average dose rate of antibiotics in this group was less than CG 1.75 fold (Table 1). In MGSET complications of pneumonia (toxic shock, acute respiratory failure) were cropped to 2.1 times faster than MG, and CGSET - 1.5 times faster than CG.

In addition, patients and MGSET and CGSET, unlike the MG and CG celebrated faster regression of initially elevated laboratory parameters of inflammatory activity (leukocytosis, ESR, CRP, seromucoid, content, α2-globulin and fibrinogen), starting from 5th day of the disease. Laboratory parameters in patients of the groups at the end of the course of antibiotic and systemic enzyme therapy (day 8) are presented in Table. 2.

In the analysis of blood parameters at the time of completion of the course of treatment would Wobenzym la showed a trend toward normalization in their groups MGSET, CGSET, approaching normal levels in the MG and store it above the norm in the CG (Table 3).

Violations of ERF in the first day of hospital treatment for obstructive, restrictive or mixed type were found in 52.2% of patients MGSET, 54.3% of patients in the MG, in 84.8% of patients CGSET and 85.2% of patients CG (Table 4).

A statistically significant difference between the above parameters indicative of the effectiveness of vaccination in patients MGSET and MG affecting the severity of pneumonia and the nature of the complications of the disease. However, data on the 8th day of treatment, not only confirmed the benefits of immunization troops organized military groups, but also showed the effectiveness of inclusion in the complex treatment of pneumonia preparation Wobenzym as in vaccinated and non-vaccinated patients. Multimodality treatment involving Wobenzym clearly depends on the recovery of external breathing. Thus, normalization of respiratory function by increasing ventilation mainly by improving bronchial obstruction was observed significantly more frequently in MGSET and CGSET than in the MG and CG. To discharge violations ERF in patients treated with additional medication Wobenzym as the previously vaccinated with pneumococcal vaccine "Pneumo-23" (MGSET group) and non-vaccinated (group CGSET) were detected in 4.5 times less likely than patients administered standard regimen (group MG, CG).

According to X-ray examination of the chest on the 14th day of treatment, complete

resolution of infiltrative changes in MGSET was found in 97.7%, in CGSET - at 93.9%, in the MG - at 93.5% in CG - in 85 3% of patients. Recovery of residual radiological signs in the form of strengthening lung pattern in MGSET noted only in one patient (2.3%), in CGSET - in 6.1% of patients. In the MG in 6.5% of patients were diagnosed with residual radiographic changes in the form of strengthening pulmonary pattern, focal fibrosis and pleural Mooring. In the CG in 14.7% of patients were ascertained recovery with residual changes in the form of the syndrome of pathological disorders lung pattern (interstitial tissue sealing, reinforcement, enrichment, strain, blurred pulmonary pattern), the expansion of the lung root on the affected side and pleural reaction in the form of its thickening .

Time resolution of infiltrative changes in the lungs according to radiographs in patients MGSET was 14,6 ± 1,6 days, length of stay in hospital - 18,1 ± 1,7 days. Similar rates of patients in the groups CGSET, MG and CG totaled respectively: 14,9 ± 1,8 and 19,4 ± 1,5 days; 16,5 ± 1,4 and 20,7 ± 1,2 days; 18,7 ± 1,3 and 24,1 ± 1,6 days. As a result, the inclusion of Wobenzym in the complex treatment of pneumonia al-lowed to reduce the time of treatment in the hospital with a 24,1 ± 1,6 to 18, 1 ± 1,7 days ($p< 0,05$).

CONCLUSION

The inclusion of the drug Wobenzym in the complex therapy of pneumonia contributed to a more rapid regression of all clinical manifestations of the disease. This is confirmed by the reduction in terms of clinical and laboratory recovery by an average of 3 days, febrile period - twice more clear positive dynamics of the X-ray is the 10th day of treatment in 87% of patients and a reduction in the amount of residual radiological manifestations of the 14th day of treatment to 9%. These clinical effects are due, presumably, the achievement of higher concentrations of antibiotic at the site of inflammation in common use with Wobenzym due to improved rheological properties of the blood and microcirculation in the lung tissue. The efficacy of Wobenzym in the treatment of pneumonia is higher in vaccinated patients.

These data suggest justified the inclusion of systemic enzyme therapy drugs in the complex treatment of pneumonia as a pathogenetically valid form of therapy.

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About the authors

Borisov Igor Michaylovich, Candidate of Medicine

Head of Pulmonology, Branch №12 1602 District Military Hospital, Znamensk

Address: 416540, Astrakhan Region, Znamensk, st. Lenin, 31

Phone: 8(85140)22762, mobile phone: 8902 1113 492.

E_mail: askbo@mail.ru.

Shapovalova Tatjana Germanovna, Doctor of Medicine

Razumovsky Saratov State Medical University, Professor of Department of Therapy of Pediatric and Stomatological Faculties, Saratov

Address: 410012, Saratov , st. Bolshaja Kazachja, 112

Phone: 8(8452)502396, mobile phone : 8927 1058 499

E_mail: t.g.shapovalova@gmail.com.

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Table 1

Indicators of clinical efficacy of Wobenzym in the treatment of pneumonia

Index (duration, days)	BGSET (n = 44)	BG (n = 46)	CGSET (n = 33)	CG (n = 34)
Fever	3,2 ± 0,3*	5,3 ± 1,1	4,5 ± 0,4**	6,3 ± 0,6
Cough	5,5 ± 1,2	7,7 ± 1,8	7,2 ± 0,6	8,1 ± 1,9
Antimicrobial therapy	6,1 ± 0,4*	6,7 ± 0,6	6,9 ± 0,7**	7,3 ± 0,9
Patient day	11,4 ± 0,7	13,6 ± 1,2	13,2 ± 0,9	17,4 ± 2,2

Note:

* - difference between BGSET and BG significantly, $p < 0,05$;

** - difference between CGSET and CG significantly, $p < 0,05$

Table 2

Laboratory findings in patients studied groups on the 8th day of treatment,%

Index	BGSET (n = 44)	BG (n = 46)	CGSET (n = 33)	CG (n = 34)
Leukocytosis, ($\geq 9{,}0 \times 10^9$/l)	0	2,1; **p =0,042 (χ^2)	0	8,8
Accelerated ESR, (more 10 mm / hr)	2,2; *p =0,001; **p =0,000001; ***p =0,017 (χ^2)	10,8; **p =0,003(χ^2)	15,1; **p =0,032 (χ^2)	29,4
Seromucoid, (more 0, 20 units)	0	0	0	8,8
The presence of CRP	0	2,1; **p =0,009 (χ^2)	0	11,7
The increase in α_2-globulin, (more 6, 9 %)	0	2,1; **p =0,009 (χ^2)	0	11,7
Fibrinosis, (more 11,7 micromoles /l)	0	4,0; **p =0,017 (χ^2)	3,0 **p =0,005 (χ^2)	14,7

Note:

* - differences are statistically significant with respect to CGSET;

** - differences are statistically significant with respect to CG;

*** - differences are statistically significant with respect to BG

Table 3

The peripheral blood of patients studied groups on the 8th day of treatment

Index	Groups of patients			
	BGSET (n = 44)	BG (n = 46)	CGSET (n = 33)	CG (n = 34)
Average Rating:				
leukocytes, × 10^9/l	5,6 ± 0,75	6,7 ± 1,21	6,3 ± 2,44	8,5 ± 1,31
neutrophils stab, %	4,2 ± 1,12	4,7 ± 1,23	4,1 ± 2,08	6,6 ± 0,75
The number of immature forms of leucocytes more 10%	0	2,1; **p =0,042 (χ^2)	0	8,8
The average number of lymphocytes, %	22,6 ± 2,4	21,2 ± 2,9	20,2 ± 2,1	17,2 ± 2,8
Average ESR, mm / hr	15,2 ± 2,3*	17,4 ± 3,6	19,1 ± 4,4	21,4 ± 5,8

Note:

* - difference to those in CG significantly, p < 0, 05;

** - the difference is statistically significant with CG

Table 4

The frequency of violations of respiratory function in patients studied groups,%

Groups of patients	The frequency of violations of respiratory function during therapy,%		
	1-е сутки	8-е сутки	14-е сутки
BGSET (n = 44)	52,2; *p =0,005; **p =0,004 (χ^2)	2,2; *p =0,001; **p =0,0000001; ***p =0,0002 (χ^2)	0
BG (n = 46)	54,3; *p =0,009; **p =0,008 (χ^2)	19,5; **p =0,000006 (χ^2)	0
CGSET (n = 33)	84,8	15,1; ***p =0,0000001 (χ^2)	0
CG (n = 34)	85,2	59,9	2,9

Note:

* - differences are statistically significant with respect to CGSET;

** - differences are statistically significant with respect to CG;

*** - differences are statistically significant with respect to BG