VARIA

EFFECTIVENESS OF IMMUNOMODULATOR LISTEN IN COMPLEX THERAPY OF PATIENTS WITH MULTIRESISTANT TUBERCULOSIS

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Summary

47 patients were involved in the research. The use of immune response modifier glucosaminilmuramilpentapeptide (LIASTEN) along with the antimycobacterial therapy resulted in speeding up abacillation in (1.7±0.2) months, dispersion of focal abnormalities and infiltration in (1.5±0.1) months and the cicatrization of destruction cavities in (1.6±0.1) months as compared to the previous indicators. It should be noted that the average treatment duration during the intensive phase might be reduced by (1.9±0.3) months.

Key words. Multi-drug resistant tuberculosis, glucosaminilmuramilpentapeptide, treatment efficiency.

Rezumat

În acest studiu au fost implicaţi 47 de pacienţi. A fost administrat imunomadulatorul glucosaminilmuramilpentapeptid (LIASTEN) în complex cu tratamentul antituberculos, care a contribuit la accelerarea abacilării în (1,7 ± 0,2) luni, rezorbţia focarelor infiltrative în (1,5 ± 0,1) luni şi cicatrizarea cavităţilor destructive на(1,6 ± 0,1) faţă de lotul de control. Rezultatele obţinute au dat posibilitate de a reduce durata medie a tratamentului în faza intensivă cu 1,9 ± 0,3 luni.

Cuvinte cheie. Tuberculoza cu multirezistenţă, glucosaminilmuramilpentapeptidul, eficacitatea tratamentului.

Резюме

В настоящее исследование включены 47 пациентов, у которых был использован иммуномодулятор глюкозаминилмурамилпентапептид (LIASTEN) вместе с антибактериальной терапией, что определило ускорение абациллирования на (1,7 ± 0,2) мес., рассасывание очаговых изменений и инфильтрации на (1,5 ± 0,1) мес. и заживление каверн на (1,6 ± 0,1) мес., в сравнении с контрольной группой, которые получали только антибактериальные препараты. Это дало возможность сократить длительность лечения в интенсивной фазе на (1,9 ± 0,3) мес.

Кдючевые слова. Туберкулез с множестенной лекарстенной резистентностью, глюкозаминилмурамилпентапептид, эффективность лечения.

The follow-up of drug resistant tuberculosis profile, prevalence and incidence in Ukraine, the spread of drug resistant forms of the specific process, in particular, multi-drug resistant being the most dangerous one causing the loss of labour capacity, health deterioration as well as the increase of disability and mortality rates have been the topical issues nowadays [4, 7, 10, 14, 15].

The favourable conditions for the selection of drug resistant tuberculosis mycobacteria are one of the reasons for the multi-drug resistant tuberculosis epidemy: the lack of full controlled cure, treatment interruptions, poor sequestration in in-patient departments (nosocomial contamination) etc [1].

The curing of patients diagnosed with multi-drug resistant and extensively drug-resistant tuberculosis is very challenging and differs from the treatment of patients releasing mycobacteria sensitive to antituberculosis drugs according to chemical therapy regimes and the relevant agents included in this therapy, the treatment duration and the frequency of undesired side effects. Thus, the treatment codes applied for chemical resistant tuberculosis [3, 11 - 13] have been constantly improved over the last years.

For this purpose, the differentiated use of pathogenetic agents have been developed for increasing the efficiency of complex chemical therapy for treating tuberculosis along with the search of new etiotropic therapy codes [8].

LIASTEN serving as a pathogenetic agent in the

complex therapy was prescribed in cases of respiratory diseases, the first diagnosed chemical sensitive tuberculosis [2, 5,], breast cancer [9], surgical infections [6] etc. Taking into consideration the necessity of raising the treatment efficiency of multi-drug resistant tuberculosis a research has been made to prove the reasonability of prescribing immune response modifier glucosaminilmuramilpentapeptide (LIASTEN).

The study the efficiency of the immune response modifier glucosaminilmuramilpentapeptide (LIASTEN) used in the complex therapy for treating multi-drug resistant tuberculosis based on some clinical, roentgenographical and laboratory research is **the objective of this scientific paper.**

Materials and methods. 47 patients took part in the research. The immune response modifier glucosaminilmuramilpentapeptide (LIASTEN) serving as a pathogenetic agent was used in combination with the antimycobacterial therapy (AMBT). The patients were divided into two groups: the 1st group consisted of 22 patients undergoing only antimycobacterial therapy (AMBT); the 2nd one consisted of 25 people undergoing the complex treatment involving LIASTEN (with the following treatment code: AMBT+LIASTEN). All the patients underwent the complex clinical roentgenographical, microbiological and general laboratory examination in the intensive phase (before curing, in 2, 4, 6 and 8 months after treatment). The antimycobacterial therapy was applied in accordance with the drug sensitivity test in the generally accepted doses with a view to kg-BM (basic treatment).

LIASTEM is an immune response modifier of natural origin with a wide spectrum of effect. It is a fragment of the lactic bacteria cell wall with the glucosaminilmuramilpentapeptide as an active substance (N- acetylglucosaminyl-N-acetylmuramil-L-alanyl-D-glutamyl-L-lysyl-D-alanyl-L-asparagile) with regard to peptides. LIASTEN was injected intramuscularly in cases of evident T-cell immunological suppression with over 30.0% decrease of T-lymphocytic pool once per 6 days, No. 5.

Intoxication decrement, the dispersion of focal abnormalities and infiltration in the lungs, cicatrization of destruction cavities, abacillation and the normalization of general laboratory parameters in the course of intensive therapy were the main criteria of efficient tuberculosis treatment.

Findings and discussion. The division of patients according to clinical forms and the evidence of destruction in the lung tissue as well as the treatment methods are shown in Table 1.

As the Table 1 shows, the groups under research were practically identical according to the clinical forms, the evidence of lung tissue destruction and the structure of pathogen's resistance to antimycobacterial agents. All the patients were first diagnosed with multi-drug resistant pulmonary tuberculosis. The frequency of the confirmed infiltrative and disseminated forms of the specific process was almost the same in all the groups.

Table 1

The division of patients diagnosed with multi-drug resistant tuberculosis according to clinical forms, the evidence of lung destructions and treatment methods.

Tuberculosis forms	The 1st group (antimycobacterial therapy)		The 2nd group antimycobacterial therapy + LIASTEN)	
	total	destruction (abs./ %)	total	Destruction (abs./ %)
Infiltrative	10	10 (100.0)	7	7 (100.0)
Disseminated	12	12 (100.0)	8	8 (100.0)
total - n %	22 100.0	22 100.0	25	15 100.0

The research proved that the toxic syndrome in cases of LIASEN prescribed at the early stage of antimycobacterial therapy for patients diagnosed with multi-drug resistant tuberculosis (the 2nd group) was interrupted 1.6 times more frequently and faster as compared to the first group (68.0% versus 40.9% $p<0.05$). Intoxication syndrome were completely interrupted in the 2nd group during the first four months.

The same tendency was also evident in the general laboratory parameters.

Table 2

Frequency and terms of intoxication syndrome interruption in cases of multi-drug resistant tuberculosis

Patient groups	The amount of examined patients	The interruption of intoxication syndrome			
duration (months)		2	4	6	8
1-a abs.	22	9 40.9	7 31.8	6 27.3	-
2-a abs. %	25	17 68.0 *	8 32.0	-	-

Notes * – the difference between the first and second groups is reliable ($p_{1,3}<0.05$).

In particular, the normalization of blood

Table 3

Frequency and terms of bacterial excretion (culturally), dispersion of focal and infiltrative abnormalities

Patient groups (n)		Positive X-ray dynamics (according to the frequency of focal and infiltrative changes dispersion)					Abacillation frequency				
duration (months)		2	4	6	8	Partial dispersion	2	4	6	8	Mycobacterium tuberculosis+
1-a (22)	abs.	3	6	5	3	5	7	5	5	3	2
	%	13.6	27.3	22.7	13.6	22.7	31.8	22.7	22.7	13.6	9.1
2-a (25)	abs.	7	7	5	3	3	12	7	4	1	1
	%	28.0 *	28.0	20.0	12.0	12.0 *	48.0	28.0	16.0	4.0*	4.0*

Note* – the difference between the first and second groups is reliable ($p<0.05$);

sedimentation rate during two months of intensive therapy was observed in 68.0% patients from the second group and in 31.8% patients from the first group. At the same time, the decrease of blood sedimentation rate was evident more often in the second group as compared to the first one. Consequently, the 2nd treatment code (AMBT + LIASTEN) was more effective as compared to the first one which was proved by the fast normalization of general blood values and the elimination of intoxication syndrome.

The microbiological research findings are shown in Table 3.

The monitoring of X-ray follow-up data proves that the faster dispersion of sites of damage and infiltration was observed in the 2nd group, in particular, the significant positive dynamics of focal abnormalities and infiltration dispersion was more evident in the second group (28.0%) as compared to the first one (13,6 %, $p<0,05$) during the first two months of intensive therapy. The average duration of focal abnormalities and infiltration dispersion was (6.1 ± 0.2) months in the first group and (5.6 ± 0.1) months in the second group ($p<0.05$). The results of destruction cavity cicatrization are shown in Table 4.

The research proved the positive impact of the immune response modifier LIASTEN used at the beginning of the intensive phase of the antimycobacterial therapy. In two months of the intensive therapy the cicatrization of the destruction cavity was observed in 18.2% patients from the first group being by 2.2 times more frequent and faster in the patients from the second group (40.0 %) as compared to the first one ($p<0.05$-0.01). After the completion of the intensive phase the evidence of cavities was reliably less frequently observed in the patients treated with LIASTEN: the destruction was observed in 18.2% patients from the first group being almost by 3.6 times more frequent than in patients from the second group 5.0 % ($p<0.01$). Consequently, subject to the research findings the second treatment code is an effective one.

The analysis of frequency and the type of residual effects proves that the insignificant abnormalities were observed reliably more often in the second group of patients cured with LIASTEN as compared

Table 4

Frequency and terms of destruction cavity cicatrization based on treatment codes in cases of multi-drug resistant tuberculosis

Patient groups		Amount of examined patients 2	Terms of destruction cavities cicaitrization (months)				The evidence of destruction cavity
			4	6	8		
1-a	abs.	22	4	5	6	3	4
	%		18.2	22.8	27.2	13.6	18.2
2-a	abs.	25	10	7	4	3	1
	%		40.0 *	28.0	16.0 *	12.0	5.0*

Note * – the difference between the first and second groups is reliable ($p<0.05$).

to the first one (28.0% versus 13.6 %, p<0.05, Table 5).

Conclusions. The treatment of patients diagnosed with multi-drug resistant tuberculosis is more effective provided that antimycobacterial therapy is combined with glucosaminilmuramilpentapeptide (LIASTEN). In case of combining LIASTEN with antimycobacterial therapy abacillation was fastened being evident in 1,7±0,2 months, dispersion of focal abnormalities and infiltration was observed in (1,5±0,1) months, cicatrization of destruction cavities was evident in (1,6±0,1) months as compared to the first group. At the same time, the research proved that the average treatment duration in the intensive phase could be shortened to (1.9±0.3) months.

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