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PECULIARITIES OF CHEMIORESISTANT MICOBACTERIUM TUBERCULOSIS IN TERNOPIL REGION IN RECENT YEARS

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The article presents the results of the study of susceptibility of M. tuberculosis isolated from patients with pulmonary tuberculosis in 2007 to 2013 in the Ternopil region (Ukraine). The positive tendency of increasing the rate of susceptibility of M. tuberculosis anti-TB drugs in 2013 in comparison 2007 in patients with new tuberculosis and other cases of tuberculosis but not recidivation was marked in Ternopil region.

In patients with new tuberculosis the number of pathogens which were susceptible to anti-TB drugs of the first line I for this period increased on 12,6 %, while in patients with re-treatment of pulmonary tuberculosis, except recidivation – increased in 1,7 times, and in patients with of pulmonary tuberculosis relapses this index fluctuated between 27,1-47,6 %.

The relative amount of multiresistant strains during this period has deeply increased. Thus, in patients with new pulmonary tuberculosis twofold increase of the rate of multidrug-resistant strains in 2012 compared to 2010-2011 years was revealed. The same trend was observed in patients with tuberculosis recidivation.

The attention was paid to the priority of the introduction of modern express methods of tuberculosis diagnosis and examination of susceptibility of its causative agents to antimycobacterial drugs. It will permit to correct antimycobacterial treatment in time, and reduce the number of relapses and appearance of chronic pulmonary tuberculosis in patients with multiresistant pathogens.

Key words: tuberculosis, Mycobacteria, susceptibility, chemoresistance, treatment.

There is threatening situation due to the spread of pulmonary tuberculosis today in Ukraine as in other countries of the world. Spread of tuberculosis has some features, including growth of tuberculosis cases frequency more than in 1,5 times during in the last decade of the past century; increasing of tuberculosis incidences in the penitentiary, and complexity of controlling for the spread and the course of tuberculosis.

The increase of number of clinical isolates with primary and secondary resistance to anti-tuberculosis

drugs significantly complicates the effective treatment of disease. That's why tuberculosis is leading reason of mortality in working bodied age [1-5].

The presence of M. tuberculosis resistant strains decreases the clinical and bacteriological efficacy of tuberculosis patients treatment, significantly increases the period of stay in hospital and significantly increases the financial costs of patients treatment [6-8]. Among drug-resistant strains clinicians mark increase in the frequency polyresistance in causative agents of tuberculosis – up to 60 % and more. These strains resistant to any two or more dugs of first line.

Multiresistance (multiple drug resistance) is a kind of poliresistance – multiple resistance to isoniazid and rifampicin in the absence or presence the resistance to other anti-TB drugs.

According to the WHO data about 50 % of such patients die within 5 years without treatment, 25 % – recover, and in 25 % of patients process becomes chronic, therefore, they are the source of infection for others [2, 5, 6].

That's why the aim of investigation was to analyze the dynamics of changes in indicators of sensitivity of causative agents of tuberculosis to antimycobacterial drugs over the past seven years in Ternopil region (Ukraine) and formulate recommendations for the of drug combinations use in this region.

Materials and methods

The examination was made in clinical and diagnostic laboratory of Ternopil regional municipal tuberculosis dispensary in a period between 2007-2013.

Sensitivity analysis was carried out on a solid medium Lowenstein–Jensen by proportion technique and in Meedlebrook liquid medium by automatic bacteriological “BACTEC” MGIT 960 analyzer with addition into the medium of anti-TB drugs of the first line according to the order of Ministry of public Health of Ukraine № 45 [9].

Inoculum 1,0 MacFarland and 0,5 MacFarland respectively for tests on solid and in liquid media were prepared. Inoculation of bacterial suspension on/in these

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media with addition of anti-TB drugs and control tube without medicines was performed.

Absence of growth or slight growth of mycobacteria (up to 1% relatively to the control growth) on media with drugs confirmed the sensitivity of this strain to the corresponding antimycobacterial drug.

For statistical processing the Microsoft Excel package program has been used.

Isolates from 2923 patients, including 1867(63,9 %) strains from the persons with first diagnosed pulmonary

TB, 405 (13,8%) ones – from patients with recidivation of pulmonary tuberculosis, and 651 (22,3%) strains from the persons with another cases of repeated pulmonary tuberculosis except relapses were examined concerning their anti-TB drugs susceptibility.

Results of examination and their discussion

Results of *Mycobacterium tuberculosis* susceptibility to I line anti-TB drugs studying in a period of 2007-2013 are shown in Table 1.

Table 1

Dynamics of changes of *Mycobacterium tuberculosis* susceptibility to anti-TB drugs of I line

Year	susceptible strains in patients with new tuberculosis		Susceptible strains from (in) the patients which were treated before			
			in patients with pulmonary tuberculosis recidivation		in patients with another cases of pulmonary tuberculosis	
	absol.	%	absol.	%	absol.	%
2007	186	58,1	25	43,9	85	23,0
2008	185	62,1	21	42,0	12	27,3
2009	164	60,1	16	27,1	26	34,7
2010	155	63,5	20	47,6	11	32,4
2011	166	65,4	17	45,9	10	27,0
2012	149	64,5	18	33,3	18	42,9
2013	167	67,6	42	39,6	16	39,0

Analysis of the results showed the presence of positive trend of increasing the rate of sensitive to anti-TB drugs *M. tuberculosis* in 2013 as compared with 2007 in patients with new tuberculosis pulmonary tuberculosis and another cases of tuberculosis but not relapses. Thus, in patients with new tuberculosis the number of susceptible *M. tuberculosis* to anti-TB drugs of I line during this period of investigation increased for about

12,6 % as in other patients with cases of repeated treatment but not except recidivation increased in 1,7 times during studied six years period (to 69,6 %), and in patients with recidivation this indices fluctuated between 27,1–47,6 % (table 1).

The number of mono-resistant in 2007-2011 fluctuated insignificantly in all three categories of observed patients (table 2).

Table 2

Dynamics of changes of *Mycobacterium tuberculosis* monoresistance to anti-TB drugs of I line

Pik	Monoresistant strains in patients with new tuberculosis		Monoresistant strains (in) patients which were treated before			
			in patients with pulmonary tuberculosis recidivation		in patients with another cases of pulmonary tuberculosis	
	absol.	%	absol.	%	absol.	%
2007	70	21,9	12	21,1	73	19,7
2008	53	17,8	11	22,0	9	20,5
2009	61	22,3	12	20,3	20	26,7
2010	49	20,1	8	19,0	6	17,6
2011	53	20,9	8	21,6	7	18,9
2012	28	12,1	11	20,4	7	16,7
2013	34	13,8	16	15,1	8	19,5

The relative amount of monoresistant *Mycobacterium tuberculosis* strains isolated from persons with new tuberculosis from 2007 to 2013 decreased in 1,6 times, and in patients with pulmonary tuberculosis recidivation – on 39,7 %. The same index

in patients with other cases of tuberculosis did not change practically (table 2).

In the structure of mycobacteria monoresistant strain isolated from the patients with new tuberculosis during all years of examination, the evaluation of the number

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of strains which were resistant to ethambutol – in 4,3 times was observed.

At the same time, partially reduced the frequency of isolation of strains with resistance to isoniazid (from

8.4 % to 6.9 %), and about in 6, 3 times with resistance to rifampicin. The frequency of isolation of strains with resistance to streptomycin changed insignificantly (Figure 1).

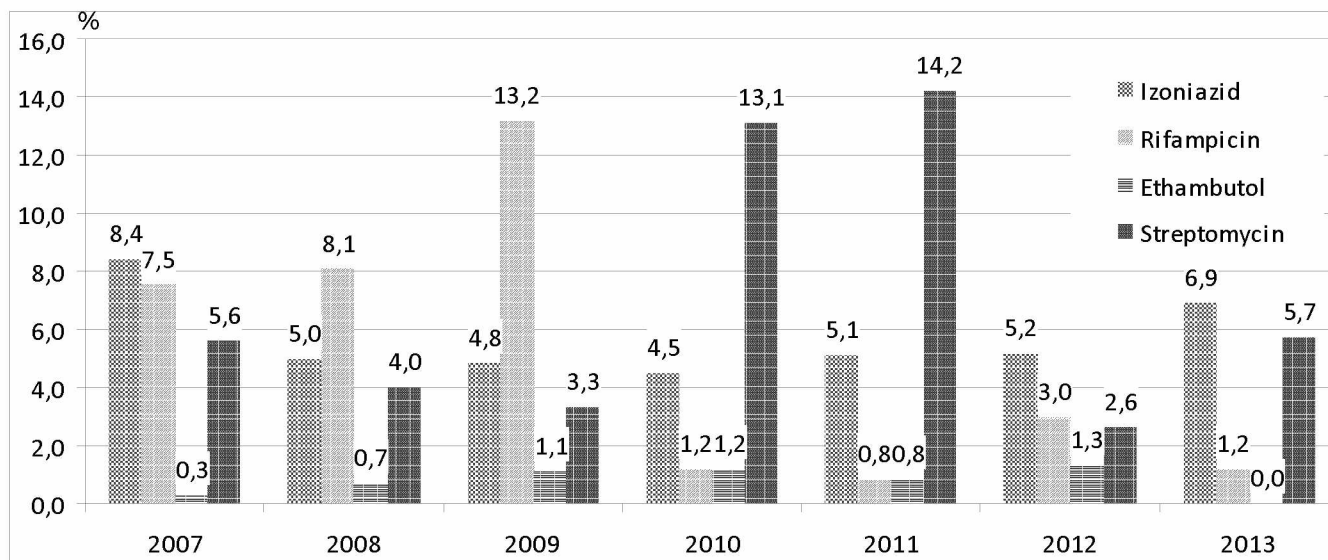


Figure 1. The changes of Mycobacteria mono-resistance in persons with new tuberculosis in 2007-2013.

As shown the data presented in Figure 2, it is necessary to pay attention to twofold increase of rate of multidrug-resistant strains of tuberculosis bacilli in patients with new tuberculosis in 2012 compared to 2010-2011.

Besides, from 2007 to 2013 about in 2 times increased the frequency of detection of multidrug-resistant tuberculosis bacilli patients with tuberculosis

recidivation, and 2013 increased incidence of multidrug-resistant strains and in patients with tuberculosis relapses.

At the same time the relative data of presence of multidrug Mycobacteria strains in patients with chronic pulmonary tuberculosis decreased over this period, about in 1, 7 times (Figure 2).

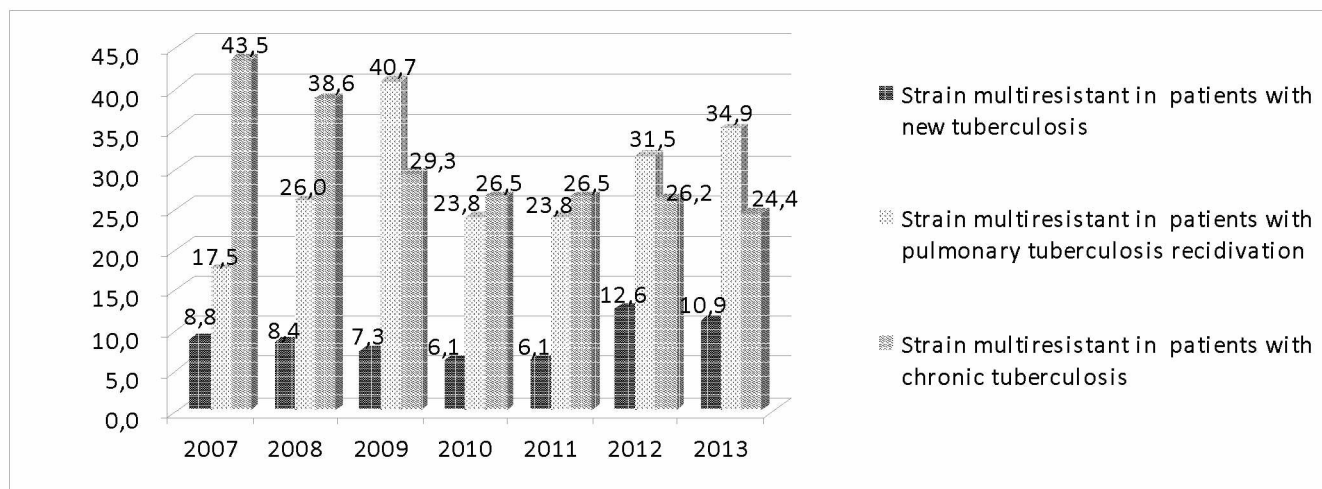


Figure 2. Dynamics of M. tuberculosis multi-resistance changes in 2007-2013.

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Conclusions

During last years the number of causative agents of tuberculosis which are susceptible to anti-TB drugs of the I line has been increased mainly due to the strains isolated from the patients with all cases of tuberculosis except recidivation. The tendency of the number of monoresistant Mycobacteria decreasing in patient with new tuberculosis and this disease recidivation is observed. The frequency of revealing Mycobacteria multiresistant strains in patients with new tuberculosis and tuberculosis relapses has increased about in 2 times.

Positive trends in the susceptibility of Mycobacteria strains isolated from patients with pulmonary tuberculosis, but not tuberculosis recidivation in Ternopol region testify to the effectiveness of antituberculosis activities in the region.

Taking into consideration the frequency of multiresistant pathogens occurrence increase in patients with new tuberculosis and this disease recidivation it is necessary to use modern express methods of tuberculosis diagnosis and examination of susceptibility of its causative agents to antimycobacterial drugs. It will allow to correct antimycobacterial therapy in time and decrease the frequency of tuberculosis recidivation and chronic tuberculosis in patients with multiresistant causative agents. With a further increased resistance to ethambutol its substitution by II line preparation is recommended for reverse of susceptibility to ethambutol.

To optimize the analysis of Mycobacteria susceptibility to anti-TB-drugs special computer program was offered by us.

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ОСОБЛИВОСТІ ХІМІОРЕЗИСТЕНТНОСТІ МІКОБАКТЕРІЙ ТУБЕРКУЛЬОЗУ В ТЕРНОПІЛЬСЬКІЙ ОБЛАСТІ ЗА ОСТАННІ РОКИ

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РЕЗЮМЕ. Спостерігалася позитивна динаміка збільшення частоти виявлення чутливих до АМБП *M. tuberculosis* у 2013 р. порівняно з 2007 р. в осіб з вперше діагностованим туберкульозом легень та іншими випадками туберкульозу, крім рецидивів, у Тернопільській області.

Відносна кількість монорезистентних штамів знизилася в осіб, які захворіли вперше, в 1,6 разу, у хворих з рецидивом туберкульозу – на 39,7 % і практично не змінилася в інших випадках повторного лікування цього захворювання.

Пріоритетним є впровадження сучасних прискорених методів діагностики та вивчення чутливості штамів до антимікобактерійних препаратів, що дозволить вчасно відкоригувати протитуберкульозну терапію і зменшити кількість виникнення рецидивів і хронічного туберкульозу легень у хворих з мультирезистентними збудниками.

Ключові слова: туберкульоз, мікобактерії, чутливість, хіміорезистентність, лікування.

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