УДЕЛЬНЫЙ ВЕС АНТИБИОТИКОРЕЗИСТЕНТНЫХ ШТАММОВ МИКОБАКТЕРИИ ТУБЕРКУЛЕЗА В ЭТИОЛОГИИ ТУБЕРКУЛЕЗА

Мануконда Ашоккумар, Ким Т.М.,
Международный Университет Кыргызстана,
Международная Высшая Школа Медицины,
Бишкек, Кыргызская Республика

Резюме: *В этой статье представлен анализ литературы по изучению резистентности микобактерий туберкулёза и удельного веса в этиологии различных форм туберкулеза. В наше время туберкулёз чаще вызывается множественно-резистентными или панрезистентными штаммами микобактерий туберкулёза.*

Ключевые слова: *микобактерия туберкулеза, туберкулез, антибиотикорезистентность.*

КУРГАК УЧУК МИКОБАКТЕРИЯСЫНЫН АНТИБИОТИКЕ ТУРУКТУУ ШТАММДАРЫНЫН КУРГАК УЧУКТУН ЭТИОЛОГИЯСЫНДАГЫ ОРУНДУУ САЛМАГЫ

Мануконда Ашоккумар, Ким Т.М.,
Кыргызстан Эл аралыкУниверситети,
Эл аралык жогорку медициналык мектеби,
Бишкек. Кыргыз Республикасы

Корутунду: *Бул макалада кургак учуктун микобактериясынын туруктуулугу жонунде изилдоо жана артуруу кургак учуктун формаларынын этиологиясын дагы орундуу салмагы адабиятарынын анализи берилген. Азыркы кунде кургак учуктун себепкери копчулук-туруктуу же пантуруктуу штаммдары козгойт.*

Негизги создор: *кургак учуктун микобактериясы, кургак учук, антибиотике туруктуулук.*

RATE OF DRUG RESISTANCE MYCOBACTERIUM TUBERCULOSIS IN TOTAL NUMBER OF TUBERCULOSIS CASES

Manukonda Ashokkumar, Kim T.M.,
International University of Kyrgyzstan,
International School of Medicine,
Bishkek, Kyrgyz Republic

Summary. *In this article presents an analysis of the literature on the study of drug resistance of M.tuberculosis and their proportion in the etiology of tuberculosis. At present tuberculosis often caused by multidrug-resistant (MDR) or extensively drug-resistant (XDR) strains of Mycobacterium tuberculosis.*

Key words: *Mycobacterium tuberculosis, tuberculosis, drug resistance*

Tuberculosis (TB) is one of the most commonest infections in the world, each year 1.7 million people are dying from TB and it is in second place after malaria among infectious disease. In the absence of effective treatment, on average, per year, each person with active TB can infect 10-15 healthy people. According to the World Health Organization, is currently a third of the world's population is infected with Mycobacterium tuberculosis (MTB), of which the number of new cases is about 9.4 million, and reached its maximum level [1].

WHO has declared recently that drug-resistant tuberculosis (TB, which is not cured by standard regimens) become a serious problem. In some parts of the world this form of the disease occurs approximately in 25% of people already with tuberculosis. Around the world in 2008, 440,000 people had MDR-TB, one-third of them died.

Currently, the most relevant forms of TB are: multidrug-resistant tuberculosis (MDR-TB) is caused by bacteria that are resistant to at least isoniazid and rifampicin. This form of disease develops either as a result of primary infection with resistant bacteria or during patient treatment [2]

Basically, an epidemic of MDR-TB cases occur globally in Asia, 50% of cases - in China and India. In Africa, has a low percentage of MDR-TB among new TB cases, as it is due to the limited laboratory capacity for the determination of drug resistance. WHO estimated that in 2008 Africa were 69 000 cases of MDR-TB.

According to WHO, in 2008 the highest rate of diagnosed cases of MDR-TB was reported in north-western regions of Russia - 28% of the total number of people with tuberculosis. Prior to this, in 2007, in Baku, Azerbaijan, the percentage of diagnosed cases of MDR-TB was 22%. [1,2,3].

Extensively drug resistant TB (XDR-TB) is caused by bacteria that are resistant to both isoniazid and rifampicin (ie MDR-TB), as well as to any fluoroquinolone and any of the anti-injecting second-line drugs (kanamycin, amikacin or capreomycin). In 2006 it was first given to the definition of XDR-TB, and by March 2010 in 58 countries were registered for at least one case of XDR-TB [4].

WHO predicts that between 2011 and 2015. More than 2 million new cases of TB are caused by multidrugresistant strains.

5.4% XDR-TB are diagnosed from MDR-TB. These two forms of TB are not curable by standard anti-TB drugs scheme of first-line. In these cases, prescribe less effective but more toxic and expensive drugs [5].

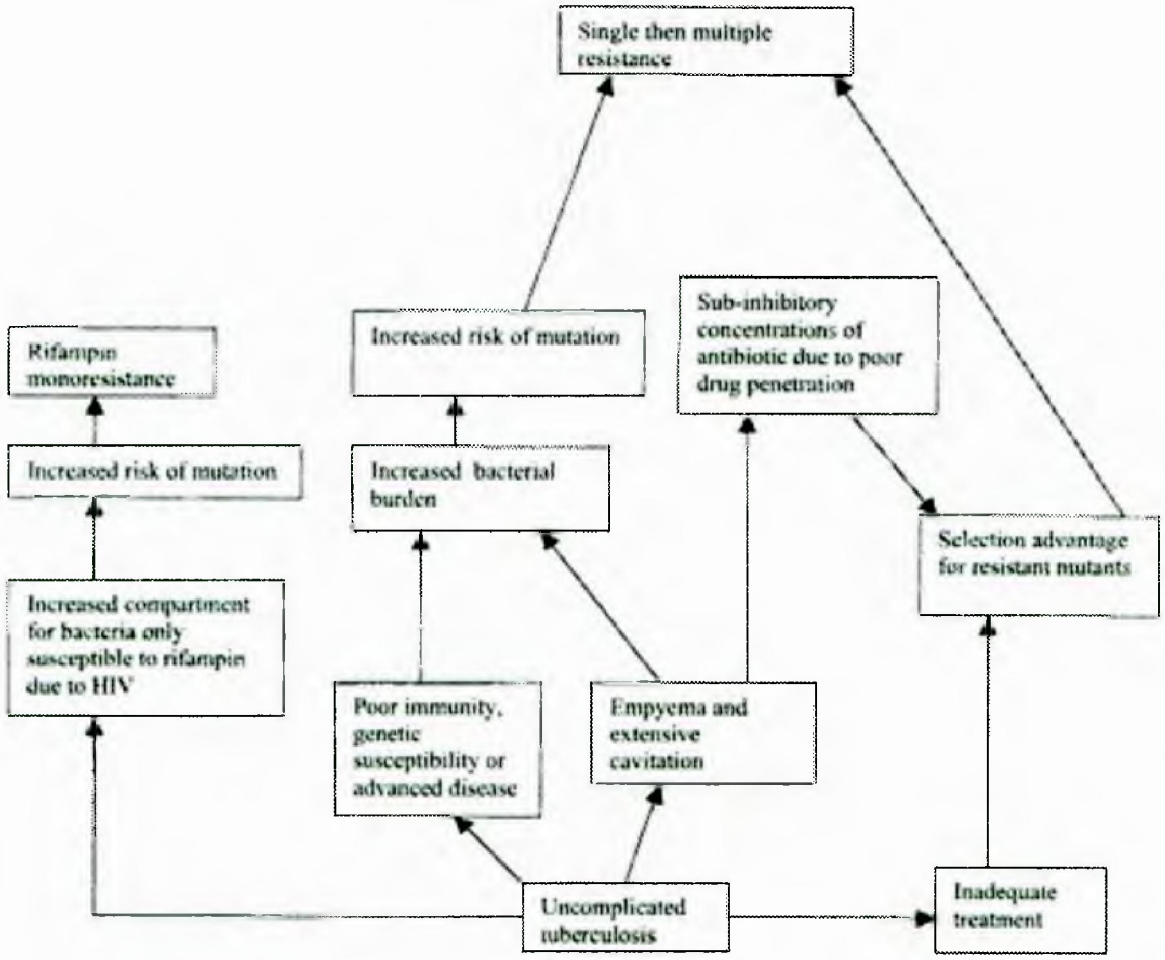
Programmes to reduce the rates of MDR-TB are facing enormous difficulties and going very slowly .

60% of patients received TB treatment are recovered, but only 7% of all patients diagnosed with MDR-TB.

Possibility to reverse the situation by activating the efforts to combat the disease and implement the recommendations of WHO of MDR- and XDR-TB

Steady decline in tuberculosis cases observed data in the Special Administrative Region of China, Hong Kong and the United States, Western Europe, the incidence remains consistently low. There is a tendency to reduce the incidence of MDR-TB in

Fig.1. Mechanism of Drug resistance (http://aac.asm.org/content/46/2/267/F1.expansion.html)



Estonia and Latvia. Significant progress has been made in the Orel and Tomsk regions of Russian Federation, where the increase in the incidence of MDR-TB was stopped and reversed [6].

Difficulties in diagnosing and reducing these forms of tuberculosis associated with drug-resistant MTB. The basis of the phenomenon of drug resistance are the molecular-biological characteristics of the MTB, the analysis of clinical isolates reveals a large number of gene mutations, some of which takes a microorganism metabolic processes in the doubling pathway.

Drug resistance develops as a result of one or more spontaneous mutations in the independent genes of the MTB, which usually occur under the influence of inadequate therapy and monotherapy [7,8].

In the early doctors are faced with resistance of MTB to streptomycin, but only in last time was decoded the nature of this phenomenon Streptomycin is a broad-spectrum aminoglycoside [9].

The development of drug resistance to isoniazid is due to mutations, inhibits the synthesis of mikoliticheskih acids, and mutations that disturb the work of the enzyme catalase-peroxidase in the cell by the MTB [10,11].

Drug resistance to rifampicin alone is rare Resistance to rifampin arises due to mutations in the beta subunit of RNA polymerase encoded by the gene *rpoB*. The most common resistance to rifampicin is associated with drug resistance to isoniazid, for that rifampicin is a marker of MDR [12,13].

On the molecular basis of drug resistance MTB to the second-line drugs is known little, except ethionamide, and fluoroquinolones.

Ethionamide and isoniazid have cross-resistance due to genetic drug resistance to multiple drugs simultaneously [14].

Agree with literature sources the features, complicating the combat against MDR and XDR: the slow rate of growth of pathogens, and their intracellular localization, high concentration of MTB in the affected organ - up to 10 billion per lung [15]. The presence of lung cavities that permit bacteria to grow in sites that are protected from the penetration of antituberculosis agents in adequate concentrations and, in empyema pus, may be compounded by low pH, which may reduce drug activity. The ability of cells to transition into a phase of growth with the absence of reactivation of a few years. All this leads to chronic infection [16,17].

If the increase in the stability of the MTB will continue unabated, in the next decade of tuberculosis patients will be impossible to treat a number of anti-TB drugs and TB doctors will be subjected to risk of contracting the deadly multidrug-resistant [18].

To prevent an epidemic of multidrug-resistant TB it is necessary all patients should be diagnosed and treated effectively, so that there will be no resistant strains.

References

1 WHO Report 2009 Global tuberculosis control. surveillance, planning, financing: A Short Update to the 2009.- Report World Health Organization, 2009.-P.411.

2 Национальный центр фтизиатрии при МЗ КР Борьба с туберкулезом в КР 20 лет – итоги: статистический сборник.-Бишкек. Национальный центр фтизиатрии, 2011. -С. 42.

3. Егоров А.М. Достижения фундаментальных наук и новые подходы к химиотерапии туберкулеза // Проблемы туберкулеза. -2000. - №5. -С. 11-15.

4 Raviglione MC, Smith IM XDR tuberculosis–implications for global public health. N Engl J Med -2007. -P.656–659.

5. Ганза В.Н., Свистунова В.П., Канин Е.С. Лекарственно резистентный туберкулез: проблемы ведения лечения // Дальневосточный медицинский журнал.-2005.-№ 4 -С 108-110.

6. WHO Global report on surveillance and response 2010. Multidrug and extensively drug-resistant TB (M/XDR-TB) Report World Health Organization, 2010.-P. 71.

7. Böttger EC, Springer B. Tuberculosis: drug resistance, fitness, and strategies for global control // Eur J Pediatr.- 2008, 167.-P. 141–148.

8 Meacci F, Orru G, Iona E et al. Drug resistance evolution of Mycobacterium tuberculosis strain from a noncompliant patient // J Clin Microbiol -2005, 43: 3.-P.114–3120.

9. Shcherbakov D, Akbergenov R, Matt T et al Directed mutagenesis of Mycobacterium smegmatis 16S rRNA to reconstruct the in-vivo evolution of aminoglycoside resistance in Mycobacterium tuberculosis // Mol Microbiol -2010, 77.-P.830–840.

10. Boehme CC, Nabeta P, Hillemann D. et al. Rapid molecular detection of tuberculosis and rifampin resistance // N Engl J Med - 2010;363(11):1005-15.

11. McNerney R., Kiepiela P., Bishop K.S.et al. Rapid screening of Mycobacterium tuberculosis for susceptibility to rifampicin and streptomycin // Int. J. Tuberc' Lung Dis. -2000.-№4 -P 69–75

12. Herrera L., Jimenez S., Valverde A.et al. Molecular analysis of rifampicin-resistant Mycobacterium tuberculosis isolated in Spain (1996–2001). Description of newmutations in the rpoB gene and review of the literature // Int. J. Antimicrob. Agents.-2003.-№ 21.-P. 403–408.

13. Jiao W W, Mokrousov I, Sun G Z, et al. (2007). Molecular characteristics of rifampin and isoniazid resistant Mycobacterium tuberculosis strains from Beijing, China. // Chin Med J (Engl). -2007.120(9). -P. 814-819.

14. Valvatne H, Syre H, Kross M, et al. (2009). Isoniazid and rifampicin resistance-associated mutations in Mycobacterium tuberculosis isolates from Yangon, Myanmar: implications for rapid molecular testing//J AntimicrobChemother. -2009, 64(4).-P. 694-701.

15. Kim HR, Hwang SS, Kim HJ et al. Impact of extensive drug resistance on treatment outcomes in non-HIV-infected patients with multidrug-resistant tuberculosis //Clin Infect Dis.- 2007, 45(10). -P.1290-5.

16. El Khechine A, Henry M, Raoult D et al Detection of Mycobacterium tuberculosis complex organisms in the stools of patients with pulmonary tuberculosis. Microbiology -2009, 155(Pt 7).-P.2384-9.

17. ВолошинаЕ.П., ХудушинаТ.А., МаслаковаМ.Г. et al. Лекарственная устойчивость микобактерии туберкулеза у впервые выявленных больных туберкулезом легких // Проблемы туберкулеза и болезней легких.- 2005.-№ 12.-С.37-39.

18. Gandhi NR, Nunn P, Dheda K. et al. Multidrug-resistant and extensively drug-resistant tuberculosis: a threat to global control of tuberculosis // Lancet. -2010;375(9728).-P.1830.