European Journal of Innovation in Nonformal Education (EJINE)
Volume 4 | Issue 8 | Aug - 2024 ISSN: 2795-8612

Current State of Treatment of Pulmonary Tuberculosis

Jumaev Mukhtor Fatullaevich
Bukhara State Medical Institute, Department of Phthisiology and Pulmonology

A B S T R A C T
The global fight against pulmonary tuberculosis (TB) faces a formidable challenge in the emergence of multidrug-resistant tuberculosis (MDR-TB). The increasing prevalence of primary MDR-TB necessitates a comprehensive approach to treatment and control efforts. While standard chemotherapy remains effective for susceptible TB strains, the development of drug resistance requires innovative strategies to ensure successful treatment outcomes.

This article explores the current state of TB treatment, highlighting the complex issue of drug resistance and the need for improved diagnostic tools and therapeutic approaches. We examine the evolution of the concept of drug resistance and discuss the ongoing research into understanding the mechanisms of drug resistance. The article emphasizes the importance of integrated public health interventions, including early diagnosis, improved access to healthcare, and the implementation of robust infection control measures to effectively manage the growing threat of MDR-TB.

A R T I C L E I N F O
Article history:
Received 11 Jun 2024
Received in revised form
10 Jul 2024
Accepted 10 Aug 2024

Keywords: Pulmonary tuberculosis, multidrug-resistant tuberculosis (MDR-TB), drug resistance, treatment, chemotherapy, diagnosis, public health, infection control.

Relevance. The spread of multidrug-resistant tuberculosis (MDR-TB) worldwide is a major obstacle to tuberculosis control and achievement of the targets set by the World Health Assembly and one of the United Nations Sustainable Development Goals. Of particular concern is the steady increase in the number of patients with primary MDR MBT.

Currently, in our country, special attention is paid to the problems of improving the functioning of the healthcare system, including a healthy lifestyle of the population, early diagnosis of diseases, treatment and prevention of tuberculosis. Scientific work is being carried out on the early detection of tuberculosis, increasing the level of provision of modern medical care, improving modern technologies for providing quality medical care using modern methods of surgical treatment.

Standard controlled chemotherapy for tuberculosis is highly effective in the treatment of tuberculosis caused by a susceptible pathogen [20; With. 44-49, 30; with. 10-13.].

Numerous studies by domestic and foreign authors are devoted to the issue of drug resistance of Mycobacterium tuberculosis [6; p., 7; With. 19-21, 78; With. 6-15]. The meaning of the concept of "drug-resistant strain" has changed as knowledge about the mechanisms of drug resistance has accumulated. At the stage of introducing anti-tuberculosis drugs, it was proposed to designate a strain as resistant if it was isolated from a patient in whom treatment did not provide improvement. This approach lost its significance after the complete abandonment of monotherapy [78; With. 6-15, 5; With. 23-25.].

Conducting a microbiological study of the drug sensitivity of MBT to the main and reserve anti-tuberculosis drugs is necessary in each case of isolating an MBT culture. After obtaining data from a microbiological study of the drug sensitivity of MBT, correction of chemotherapy and the prescription of individualized treatment regimens is mandatory. [63; With. 39-41.].

Drug resistance of MBT has not only clinical and epidemiological, but also economic significance, since the treatment of such patients is more expensive than patients with MBT who are sensitive to the main anti-TB drugs. With the introduction into practice of rapid methods for diagnosing drug resistance of Mycobacterium tuberculosis, it became possible to timely prescribe a chemotherapy regimen with reserve anti-inflammatory drugs to patients with primary MDR Mycobacterium tuberculosis [2]. The development of standards for the treatment of drug-resistant tuberculosis is one of the priorities of modern phthisiology [30; With. 10-13, 69; With. 375-378.].

The history of the development of resistance to anti- tuberculosis drugs is relatively short and arose only 60 years ago with the advent of drugs for the treatment of tuberculosis [127; With. 33-44.]. Over the decades, this problem has become evident in certain areas among patients treated in specialized centers in industrialized countries [126; With. 829-837]. With the discovery of rifampicin (RMP) in 1966[127; With. 33-44.] and its widespread use in the period 1970-1990. patients who were already carriers of - isoniazid (INH) -resistant Mycobacterium strains tuberculosis acquired resistance to RMP. This marked the beginning of the gradually growing problem of multidrug-resistant tuberculosis (MDR-TB, the essence of which is the presence of resistance to at least both INH and RMP) [182; With. 1-120.], and in some countries it reached epidemic proportions. Curing TB in these patients is challenging because they are infected with strains that are resistant to the two most effective anti-TB drugs. Over the past two decades, due to disruptions in the use of other anti-TB drugs, particularly fluoroquinolone drugs (FQs), which are the most effective second-line drugs, the range of TB pathogen resistance has increased to extensively drug-resistant TB (XDR-TB, defined as MDR-TB plus resistance to any FQ drug and at least one second-line injectable drug) [181; With. 1-51, 125; With. 1413-1415.]. This gradual transition to the - modern epidemic occurred only 15 years ago, that is, in the second half of the 1990s, and its spread was uneven throughout the world. Thus, if in many regions this situation causes concern, in a number of other territories the problem of MDR-TB is barely noticeable and may never reach epidemic levels [127; With. 33-44.].

Treatment of patients with MDR-TB is long-term with multicomponent chemotherapy regimens, often accompanied by adverse reactions (ARs) to the drugs used and their combinations. This, especially in the absence of proper motivation and psychological support, increases the risk of withdrawal from treatment among patients, thereby increasing the likelihood of an unfavorable outcome [135; With. 36-45, 145; p., 185; With.]. Even an improvement in the patient's condition and a decrease/disappearance of symptoms of the disease can be the reason for the patient's premature termination of chemotherapy due to an incorrect assessment of his condition [99; with. 52-55.].

In the complex treatment of young patients with newly diagnosed destructive pulmonary tuberculosis for the purpose of detoxification, immunomodulatory and reparative effects, it is recommended to include MIL therapy within 1 to 4 months from the start of chemotherapy in laser mode at 5 and 50 Hz, maximum power of continuous infrared radiation with constant magnetic field for 3-5 minutes for every 3 zones of the irradiated lobe of the lung. Procedures are carried out daily for 2-3 weeks with a 1-2 day break per week. The duration of the procedure is 15 minutes per day, the course of treatment is 10-15 procedures. If processes with an exudative type of inflammation predominate, it is recommended to include polyoxidonium in the complex treatment of young patients with newly diagnosed pulmonary tuberculosis within 1 to 6 months from the start of chemotherapy according to the scheme: the drug is administered intramuscularly at 6 mg 2 times a week, the course of treatment is 10 injections during 5 weeks with immunomodulatory, detoxifying, antioxidant effects. In the complex treatment of young patients with newly diagnosed destructive pulmonary tuberculosis and in processes with a productive type of inflammation, it is recommended to include longidase within 1 to 6 months from the start of chemotherapy according to the scheme: 3000 IU intramuscularly once every 5 days in a course of 10 injections in order to improve reparative processes in lung tissue [63; With. 39-41.].

A number of studies show that early sputum culture negative and conversion status at 6 months. May serve as a prognostic marker for successful treatment in patients with MDR-TB [123; With. 1060-1067, 151; With. 201-209, 155; With.]. According to pooled WHO data, the proportion of patients with MDR-TB, including extensively drug-resistant tuberculosis (XDR), who were treated with bedaquiline-containing regimens, had sputum culture conversion after 6 months. Treatment reaches 79.7% (95% CI

75.2-83.5) [138; p., 83; with. 57-66.].

In organizing tuberculosis treatment, special attention should be paid to the scrupulous implementation of standard chemotherapy regimens and solving the problem of treatment evasion. It is necessary to further improve anti-epidemic measures among the migrating population [5; with. 23-25.]. Empirical administration of a standard combination of first-line chemotherapy in the case of primary MDR leads to increased resistance and its wider spread [109; With. 21-24.].

WHO in a standardized short-term treatment regimen for MDR-TB [128; With. 229-230, 130; p., 173; with. 907-916.]. A study in Haiti, based on drug susceptibility testing of MTB isolates obtained from 239 patients with MDR-TB, revealed resistance of the pathogen: 95% to high doses of isoniazid , 57% to pyrazinamide , 77 % to ethambutol and 16% - to ethionamide . Based on data on the resistance spectrum of MBT, the authors predicted that only 118 (49.2%) patients would receive at least four effective drugs in the intensive phase of therapy and at least three effective drugs in the continuation phase, and the empirical use of short-term regimens would entail carries a high risk of treatment failure [128; With. 229-230.]. Among MDR-TB patients in China, pathogen resistance to pyrazinamide was common, which was detected in 47.5% of MTB isolates obtained [183; with. 19.], and pyrazinamide is an extremely important component of the treatment regimen to achieve tuberculosis cure without relapse [136; with. 1206-1211.].

Increasing the effectiveness of treatment of drug-resistant tuberculosis is possible through the use of accelerated methods for detecting drug resistance of MBT, which allows timely changes in the chemotherapy regimen. The possibility of effective treatment of MDR tuberculosis up to 70% is confirmed by published studies in other regions [20; with. 44-49.]. of no small importance is the fact that reserve-line anti-TB drugs are well tolerated in primary MDR, which will not negatively affect the effectiveness of treatment. Amplification of the MTB resistance spectrum with untimely detection of MDR and a non-standardized approach to its treatment contributes to the development of XDR, which in prognostic terms is an unfavorable factor in the deterioration of the epidemiological situation with tuberculosis [69; With. 375-378.].

In recent years, more and more attention when drawing up treatment regimens for MDR-TB has been given to the priority use of oral forms of drugs with the inclusion of new anti-tuberculosis drugs and antibacterial drugs with anti-tuberculosis activity [148; With. 535-546, 153; With., 178; With.] . In a meta-analysis of 50 studies from 25 countries, including 12,030 patients, the use of kanamycin and capreomycin (at least 1 month) was associated with worse treatment outcomes compared with regimens that did not include them. At the same time, the use of amikacin (for at least 1 month) provided slight advantages [83; With. 57-66, 122; with. 821-834.].

According to domestic studies, almost 90% of patients with pulmonary tuberculosis develop at least one undesirable side reaction. The presence of side effects requiring a change in the specific therapy regimen or its temporary withdrawal is accompanied by treatment, according to various sources, from 60 to 80% of newly diagnosed patients [41; With. 15-22, 38; With. 15-19, 106; With. 48.]. It has been established that drug complications arising during the treatment of pulmonary tuberculosis seriously impede the formation of therapeutic cooperation of the patient [28; with. 4-12.], significantly reduce the clinical and economic effectiveness of therapy [44; With. 16-21, 93; 42-45, 98; With. 50-53, 103; with ..], and are also associated with a high risk of treatment failure and patient mortality [40; With. 25-31.].

Patients with an unfavorable psychological status should be considered a potential risk group for side effects during chemotherapy. The complex of basic treatment measures in such patients shows normalization of their psychophysiological state, which will contribute to the implementation of the principle of continuity of chemotherapy as one of the factors of its effectiveness [38; p.15-19].

Standard and individual chemotherapy regimens adapted taking into account the regional drug resistance of the tuberculosis pathogen can significantly increase the frequency of effective courses of treatment for patients with pulmonary tuberculosis with MDR MBT. Thus, determining the regional drug resistance of the pathogen is important for choosing optimal chemotherapy regimens [17; p.19-21.].

Authors from Ecuador observed 43% of all cases lost to follow-up after 9 months. treatment in patients with rifampicin -resistant tuberculosis (RR-TB) and MDR-TB using long-term (18-24 months)

chemotherapy regimens. In total, the proportion of “losses to follow-up” was 39.6% of all those who started treatment [170, p.]. A study by A. O. Maryandyshev et al. recorded a decrease in the incidence of “interrupted treatment” from 13.3 to 9.5% when using 12-month short-term treatment regimens (STR) instead of the recommended 24 months. [161; With. 5-10.]. Study by S. Abidi and et al . based on data from 5,342 MDR/RR-TB patients demonstrated a significant reduction (4.2% versus 14.6%) in the rate of “loss to follow-up” when using CSL versus long-term regimens [120; With.]. In the case of the use of CFL for MDR-TB, cost analysis indicates a significant reduction in health system costs and the possibility of reducing the financial burden for patients [156; With. 306-314, 157; with. 376-382.]. A study in the USA demonstrated a reduction in treatment costs of 37-46% with the possibility of prescribing CSL [173; with. 907-916.]. In addition to cost-effectiveness, the use of CFL can have a beneficial effect on the epidemic situation of MDR-TB on a global scale [149; With. 191-199, 166; with. 159-161.].

The use of CSLs for the treatment of MDR-TB containing injectable drugs is not contraindicated in people living with HIV, but hearing impairment when using aminoglycosides was more common in patients in this category [144; With. 667-674, 172; With. 55, 177; With.]. The use of CSL should be accompanied by increased access to testing for MBT sensitivity to second-line drugs [134; With. , 135; With. 36-45, 160; With. , 154; With. 1035-1036 .]. The high level of MBT resistance to drugs recommended by WHO for short-term regimens may be an obstacle to the widespread use of a standardized short-term regimen within national tuberculosis control programs [154; With. 1035-1036, 173; With. 907-916, 174; With.]. In conclusion, it should be noted that, despite the enormous strides made in the development and implementation of CSLs for MDR-TB, none of them is ideal yet, so the search must continue. Convenient, effective and affordable CSLs will be the key to successfully combating the MDR-TB epidemic [83; with. 57-66.].

Thus, the course of pulmonary tuberculosis with multiple and extensively drug-resistant mycobacteria is accompanied by the development of a systemic inflammatory response, the severity of which depends on the drug resistance profile [10; with. 31-36.].

1.6. Prognosis and long-term results of treatment

According to the Central Scientific Research Institute of Public Health, if the current trend in morbidity and mortality from TB continues until 2020, losses in the country’s EAP will amount to at least 3.5 billion dollars. According to the expert community, the global epidemic of M/XDR TB can only be stopped using a systematic approach aimed at improving the detection and treatment of these forms of tuberculosis [73; p., 108; With. 25-34].

Several decades ago, P. Farmer et al. expressed the following point of view: “In choosing to ignore MDR-TB as a priority problem worldwide, we are acting shortsighted. Such restriction will lead to millions of deaths and the persistence of resistant M. tuberculosis in the human population" [8; With. , 67; With. 296-302.].

The use of pathogenetic methods in combination with chemotherapy in newly diagnosed patients with bacterial excretion at the end of the intensive phase allows for complete relief of intoxication syndrome and shortness of breath; normalize percussion and auscultation data in more than 90% of cases; achieve the disappearance of inflammatory markers in a general blood test in 80-90% of cases; completely stop bacterial excretion by bacterioscopy, and by culture in more than 90% of cases, even in the presence of DR MBT; achieve resorption of infiltration in the lungs significantly more often (in 80% of cases); significantly more often register reduction and closure of cavities in the lungs (more than 75% of cases) [63; With. 39-41.].

Thus, against the backdrop of the global epidemic of M/XDR-TB, it is necessary to both optimize the diagnosis of DR-TB and early prescribe a course of controlled chemotherapy, selected based on the drug sensitivity (DS) of the pathogen, and include in the course of chemotherapy new drugs effective against M/XDR-TB [109; With. 21-24, 84; p., 175; With. 472.]. The steady increase in the number of cases of M/XDR TB poses a threat to public health and has the nature of a global epidemic, which is recognized by both the WHO and the international community and domestic phthisiology [131; With. , 14; p., 139; With.]. The low level of effectiveness of treatment for TB patients is due to the lack of timely diagnosis

and monitoring of chemotherapy, as well as effective modern drugs. WHO experts, considering MDR-TB a public health crisis, name as priority areas for combating the epidemic, in particular, expanding the use of rapid testing methods and identifying MDR-TB cases, as well as conducting scientific research to develop new diagnostic tools, drugs and treatment regimens [139; With. , 108; With. 25-34].

The analysis suggests that timely administration of an adequate chemotherapy regimen to patients with pulmonary tuberculosis with MDR MBT contributes to the achievement of treatment effectiveness in a shorter period of time in terms of sputum smear negativity and sputum smear conversion in 77.8% and 78%, respectively, as well as in the outcome of the course of treatment - “cure” in 26% [69; With. 375-378.].

Thus, in the world literature, scientific works devoted to the problem of drug-resistant forms of tuberculosis are often found, but Mycobacterium tuberculosis will not remain from science, it also changes its properties and structure, while the territory, environmental factors, continent and way of life of peoples are especially important in development of the disease or spread of the Koch bacterium among the population. The problem is relevant and requires further research, with the search for new diagnostic methods and improvement of modern treatment methods. Rehabilitation methods and methods that improve the psycho-emotional state of patients in this category have not been sufficiently studied and require further research.

References:

1. Abidi S. et al. Standardised shorter regimens versus individualised longer regimens for rifampin- or multidrug-resistant tuberculosis // Eur. Respir. J. European Respiratory Society. – 2020. – Vol. 55, № 3.
2. Adanin S., Yalovetskiy, Nardulli B.A., et al.. Inhibiting adenosine deaminae modulates the systemic inflammatory response syndrome in endotoxemia and sepsis. Am J Physiol. 2002; 282:1324–1332.
3. Ahmad N. et al. Treatment correlates of successful outcomes in pulmonary multidrug-resistant tuberculosis: an individual patient data meta-analysis //Lancet. Lancet Publishing Group, 2018. – Vol. 392, № 10150. – P. 821-834.
4. Bastard M. et al. What is the best culture conversion prognostic marker for patients treated for multidrug-resistant tuberculosis? // Int. J. Tuberc. Lung Dis. NLM (Medline). – 2019. – Vol. 23, № 10. P. 1060-1067.
5. Calligaro G., Moodley L., Symons G., Dheda K... The medical and surgical treatment of drugresistant tuberculosis. J. Thorac. Dis. 2014; 3 (6): 186–95.
6. Caminero J.A... Extensively drug-resistant tuberculosis: is its definition correct? (Correspondence). Eur Respir J 2008; 32: 1413–1415.
7. Caminero J.A... Treatment of multidrug-resistant tuberculosis: evidence and controversies. Int J Tuberc Lung Dis 2006; 10: 829–837.
8. Caminero J.A... Туберкулез с множественной лекарственной устойчивостью: эпидемиология, факторы риска и выявление случаев// Международный журнал «Туберкулез и легочные заболевания». Том-2, №1, 2011.-С.33-44.
9. Campbell J. R., Menzies D. What’s next for the standard short-course regimen or treatment of multidrug-resistant tuberculosis // Am. J. Trop. Med. Hygiene. American Society of Tropical Medicine and Hygiene. – 2019. – Vol. 100, № 2. – P. 229-230.
10. Chakraborty N.J. et al.. A rapid immunochromatographic assay for the detection of Mycobacterium tuberculosis antigens in pulmonary samples from HIV seropositive patients and its comparison with conventional methods /Methods. – 2009 Jan. – Vol. 76, N 1. – P. 12–17.
11. Chee C. B. E. et al. The shorter multidrug-resistant tuberculosis treatment regimen in Singapore: Are patients from South-East Asia eligible? // Eur. Respir. J. European Respiratory Society. – 2017. – Vol. 50, № 2.

12. Cochrane L... Drug-resistant-tuberculosis outbreak would be equal to Ebola threat: Costello. ABC News. 2015. Available at: http://www.abc.net.au/pm/content/2015/s4181008.htm.
13. Companion handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis /World Health Organization; 2014. – 448 p.
14. Conlon B.A., Law W.R... Macrophages are a source of extracellular adenosine deaminase-2 during inflammatory responses. Clin Exp Immunol. 2004; 138:14–20.
15. Dalcolmo M. et al. Resistance profile of drugs composing the "shorter" regimen for multidrug-resistant tuberculosis in Brazil, 2000-2015 // Eur. Respir. J.European Respiratory Society. – 2017. – Vol. 49, № 4.
16. Dheda K. et al. Recent controversies about MDR and XDR-TB: Global implementation of the WHO shorter MDR-TB regimen and bedaquiline for all with MDR-TB? // Respirology. Blackwell Publishing. – 2018. – Vol. 23, № 1. – P. 36-45
17. Dowdy D. W. et al. Of Testing and treatment: implications of implementing new regimens for multidrug-resistant tuberculosis // Clin. Infect. Dis. Oxford University Press. – 2017. – Vol. 65, № 7. – P. 1206-1211.
18. Dye C., Williams B.G... Criteria for the control of drugresistant tuberculosis // Proc. Natl. Acad. Sci. USA. – 2000. – Vol. 97, No. 14. – P. 8180–8185.