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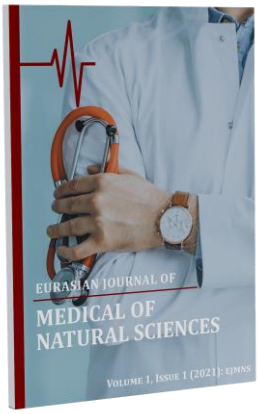

SPECIFIC PREVENTION AND DIAGNOSIS OF TUBERCULOSIS

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ABSTRACT
The paper presents data on the state of tuberculosis in developed, developing countries and in the Republic of Uzbekistan; on the methods of prevention and diagnosis of tuberculosis used in the world health community to date; on WHO reports on tuberculosis; on the implementation of the WHO tuberculosis eradication strategy; data on the dynamics of the prevalence of tuberculosis in various countries.

Relevance

In recent years, tuberculosis has been one of the big problems of modern medicine. The World Health Organization (WHO) has recognized tuberculosis as one of the five global problems of mankind. WHO estimates that 10 million people worldwide fell ill with tuberculosis in 2019, including 5.6 million men, 3.2 million women and 1.2 million children. Tuberculosis is common in all countries and age groups. Tuberculosis is curable and preventable.

It can be difficult to diagnose and treat tuberculosis in children and adolescents, and the disease at this age often remains unrecognized by health workers.

In 2019, the 30 countries with a heavy burden of tuberculosis accounted for 87% of new cases of tuberculosis. Two-thirds of the cases occurred in eight countries, among which India ranked first, followed by Indonesia, China, the Philippines, Pakistan, Nigeria, Bangladesh and South Africa.

Purpose of research

To study the methods of specific prevention and diagnosis of tuberculosis in developed and developing countries and compare them with the methods in the Republic of Uzbekistan.

Study of articles by international authors in the field of specific prevention and diagnosis of tuberculosis.

Materials and methods

The research materials are the reporting data of the Sanitary and Epidemiological Welfare and Public Health Service of the Republic of Karakalpakstan, articles by international authors on the topic "Diagnosis and specific prevention of tuberculosis", articles on the official WHO website.

The research method is a meta-analysis based on the above data.

Results and discussions

With the development of science, the BCG vaccine was developed. In Uzbekistan, this vaccine is used only once on the 2-5 birthday of a child, and is administered directly in Prenatal centers. It has been proven that this vaccine protects only from tuberculous meningitis, rather than from tuberculosis itself. In an article called "The impact of a change in infant BCG vaccination policy on adolescent TB incident rates: A South African population-level cohort study" (The impact of a change in BCG infant vaccination policy on the incidence of tuberculosis among adolescents: a cohort study at the population level of South Africa), it was concluded that a change in policy regarding vaccination of children with BCG was associated with a moderate decrease in the incidence of tuberculosis among HIV-negative adolescents aged 10 to 17 years. However, the incidence of TB increased rapidly with age in both cohorts of adolescents and remained high despite BCG vaccination at birth [1].

Scientists from the People's Republic of China have proved that the introduction of BCG vaccine significantly reduces the risk of asthma by 23%, which indicates its protective effectiveness against the development of asthma among vaccinated children. However, early administration of the BCG vaccine did not significantly reduce the risk of eczema and rhinitis (BCG vaccination in early childhood and the risk of atopic diseases: a systematic review and meta-analysis) [2].

BCG vaccine is also used in the field of oncology in the treatment of various tumor diseases. An example of this is the following article by Bacillus Calmette-Guérin (BCG) and alternatives: Drug treatment of high-risk non-muscle invasive blade cancer (Drug treatment of high-risk non-muscle invasive bladder cancer [4].

In any infectious diseases, its diagnosis is important. At the present stage, there are several ways to diagnose tuberculosis in children: tuberculin test (Mantoux test), Diaskin test, Quantiferon test. The very first and widely used diagnostic method is the Mantoux test. Advantages of this method: availability and cheapness of the drug; the disadvantages include: the need for special care of the injection site, allergic reactions to tuberculin often occur, children scratch the injection site, after which a false positive reaction may appear, including false negative results are also not excluded. But currently, this test has been canceled in Uzbekistan, the effectiveness of the diagnosis of tuberculosis, which is only 0.03% of cases.

To completely exclude false positive reactions, you can resort to a Diaskin test. Often in practice there are cases when the parents of a child refuse a tuberculin test, considering it toxic. In this regard, the Diaskin test is much "Cleaner" than the Mantoux test, since it does not have mycobacterium components, and contains proteins identical to mycobacterium proteins. The disadvantages of the Diaskin test include: the high cost of the test, it is not able to detect hidden and latent forms of the disease, it can also be false negative. According to the latter criterion, the Quantiferon test is one of the most reliable, since it can make an early diagnosis of tuberculosis. The first methods of diagnosing tuberculosis listed above have one common drawback: you need to inject the drug into the body and wait for the

result, which can be influenced by many factors that will directly affect the result. In this regard, the Quantiferon test is considered independent of the state of the body at that time, and blood from a vein is needed for diagnosis. Also, the most significant advantages of the Quantiferon test are: the ability to carry out diagnostics in children's institutions during quarantine, in HIV-infected people, with contraindications to many drugs. A significant disadvantage of this diagnostic method is the inability to distinguish cow tuberculosis from human tuberculosis, and it also does not distinguish between ordinary infection and disease.

With these data, we can say that there is no ideal method for diagnosing tuberculosis at the moment. It is necessary to diagnose this disease in stages and systematically. The above methods make it possible to identify children who need a phthisiologist's consultation, preventive treatment or full-fledged anti-tuberculosis care.

In the diagnosis of tuberculosis in Uzbekistan, the main method is mass fluorography.

Guidelines for the diagnosis and treatment of tuberculosis developed by the American Thoracic Society, the American Society of Infectious Diseases Specialists and the Centers for Disease Control and Prevention (CDC) have been updated in the United States. They recommend using the new immunological diagnostic method IGRA (Interferon Gamma Release Assays) instead of a standard skin test with a tuberculin solution (Mantoux test). The IGRA method is based on measuring the immune response of T-lymphocytes to highly specific mycobacterial antigens ESAT-6 and CFP-10, expressed by the production of gamma interferon in a 24-hour whole blood culture. Its use increases the specificity of the results obtained, especially in patients who have received preliminary BCG vaccination. In addition, one visit to a medical institution is enough for this examination. After the diagnosis of latent tuberculosis, preventive treatment with isoniazid is recommended [3].

The European Tuberculosis Laboratory Initiative (ELI), together with the secretariat at the WHO Regional Office for Europe, has developed a technical document to meet the needs for more timely and accurate detection of tuberculosis (TB), including multidrug–resistant tuberculosis (MDR-TB) in the WHO European Region by scaling up the appropriate use of rapid molecular methods diagnostics recommended by WHO [5].

Scientists believe that in conditions of high risk of transmission of TB and/or MDR-TB (for example, penitentiary institutions of the former Soviet Union), annual sputum screening by PCR (GeneXpert MTB/RIF) has demonstrated greater cost-effectiveness for reducing TB and MDR-TB compared to traditional methods.

In the Russian Federation, molecular diagnostics of tuberculosis is widely used, which include IS6110-RFLP typing, VNTR typing, spoligotyping and sequencing. The first three can be attributed to obsolete, and sequencing — to modern methods. With the help of genome-wide sequencing, both neutral markers and mutations leading to drug resistance can be detected. Molecular genetic methods in phthisiology are used to solve the following tasks: detection of MBTC, detection of non-tuberculosis mycobacteria (NTMB), identification of mycobacteria to the species and determination of drug

sensitivity (HP). Kits for detecting MBTC using real-time PCR are widely available on the market [6].

Treatment recommendations that have been updated in new WHO protocols:

- For the treatment of patients with drug-sensitive pulmonary TB, the use of treatment regimens containing fluoroquinolones lasting 4 months is not recommended. It is recommended to use rifampicin–based regimens lasting 6 months (2 months – isoniazid + rifampicin + pyrazinamide + ethambutol and 4 months - isoniazid + rifampicin).
- All patients with HPV TB are not recommended to take medications three times a week in both phases of treatment, intensive and continuation phase, but daily medication is recommended.
- Patients who need repeated TB treatment should not receive a second-category treatment regimen (standard TB treatment regimen + streptomycin). Such patients need to be tested for drug sensitivity in order to choose the appropriate treatment.
- In the treatment of drug-sensitive TB, the use of combination drugs with a fixed dosage, rather than monocomponents, is recommended.
- All patients with TB and HIV should start ARV therapy regardless of the amount of DM4. TB treatment should be started first, and then ARV drugs should be started as soon as possible during the first 8 weeks of treatment. HIV-positive patients with CD4 of less than 50 cells should start ARV therapy within the first two weeks from the start of TB treatment[7].

In Uzbekistan, until 2019, the DOTS (Directly Observed Treatment, Short-course) strategy functioned — this is "treatment under direct control with a short course"). Political support of this strategy by the authorities at all levels and the government's commitment to ensure the implementation of measures to combat tuberculosis:

— detection of tuberculosis cases using bacterioscopic examination of sputum smears in patients with symptoms of the disease (according to the treatment);

— Conducting treatment according to standardized regimens under direct supervision during the entire course of chemotherapy;

— Regular, uninterrupted supply of all major anti-tuberculosis drugs;

— A standardized system of registration and reporting, which allows assessing the results of each patient and the effectiveness of the tuberculosis control program as a whole.

In some post-Soviet countries (Russia, Ukraine) a number of experts consider the DOTS strategy to be insufficiently effective and significantly inferior to the comprehensive anti-tuberculosis strategy developed and implemented in the USSR, based on a developed network of anti-tuberculosis dispensaries. (V. M. Melnik, "Tuberculosis and DOTS") According to WHO statistics, a total of 1.4 million people died from tuberculosis in 2019 (including 208,000 people with HIV infection). Worldwide, tuberculosis is one of the 10 leading causes of death and the main cause of death due to any one causative agent of infection (ahead of HIV/AIDS). Tuberculosis is common in all countries and age groups [9].

Drug-resistant tuberculosis continues to pose a serious threat to public health. In 2019, almost half a million people worldwide fell ill with Rifampicin-resistant

tuberculosis (RU-TB),8 of which 78% contracted multidrug-resistant tuberculosis (MDR-TB)9. Three countries accounted for the largest share of the global burden: India (27%), China (14%) and the Russian Federation (8%). The proportion of MDR/RU-TB cases worldwide was 3.3% among new cases and 17.7% among previously treated cases of tuberculosis and was the highest (over 50% among previously treated cases) in the countries of the former Soviet Union.

The main measure in the field of health care, which reduces the risk of tuberculosis infection becoming active, is preventive treatment. In accordance with the WHO guidelines, preventive treatment of tuberculosis is recommended for the following groups: people living with HIV; people in contact at the household level with patients with bacteriologically confirmed pulmonary tuberculosis; and people at risk by clinical status (for example, dialysis patients). In 2019, 4.1 million people worldwide received preventive treatment for tuberculosis, whereas in 2018 there were only 2.2 million of them.

Drug-resistant forms of tuberculosis are also important, which need full-fledged treatment not only to prevent the further spread of the disease, but also to prevent the conversion of drug-sensitive forms into XDR or MDR tuberculosis. Due to the toxic manifestations of tuberculosis drugs, patients often refuse to use them. In order to mitigate the situation, active psychological educational work is being carried out with tuberculosis patients. In 2019 77% of the difference between the number of patients referred for treatment and the estimated number of new MDR/RU-TB cases in the world occurred in 10 countries, which largely determine how successful the process of closing this gap will be. Forty-one percent of this difference is only in China and India. According to the latest data on the results of patient treatment, the success rate of MDR/RU-TB treatment in the world was 57%. Examples of countries with a heavy burden of MDR-TB and relatively high rates of successful MDR/RU-TB treatment (over 75%) are Ethiopia, Kazakhstan and Myanmar.[8]

According to the Implementation of the WHO tuberculosis eradication strategy, countries with a high burden of tuberculosis will have to ensure by 2025: the development and implementation of a national tuberculosis research plan; the creation of stable funding mechanisms for national tuberculosis research; the creation of significant scientific potential; the formation of a strong and autonomous community for tuberculosis research [10]

Tuberculosis of children is important. It can be difficult to diagnose and treat tuberculosis in children and adolescents, and the disease at this age often remains unrecognized by health workers.

According to official statistics, the incidence of tuberculosis in the Republic of Karakalpakstan in 2011, approximately 7% of all primary registered cases of tuberculosis were tuberculosis in children under 14 years of age. The intensive indicator among all those who were initially infected in 2011 was 103.6 per 100 thousand of the population, compared with 2020, in which this indicator was 58.1 per 100 thousand of the population. Over 10 years, the incidence has decreased by 36% overall, by 41% in children. These figures undoubtedly speak about the effectiveness of the tuberculosis control strategy in the Republic of Uzbekistan.

Conclusions

According to all the above data, we can say that tuberculosis is still considered one of the main unresolved problems not only at the state level, but also at the international level. The most leading factor in the development of the incidence of tuberculosis is the social factor. This can be answered by the widespread prevalence of tuberculosis in developing countries. Despite the development of many methods of diagnosing tuberculosis, diagnosis is considered to be one of the leading problems, since no method is fully accurate and practical. In addition, we can say that methods of treating tuberculosis have already been developed, but due to the refusal of patients from a full course of treatment, forms with broad and multidrug resistance are developing that are almost untreatable. Thus, tuberculosis remains an urgent problem of world health.

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