

APPROACHES TO IMPROVING TUBERCULOSIS CARE IN HIV-INFECTED PATIENTS AND CRITERIA FOR ITS EVALUATION

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Despite various anti-tuberculosis measures in the setting of HIV infection, the epidemiological situation of tuberculosis in Russia is deteriorating. We have analyzed the data of statistical report form no.61 for years 2004-2014, surveillance data on individual TB cases with HIV coinfection for years 2004-2014 (personal data) and TB care arrangements for patients with HIV in 20 regions. The main causes of the deteriorating epidemiological situation are the growing immunodeficiency in patients with TB coinfection, unseparated epidemiologically dangerous patient flows (patients with tuberculosis and HIV-infected patients) and low quality preventative measures in special care medical facilities. Chemoprophylaxis can be an effective method of controlling the spread of tuberculosis among HIV-infected patients if it is recommended by a qualified tuberculosis therapist to patients adhering to regular drug intake under supervision of medical personnel. Otherwise a large scale chemoprophylaxis can result in an increased proportion of patients with drug-resistant tuberculosis. This works suggests criteria for the evaluation of tuberculosis care effectiveness considering the pathogenesis of the disease during late stages of HIV.

Keywords: tuberculosis, HIV-infection, tuberculosis care, tuberculosis chemoprophylaxis

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ПОДХОДЫ К УСОВЕРШЕНСТВОВАНИЮ ПРОТИВОТУБЕРКУЛЕЗНОЙ ПОМОЩИ БОЛЬНЫМ ВИЧ-ИНФЕКЦИЕЙ И КРИТЕРИИ ЕЕ ОЦЕНКИ

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Несмотря на различные меры по борьбе с туберкулезом, сочетанным с ВИЧ-инфекцией, эпидемиологическая ситуация по заболеванию в России продолжает ухудшаться. Нами были проанализированы данные отчетной формы № 61 за 1999-2014 гг., данные персонифицированного мониторинга больных туберкулезом, сочетанным с ВИЧ-инфекцией, за 2004-2014 гг. (личные данные) и организация противотуберкулезной помощи больным ВИЧ-инфекцией в 20 регионах. Основными причинами ухудшения эпидемиологической ситуации являются нарастание иммунодефицита среди пациентов с сочетанным туберкулезом, отсутствие разделения эпидемиологически опасных потоков пациентов (больных туберкулезом и больных ВИЧ-инфекцией) и невысокий уровень профилактической работы в специализированных медицинских учреждениях. Химиопрофилактика может быть эффективным средством борьбы с распространением туберкулеза среди больных ВИЧ-инфекцией, если она будет назначаться подготовленным врачом-фтизиатром пациентам, готовым принимать лекарства под наблюдением медицинского персонала. Иначе масштабная химиопрофилактика может вызвать рост доли пациентов с туберкулезом с лекарственной устойчивостью. Предложены критерии оценки эффективности противотуберкулезной помощи с учетом патогенеза заболевания на поздних стадиях ВИЧ-инфекции.

Ключевые слова: туберкулез, ВИЧ-инфекция, противотуберкулезная помощь, химиопрофилактика туберкулеза

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The World Health Organization defines the fight against tuberculosis among HIV-infected patients as one of the priorities in health care, while high-quality epidemiological surveillance is an important aspect here [1]. Russia is also developing a strategy for combating tuberculosis among persons with HIV infection [2]. Discussions on the epidemiological situation and approaches to tuberculosis care delivery to HIV-infected TB patients began in the late 1990s [3, 4].

Russia began in 1999 to keep records of TB patients with HIV infection according to report form No 61 of the Federal statistical surveillance "Information About HIV Patient Population". In 2001, the first results of its analysis were published [5], while in 2002, the first doctor's TB care manual for HIV patients was published [6]. Later, approaches developed by Russian researchers were approved by WHO experts and issued by joint recommendations [7, 8]. Russia became the first and still the only country that introduced a personalized monitoring system for TB patients with HIV infection [9]. In 2008, doctors in the regions started entering a number of information about cases of tuberculosis in HIV-infected patients into report form No 61 based on personalized monitoring data. In 2004, under the auspices of the Russian Ministry of Health, the country launched a training program for TB specialists and infectious disease experts working with HIV-infected patients. In 2014, Russian Society of Phthisiologists issued the Federal Guidelines for the Diagnosis and Treatment of Tuberculosis in HIV-Infected Patients. The Guidelines expanded and modernized the approaches to tuberculosis chemoprophylaxis [10]. A draft instruction on TB chemoprophylaxis in HIV-infected patients is currently being discussed. It has been sent to regional centers for prevention and control of AIDS. The authors of this article have a copy. However, despite the measures taken, the epidemiological situation of the disease continues to worsen.

We analyzed the data from report form No 61 collected between 1999 and 2014 and data obtained from personalized monitoring of TB patients with HIV infection for 2004-2014 (personal data). We also examined how provision of TB care to HIV patients is organized, as well as information materials about the disease provided to patients in 20 regions. The aim was to identify possible causes of inefficiency of the existing TB care approaches for HIV patients. Based on the analysis, some measures on how to improve TB care to HIV patients were proposed.

Analysis of the epidemiological situation

According to report form No 61, there were 0.2 TB cases per 100,000 persons with HIV infection in 1999. The figure rose to 9.8 in 2014. Prevalence of the disease has also risen from 0.35 to 25.8 cases per 100,000 persons. Tuberculosis is increasingly becoming a cause of death in HIV-related severe immunodeficiency: in 2008 (the beginning of record keeping in form No 61), tuberculosis accounted for 75.7 % of deaths in patients with advanced HIV infection. By 2014, the figure has risen to 86.9 %. Considering the pathogenesis of tuberculosis in the late stages of HIV infection, it can be assumed that the main cause of a rise in tuberculosis in Russia is precisely an increase in immune deficiency among HIV patients.

Another reason for the deterioration of the epidemiological situation is the low level of preventive measures among TB patients with HIV infection. For example, in 2014, 7.8 % of such patients had HIV-infected family members. However, in the information materials for them, we found no information about tuberculosis preventive measures in the family and about TB peculiarities in the late stages of HIV infection. This led to a

rise in the incidence of tuberculosis in children with early stages of HIV infection: 143 children with TB infection in 2014 and 47.5 % of them had early-stage HIV infection. This means that tuberculosis in these children was not caused as a result of immunodeficiency.

Survey of HIV patients for tuberculosis in different regions showed that it is often at the stage of examination that conditions for the spread of tuberculosis are formed. For instance, for the exclusion of TB, persons with severe immune deficiency were hospitalized for diagnosis in the TB unit, where there may be patients with yet undiagnosed tuberculosis with bacterial excretion. Sometimes, all HIV-infected patients are hospitalized in one unit regardless of whether there is bacterial excretion or indications for hospitalization (diagnosis or treatment). This procedure aggravates the epidemiological situation of tuberculosis among HIV-infected patients. For example, among patients with mycobacteriosis (with HIV infection) who were treated in TB facilities, 9 % were infected and fell sick of tuberculosis [12].

Efficacy of tuberculosis chemoprophylaxis

Tuberculosis chemoprophylaxis in HIV-infected persons is undoubtedly one of the most effective means of preventing the spread of the disease if drug administration is controlled by a doctor. However, ensuring such a control is extremely difficult because most of the patients with HIV infection are socially disadvantaged individuals. For instance, in 2014, among HIV patients with tuberculosis, 75.5 % were of working age who were not working for a long time, 66.2 % were infected through drug injection, 42.1 % were currently or previously in prisons. In this connection, an indication to provide coverage of tuberculosis chemoprophylaxis for at least 50 % of HIV-infected patients [13] is worrying because it can trigger increase in drug resistance in mycobacterium tuberculosis.

This assumption is supported by data obtained from personalized monitoring conducted by us: in 2011, primary multidrug-resistant tuberculosis (caused by an organism that is resistant to at least isoniazid and rifampin) was detected in 41 % of patients, while in 2014, the figure increased to 42.1 %. Besides, primary drug-resistant tuberculosis (caused by an organism that is resistant to other two or more drugs) was observed in 15.4 % of patients in 2011 and 15.9 % in 2014. The situation is worse in prisons: in 2014, primary multidrug-resistant TB (MDR-TB) was identified in 55.9 % of patients, while primary multidrug-polyresistant TB in 16 % (obviously due to the fact that patients in such places are extremely socially disadvantaged, and that the infection source is a person at the same place). It is important to note that these parameters are not decreasing.

The question now is whether uncontrolled TB chemoprophylaxis of HIV patients will be an additional reason for emergence and spread of mycobacterium strains that are resistant to anti-TB drugs. Will this uncontrolled TB chemoprophylaxis be effective even when drugs are taken regularly, if the draft instruction on TB chemoprophylaxis encourages HIV patients to take rifampicin to which there is primary drug resistance in many of the patients and which is not combined with antiretroviral drugs included in the basic HIV treatment scheme? In addition, there are doubts over whether it is possible to cover such a number of HIV-infected patients (at least 50 %) since, according to our data, about 30 % of them are not included in records at HIV/AIDS prevention and control centers (HAPCC). Moreover, over 12 % of patients on record do not undergo medical examination. At the same

time, requiring HIV-infected patients to visit a clinic without their consent has been prohibited by law since 1995 [14].

In our opinion, only a TB doctor can prescribe tuberculosis chemoprophylaxis to HIV patients. Such doctor must be trained on this problem and the patients must be only those who are committed to regular use of drugs. Drug administration itself should be under the supervision of an HAPCC medical staff or personnel of a unit providing such functions at the municipal level. Tuberculosis chemoprophylaxis of HIV-infected patients at TB facilities, that is, at the infection source, is unacceptable.

Ways of improving the quality of TB care to HIV-infected patients

It is necessary to deploy a procedure for TB care to HIV patients that would minimize the likelihood of contact with severely immunocompromised persons and TB patients.

Medical care to TB patients with HIV infection should be provided at different TB facilities, depending on whether the patient has bacterial excretion and there is drug resistance in mycobacterium tuberculosis. For their treatment at a TB clinic, the salaries of TB doctors and infectious disease physicians must be provided for. Doctors may be taken into these positions only after occupational retraining. Their number should be determined by load (number of patients). Both specialists must be staff of the entire clinic and not just of a single ward, and manage HIV-infected patients distributed in the wards.

To minimize the likelihood of contact with patients with advanced HIV infection and tuberculosis patients with bacterial excretion, only TB specialists should terminate a TB treatment in the continuation phase at persistent absence of bacterial excretion. But this should be done at facilities providing specialized care to HIV patients. The same is true of follow-up of patients from the third record group. Treatment of HIV-infected patients with chronic forms of tuberculosis with bacterial excretion should be done only at a TB clinic.

Thus, most of the work on prevention, detection and diagnosis of tuberculosis, as well as differential diagnosis of tuberculosis and other secondary diseases in HIV infection should be conducted by HIV care facilities.

Criteria for assessing the efficiency of TB care in HIV-infected patients

Some standard criteria in TB are not relevant in the later stages of HIV infection and may compromise the work of TB facilities. For example, it is not proper in cases where TB detection in patient at the later stage is considered as not satisfactory. This is so because in a person with severe immune deficiency, clinical manifestations of the disease often develop before

the radiographic changes appear. Therefore, it is typically not possible to identify the disease through scheduled X-ray diagnostics. Deaths from TB can occur in persons without chest radiography changes. Even with a small delay by the patient in seeking medical care, death occurs as a result of acute progression of the disease. It is impossible to consider death from tuberculosis in these cases as a result of poor diagnosis. For detection of tuberculosis in the late stages of HIV infection, HIV awareness programs on the need to seek immediate treatment at a specialists hospital when the first symptoms of the disease appear are particularly important [15].

In connection with the above, criteria for evaluating the efficiency of TB care in HIV patients should be formed taking into account peculiarities of the pathogenesis of tuberculosis in the late stages of HIV infection. Perhaps to this end, it is advisable to consider the following: the proportion of TB focal points examined by medical staff during the first three days (of the number of detected focal points of tuberculosis which are home to patients with HIV infection); the proportion of children born to women with HIV infection, who are isolated from the focal points of tuberculosis (among the patients in the focal points); the proportion of discrepancies between clinical and pathologic diagnosis (if the patient was in the clinic for a month or more) taking into account the frequency of autopsies in cases of death with combined infection; the proportion of cases in which autopsy in patients with tuberculosis detected no other secondary diseases characteristic of HIV infection (if the patient was in the clinic for a month or more).

CONCLUSIONS

The spread of tuberculosis among HIV-infected patients is often caused by a breach in anti-epidemic requirements for assistance of such patients, in particular: lack of separation of epidemiologically dangerous patients (TB patients and those with immunodeficiency). Prevention, detection and diagnosis of tuberculosis in patients with advanced HIV infection should be performed at HIV/AIDS prevention and control centers or specialist institutions.

Uncontrolled TB chemoprophylaxis among socially disadvantaged patients may contribute to the spread of mycobacterium tuberculosis strains that are resistant to anti-TB drugs. Chemoprophylaxis should be done on those who are willing to regularly take medication under medical supervision. Chemoprophylaxis should be prescribed by specially trained phtthisiologists only.

Standard TB criteria for evaluating the efficiency of TB care in patients with late-stage HIV infection are biased. Criteria factoring in the peculiarities of tuberculosis pathogenesis in severe immunodeficiency should be used.

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