

Active Pulmonary Tuberculosis Despite Isoniazid Chemoprophylaxis in Children Who Were Exposed to Smear Positive Pulmonary Tuberculosis: Case Series

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Introduction: Children, especially those younger than six years old are very susceptible to tuberculosis (TB); therefore, there is need for preventive intervention to face active pulmonary tuberculosis (PTB). Using chemoprophylaxis as an effective intermediation against latent TB was proven during the last decades.

Case Presentation: Here, we presented three children of a mother, referred to our clinic due to smear positive PTB. Their mother was being treated with a four-drug regimen since one month before. All the close contacts were evaluated for TB and isoniazid was started for her daughters aged four and six, who had positive tuberculin test results and did not show any signs and symptoms of active TB. Later, these two children and her 19-year-old son were involved with active PTB.

Discussion: Isoniazid chemoprophylaxis dose not completely prevent from TB development. Therefore, we should observe and evaluate all the cases that have a history of close contact with smear positive PTB using isoniazid prophylaxis.

Keywords: Chemoprophylaxis; Isoniazid; Tuberculosis

1. Introduction

The general agreement in review of literature is that children younger than five years old, teenagers, and adolescents who are tuberculin reactors form high-risk groups should receive chemoprophylaxis (1, 2). Tuberculosis (TB) chemoprophylaxis with isoniazid (INH) to avoid development of the disease is the first choice. However, other drugs such as rifampin (RIF) can also prevent from TB in high-risk groups (1, 2). Isoniazid prophylaxis can reduce the risk of developing tuberculosis by 60% among children aged 15 years old or younger (3). In Iran, it is recommended that all the children younger than six years old who are exposed to a known case of smear positive PTB and have close contact (a close contact is someone living in the same household as a source case or someone in frequent contact with the source case) should receive isoniazid prophylaxis, even when their tuberculin test result is negative (4). Chemoprophylaxis usage is very important, because children are very susceptible to infection, and once infected, are at higher risk of progression to active TB than adults. Other high-risk people and situations include alcoholics; patients with diabetes, severe kidney disease, sarcoidosis, silicosis; long-term corticosteroid usage, malignant disease, use of immunosuppressant, and a chest X-ray image which shows latent TB (2-7). Here, we reported a mother

who had smear positive PTB, and then three of her children acquired active PTB.

2. Case Presentation

In June 2013, a 45-year-old woman from Saravan, south-eastern Iran, referred to our infection clinic because of active PTB and started been treated with a four-drug regimen since one month ago (8). She asked the physician to check her liver function. According to the guide line of TB in Iran, her children younger than six years old also started receiving isoniazid chemoprophylaxis when they had not shown any sign and symptom of active TB. It was advised to consume the drugs for six months. Two months later, these two children referred to our clinic with cough, weight loss and chest X-ray images that showed infiltration in their lungs. Although gastric lavage was negative and white blood count was normal, erythrocyte sedimentation rates (ESR) were high (60 and 75) and we started a regimen consisted of four drugs for active PTB. One month later, they responded to the treatment and were in good conditions.

In December 2014, a 19-year-old man referred to the infection clinic because of weight loss, loss of appetite and chronic cough lasting two months. Family history

showed that his mother and sisters had been treated due to active TB. He was tested for TB and all three sputum smears were positive for *Mycobacterium tuberculosis*. Chest X-ray image revealed diffuse infiltrations in both lungs. At this time, he was referred to TB center to receive TB drugs and be monitored monthly.

3. Discussion

TB, a systemic disease with various presentations and manifestations, is the most common cause of infectious diseases-related mortality worldwide. Classic clinical features associated with active PTB include: cough, weight loss, anorexia, fever, night sweats, and sometimes hemoptysis. TB chemoprophylaxis is a therapeutic measure to avoid development of the disease in individuals already infected with TB. Isoniazid is the most commonly used therapy and follow-up should be at least twice a month until the treatment is complete (1-7, 9). However, the use of RIF and pyrazinamide (PZA) has recently been introduced (9, 10). The effectiveness of INH usage, 5 mg/kg (maximum 300 mg/day) in chemoprophylaxis, has been established since 1960s (2-7, 10). Moreover, poor compliance with the treatment due to its long duration (6-12 months) and on the other hand, the occurrence of co-infection with HIV/AIDS and TB infection have stimulated studies on the effectiveness of chemoprophylaxis using other drugs such as PZA or combination of INH and RIF. In 2000, it was recommended to use a two-month course of RIF and PZA or combination of INH and RIF as a substitute for INH. These findings were based on clinical trials and experiments on animals (9, 10). Isoniazid prophylaxis significantly reduced mortality in children with HIV who were living in an area with a high prevalence of TB (11). The results of the study by Madhi revealed that isoniazid prophylaxis reduced mortality and the incidence of TB by 54% and 79%, respectively, in children infected with HIV (11). Chemoprophylaxis in adults with HIV has been significantly effective only in those with positive results of tuberculin skin test, reducing the risk of active TB by about 60% (12, 13). Recently, it has been observed that treatment for latent TB with isoniazid (but not RIF) improved the immune response, resulting in an increase in the number of interferon γ -producing T cells within a month of therapy (13). Therefore, isoniazid prophylaxis, by enhancing the host immune response, can produce a persistent protection. In our study, firstly, two children with close contact were evaluated for active TB, and then received isoniazid prophylaxis. However, despite chemoprophylaxis consumption, they acquired the active disease. There is a question: why did they get involved? They had been receiving chemoprophylaxis at the time of diagnosis of TB in their mother and on the other hand, they used the drug on time with a proper dosage. It did not seem that the microorganism was resistant to INH because their mother responded to the treatment. Although, we can say that *M. tuberculosis* was resistance to

INH and the mother responded to the other three drugs. We could not test the sensitivity of microorganism and resolve this question. On the other hand, they refused to check HIV infection or any more evaluation for co-morbidity. The Joint Tuberculosis Committee of the British Thoracic Society, the American Thoracic Society, and the Centers for Disease Control and Prevention have recommend preventive therapy for a minimum of six months in patients at increased risk of developing TB, such as recent skin test converters, close contacts of known TB cases, or patients with positive skin tests and chronic medical conditions (1, 7, 14). Although isoniazid chemoprophylaxis is a therapeutic measure to avoid development of the disease, this drug dosage did not completely prevent from developing TB. Therefore, we should observe and evaluate all the cases that have a history of close contact with smear positive PTB and use isoniazid prophylaxis.

Authors' Contributions

All the authors had equal roles in study design, practical work and manuscript writing.

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