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Risk of drug-drug interaction; analysis of tuberculosis treatment versus hepatitis B and C treatment

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ABSTRACT

Mycobacterium infection is an important problem in clinical medicine. Tuberculosis is worldwide observable. The infection has to be managed by an anti-tuberculosis drug. For management of the patients with tuberculosis, the important consideration is the management of the concurrent infections. Several infections might co-occur with tuberculosis. In the tropical endemic area, the hepatitis virus infections are common and might concomitantly occur with tuberculosis. The complex scenario of tuberculosis with hepatitis B infection of hepatitis C infection is not uncommon. To manage the patient with concurrent infection, the use of anti-hepatitis drug is necessary. The important pharmacological consideration is the possible drug-drug interaction due to the several drug administration. In the present study, the authors assess the risk of risk drug-drug interaction in case of tuberculosis treatment versus hepatitis B treatment and hepatitis C treatment. According to this study, the drug–drug interaction between anti-tuberculosis drug and anti-hepatitis B drug or anti-hepatitis C drug is possible and can occur at various degrees. Additionally, there is a difference in identified risks regarding drug–drug interaction between anti-tuberculosis drug and anti-hepatitis B drug or anti-hepatitis C drug.

Brief Report

Core tip: The drug-drug interaction between anti-tuberculosis drug and anti-hepatitis B drug or anti-hepatitis C drug is possible and can occur at various degrees. Additionally, there is a difference in identified risks regarding drug-drug interaction between anti-tuberculosis drug and anti-hepatitis B drug or anti-hepatitis C drug.

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Introduction

Pathogenic mycobacterium infection is an important clinical problem. Several medical problems are due to pathogenic mycobacterial pathogen. Tuberculosis is a worldwide infection caused by pathogenic mycobacteria. This infection is a chronic life-threatening infection and required good clinical management by anti-tuberculosis drug therapy (1,2). For management of the patients with tuberculosis, an important clinical consideration is the management of the concurrent infections. Clinically, there are several possible coinfections with tuberculosis.

In the tropical endemic area, the hepatitis virus infections are common while there is a chance that hepatitis virus infection might occur along with tuberculosis (3-5). The complex scenario of tuberculosis with hepatitis B infection of hepatitis C infection is observable. To manage the patient with concurrent infection, the use of anti-hepatitis drug is indicated. In clinical pharmacology, an important consideration is the possible drug-drug interaction due to

the several drugs altogether used.

Objectives

In the present study, the authors assess the risk of risk drug-drug interaction in case of tuberculosis treatment versus hepatitis B treatment and hepatitis C treatment based on a standard pharmacological bioinformatics approach.

Materials and Methods

The authors perform a standard clinical informatics assessment to predict the drug-drug interaction between anti-tuberculosis drug and anti-hepatitis B drug and between anti-tuberculosis drug and anti-hepatitis C drug. In this study, the included drugs for studies were anti-tuberculosis drugs (rifampicin, isoniazid, pyrazinamide and ethambutol), anti-hepatitis B drugs (Lamivudine, Tenofovir and Entecavir) and anti-hepatitis C drugs (Peginterferon alfa-2aPeginterferon alfa-2b, Ribavirin, Sofosbuvir and Ledipasvir). The possible number of interaction along with

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corresponding severity was predicted. All predictions were performed using a standard bioinformatics tool namely Interaction Checker, which can be accessible online at https://www.webmd.com/interaction-checker.

The specific risks for the studied two groups of drugs are further assessed. For each two groups of drug, two important parameters implying the risk are hereby assessed. First, the chance of drug-drug interaction, which is calculated by "overall number of predicted drug-drug interaction/number of possible drug pairs" is calculated. Second, the possible severity score of drug-drug interaction is calculated by "summation of all predicted severity score for all possible drug-drug interaction/the possible highest severity core in cases that all pairs of drugs have the highest severity of drug-drug interaction." This research followed the Tenets of the Declaration of Helsinki.

Results

According to the study, the drug-drug interaction between anti-tuberculosis drug and anti-hepatitis B drug and between anti-tuberculosis drug and anti-hepatitis C drug are presented in Table 1. For the drug-drug interaction between anti-tuberculosis drug and anti-hepatitis B drug, the chance of drug-drug interaction and the possible severity score of drug-drug interaction are equal to 0 % and 0%, respectively. For the drug-drug interaction between anti-tuberculosis drug and anti-hepatitis C drug, the chance of drug-drug interaction and the possible severity score of drug-drug interaction are equal to 10 % and 10 %, respectively (Tables 1 and 2).

Discussion

The concurrence between tuberculosis and other infection is an important problem in clinical mycobacteriology. To manage any concurrent infection is a general rule in the management of tuberculosis. However, there is usually a difficulty in clinical management. The use of several drugs aiming at tuberculosis treatment and other concomitant problem is necessary and this might lead to an unexpected adverse effect of co-treatment.

In the present report, the authors focus on the specific scenarios of co-occurrences between tuberculosis and hepatitis B virus or hepatitis C virus infections. In fact, the three infections are the important public health threatens globally (3-5). The co-occurrence usually results in difficulty in clinical management (3-5). Here, the authors focus interest on the possible drug-drug interaction, which is a common problem in clinical pharmacology. This problem can occur in any case with many drugs usage. Based on the present study, there were many possible drug-drug interactions. The risks are different for case of concurrence between tuberculosis and hepatitis B infection versus tuberculosis and hepatitis C infection. It can be shown that the concomitant management of tuberculosis and hepatitis B virus using both anti-tuberculosis drugs and anti-hepatitis B drugs had no problem of drug-drug interaction. Nevertheless up to one-tenth of the concomitant management of tuberculosis and hepatitis B virus using both anti-tuberculosis drugs and anti-hepatitis C drugs might result in drug-drug interaction. There should be a special follow-up for any patient infected with both tuberculosis and hepatitis C infection treated by anti-tuberculosis drugs and anti-hepatitis C drugs.

Conclusion

The drug-drug interaction between anti-tuberculosis drug and anti-hepatitis B drug or anti-hepatitis C drug is possible and can occur at various degrees. Also, there is a difference in identified risks regarding drug-drug interaction between anti-tuberculosis drug and anti-hepatitis B drug or anti-hepatitis C drug.

Table 2. Predicted drug-drug interaction due to concomitant use of anti-tuberculosis drug and anti-hepatitis C drug

Anti-hepatitis C drugs	Anti-tuberculosis drugs			
	H	R	Z	E
Peginterferon alfa-2a	N/A	N/A	N/A	N/A
Peginterferon alfa-2b	N/A	N/A	N/A	N/A
Ribavirin	N/A	N/A	N/A	N/A
Sofosbuvir	N/A	4	N/A	N/A
Ledipasvir	N/A	4	N/A	N/A

The studied anti tuberculosis drugs include rifampicin (R), isoniazid (H), pyrazinamide (Z) and ethambutol (E). The studied anti hepatitis C drugs include Peginterferon alfa-2aPeginterferon alfa-2b, Ribavirin, Sofosbuvir and Ledipasvir.
The number in the table represent severity degree of possible drug – drug interaction: 1 = minor, 2 = monitor closely, 3= serious and 4 = don't use together. N/A means no predicted interaction

Table 1. Predicted drug-drug interaction due to concomitant use of anti-tuberculosis drug and anti-hepatitis B drug

Antiretroviral drugs	Anti-tuberculosis drugs			
	H	R	Z	E
Lamivudine	N/A	N/A	N/A	N/A
Tenofovir	N/A	N/A	N/A	N/A
Entecavir	N/A	N/A	N/A	N/A

The studied anti tuberculosis drugs include rifampicin (R), isoniazid (H), pyrazinamide (Z) and ethambutol (E). The studied anti hepatitis C drugs include Lamivudine, Tenofovir and Entecavir.

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