Case Report

Antituberculosis Drugs Induced Hepatitis

Niyati Patel, Riya Gandhi, Padmja Dave, Mahek Mistry

Department of Pharmacy, Sumandeep Vidyapeeth (Deemed To Be University), Pipariya, Waghodiya, Vadodara, Gujarat, INDIA.

ABSTRACT

Background: Tuberculosis, also called as TB, is a highly contagious bacterial infection and can be found nearly anywhere in the body, but lungs are the most common site of infection. Among the first line combination therapy drugs (INH, RMP, PZA, EMB), INH, RMP, and PZA are hepatotoxic as they are potentially metabolized mainly by the liver. **Case:** This is a case report of 18 years old male patient who was diagnosed with hepatitis after administration of anti TB drugs. He was admitted to the hospital for dry cough, loss of appetite, weight loss 3-5kg before 1 month. Laboratory investigations and other reports confirmed hepatitis. In this case, patient was receiving the anti TB drugs since 1 month and then later developed hepatitis which is a severe adverse drug reaction. **Conclusion:** Although hepatotoxicity is severe side effects of antituberculosis drugs. Following standard treatment and care of the patient we archive favourable outcome.

Key words: Anti tubercular drugs, Hepatitis, SGOT, SGPT, Adverse Drug Reaction.

INTRODUCTION

- According to WHO, India has the world's largest tuberculosis epidemic.[1] In India, TB causes the death of every third aids patient. Furthermore, india accounts for around one fourth of the global tuberculosis burden.[2]

Tuberculosis also called as TB, is a contagious bacterial infection and is found nearly anywhere in the body, but most commonly it is found in the lungs. This is because, mycobacterium tuberculosis, the bacteria that is responsible for TB infection is spreadthrough the air as it cannot live long on surfaces. When people suffering with lung TB sneeze, cough or spit, they propel these micro-organisms in their immediate surroundings. Upon the inhalation of only a few germs a person can become infected. Although discovered more than a 100 years ago, tuberculosis still one of the disease that cause the most deaths every year. Tuberculosis is a curable and preventable.[2]

Currently, the recommended first-line treatment for TB isisoniazid (INH), rifampicin (RMP), pyrazinamide (PZA) ethambutol (EMB) given for 2 months, followed by isoniazid and rifampicin or ethambutol for 4 months. Hepatotoxicity is most occurring serious adverse effect of anti-TB medications and may reduce treatment effectiveness by compromising the treatment regimens.[2,3]

Among the first-line quadruple therapy of drugs these INH, RMP, and PZA drugs are metabolized mainly by the liver and responsible for causing hepatotoxicity. According to many studies 2 – 28% cases were reported for Anti-TB Drug-Induced Hepatotoxicity.[4]

The risk factor for anti-TB induced hepatotoxicity includes history of chronic liver disease, or an infection of the liver like chronic viral infection, hepatitis B (HBV), hepatitis C (HCV), high intake of alcohol, elderliness, advanced TB, HIV infection, associated administration of

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Address for correspondence:
Niyati Patel,
Pharm.D Intern, Department of Pharmacy, Sumandeep Vidyapeeth (Deemed To Be University), Pipariya, Waghodiya, Vadodara, Gujarat, INDIA.
Phone no: +91-9638782155
Email id: niyatipatel640@gmail.com

www.ijopp.org

enzyme-inducers, drug dependence and malnutrition status.[2,5,6] The aim of the study was to assess the risk factors, observe the approach and outcome of anti-TB medication, assess alteration ion liver enzyme and report the adverse effect of hepatotoxicity associated with anti-TB medication in a tertiary care hospital patient.

CASE REPORT

A 18-year-old male patient came with complaints of dry cough, weight loss 3-5 kg, jaundice since 4 days, loss of appetite, yellowish discoloration of skin since 4 days. The patient was addicted to alcohol. The patient was diagnosed with pulmonary TB since 1 year, he had taken anti-TB drug.

On the 1st day patient was came to the hospital with pulse rate 96/min, BP is found to be 110/68 mmHg with SPo_2 96% with high flow oxygen. The patient was asked for following investigations: serum creatinine, blood urea, liver function test, USG rest, chest X ray. Based on laboratory findings and USG reports patient diagnosed with borderline hepatitis. On the basis of medicine reference patient was diagnosed with pulmonary thromboembolism with anaemia and advise on further management by giving the patient IV iron parenteral therapy of blood transfusion(B^{+ve}). The patient received the following medications,

- Inj. Streptomycin 0.75gm (1-0-0)
- Tab. Levofloxacin 750 mg (1-0-0)
- Tab. Ethambutol 1000 mg(1-0-0)
- Neb. Levosalbutamol(1.25mcg) + Ipratropium bromide (500mcg) (1-1-1-1)
- Neb. Budesonide 0.5 mg (1-0-1)
- Inj. Normal saline 1 amp
- Inj. Ondansetron 4 mg (1-0-1)
- Tab. Paracetamol 500 mg (1 tab SOS)

On the 2nd day physician prescribed medicine that is Tab. Folic acid (5mg) + mecobalamine (1500mg) + pyridoxine (20mg) with frequency of (0-1-0) to the patient after examination.

On the 3rd day BP was recorded 102/70mmHg and pulse rate was 110/min. The patient was received following medicine and rest of the treatment was continued same as before.

- Inj. Etophyline (84.7mg) + Theophyline(25.3mg) (1-0-1)
- Inj. Enoxaparine 60 mg (1-0-1)
- Tab. Potassium chloride (2 tsf in 1/2 glass of water) (1-1-1)
- Tab. Ferrous ascorbate (100mg) + Folic acid(1.5mg) (1-0-1)
- Inj. Hydrocortisone (100mg) (1/2-1/2-1/2)

Parameter	Test values		Normal range
	Day 1	Day 2	
LFT			
SGOT	41	45	Upto 40 IU/L
SGPT	39	43	Upto 40 IU/L
Total Bilirubin	1.3	1.0	1.2 mg/dl
Direct Bilirubin	0.4	0.4	0.3 mg/dl
Lymphocytes	16		20 to 40 %
Platelets	1.3		1.5 to 2.5 Lac
Urine Analysis			
Albumin	++		
Sugar	++++		
Acetone	++		
Calcium Oxalates	1-2		
USG			
Abdomen		Borderline hepatitis	

On the 4th day BP was recorded 110/68mmHg and Pulse rate 90/min with SPo_2 concentration 95%, other examination that is sputum for AFBRNTCP – is CABNAAT positive (Rifampicin sensitive). The patient was prescribed with Tab. Isoniazid (300mg) and rest of treatment was continued.

On the 5th day, nutritional assessment was performed, the patient was on low protein, low fat liquid, liquid food, same treatment was continued.

On the 6th day, No fresh complain was seen and the same treatment was continued.

On day 7, the patient was diagnosed with anti-tuberculosis drugs induced hepatitis.

On the 8th day, the patient complains of episode of anxiety, sadness of mood and panic attack, which was evaluated by psychiatrist who prescribed the following medication and plan for discharge was made.

- Tab. Fluoxetine 60mg(1-0-1)

- Tab. Clonazepam (0.5mg) (0-0-1)

On the 9th day patient was discharge with discharge medication chart and counselling on his medication.

Causality Assessment

Causality and severity assessment has done with the help of five different scales and results are following:

Scale's Name	Result
WHO	Probable
Naranjo's algorithm	Probable
Shumock and thronton	Definitely
Karch and lasagne	Probable
Hartwigs and siegel	Predictable

DISCUSSION

Anti-Tuberculosis drugs induced hepatotoxicity is a serious problem and 2-28% cases reportedAnti-TB drug-induced Hepatotoxicity (DIH) during their course of treatment. Viral hepatitis has been replaced with Drug induced liver disorder even acute liver failure. Drug-induced liver disorder is diagnosed only after excluding viral hepatitis. The prevalence of drug induced hepatotoxicity in India is found to be around 8-36%.[7] Asian countries have higher incidence of DIH which may be due toasian ethnic susceptibility and/or the presence of various known predisposing factor such as HBV infection, and undernutrition and anemia in these regions. According to a studyconducted, the overall frequency of serious adverse effects was three times higher with Pyrazinamide than with isoniazid, or rifampicin. It is also found that malnutrition is the main risk factors that lead to hepatotoxicity due to anti-TB medications. In our case upon nutritional assessment, patient was found with lacking protein and other nutrients consistent with history of malnutrition. Patient was also found to be underweight.[7,8] Many studies show strong evidence that malnutrition is strong predictor of ATT induced hepatoxicity.[9-11]

The risk factors for Anti TB drug induced hepatotoxicity also include geriatric patients, female gender, under nourishment, alcohol consumption, history of liver diseases, Extra pulmonary Tb affecting abdomen and infections such as HIV and Hepatitis B and C. However, the mechanism of biochemical reaction and pathogenesis of Anti TB drug induced hepatotoxicity remains uncertain. Liver is an important body organ according to physiological point of view as it is responsible for metabolism of many xenobiotic. The prevalence of hepatotoxicity is found to be 2.6% with combination of INH (Isoniazid) and Rifampicin, 1.1% with Rifampicin Monotherapy and 1.6% with isoniazid Monotherapy only.[12]

According to Naranjo Causality Assessment Algorithm Antitubercular agents are probable to cause hepatotoxicity.Upon discharge, the patient was counselled regarding the medications and duration of the treatment.

CONCLUSION

We reported a case of anti-tuberculosis drugs induced hepatitis in 18-year-old male patient. Although hepatotoxicity is severe side effects of anti-tubercular drugs. Following standard treatment and care we have archive outcome. It is important for physician and pharmacist to follow up patient, counsel them about signs and symptoms of of hepatitis and encourage them to report it.

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The present study reviews the prescribing pattern for anti tuberculosis drug induced hepatitis. The study can be utilized by the researchers in direct to carry out the same at larger sample size.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

AFB: Acid Fast Bacili; **ADR:** Adverese Drug Reaction; **ATT:** Anti Tuberculosis Treatment; **AMC:** Adverse Drug Reaction Monitoring Centre; **BP:** Blood Pressure; **CABNAAT:** Cartridge Based Nucleic Acid Amplification Test; **EMB:** Ethambutol; **gm:** Gram; **HBV:** Hepatitis B Virus; **HIV:** Human Immunodeficiency Virus; **INH:** Isoniazid; **Ing:** Injection; **Mg:** Miligram; **Mcg:** Microgram; **Neb:** Nebulizer; **PZA:** Pyrazinamide; **RMP:** Rifampicin; **RNTCP:** Revised National TB Control Programme; **SGOT:** Serum Glutamic Oxeloacetic acid; **SGPT:** Serum Glutamic Pyruvic Transaminase; **SOS:** Si Opus Sit (Immediately); **TB:** Tuberculosis; **Tab:**

Tablet; **USG:** Ultrasonography; **WHO:** World Health Organization.

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