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Review on tuberculosis

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Article History	Abstract
	Tuberculosis has been one of the contagious diseases in human communities during the past 50 years. World Health Organization (WHO) has been reported that one third of the world's population is infected with Mycobacterium tuberculosis this high occurrence of infection has caused a large number of morbidity and mortality. Which is partly due to serious adverse reactions induced by Anti-TB drugs. Mycobacterium tuberculosis normally affects the lungs along with other parts of the body examples: lymph nodes, spin, cervix and kidney etc. India is the highest TB burden country accounting more than one third of the global occurrences. There are many adverse drug reactions (ADR's) are developed during the treatment of Tuberculosis with anti-tubercular drugs. The detection of adverse drug reactions (ADR's) has become increasingly significant because of introduction of a large number potent toxic chemicals. Pharmacovigilance is an arm of patient care and surveillance ADR'S effect both the children and adults with carrying the magnitudes causing morbidity and mortality. A good pharmacovigilance study will identify the risks within the shortest possible time after the medicine has been marketed and will help to establish or identify the risk factors. The current prospective observational study of six months duration was designed to assess the rate of adverse drug reactions (ADRs) occurrence by anti-tubercular drugs in patients admitted in the department of Chest & Tuberculosis from whom a proper consent obtained. The results of the study showed that the incidence of all major adverse effects was 1.08 per 50 person's month of exposure. The occurrence of any major side effect in the study was associated with female sex and increase in age. In our study the major cause of admission was adverse drug reactions 47(47%).In our study Hepatitis was observed in 11 (11.56%) patients, leading to the death of 3 patients. In conclusion, Anti-TB drugs that used in tubercular treatment were result in significant adverse effects both in quantity and severity. These reactions may lead to hospitalization, and even death. To confirm this hypothesis many more studies with large population is needed.

Introduction

Tuberculosis is a contagious disease caused by Mycobacterium tuberculosis. The disease spreads by droplet infection. Every sputum positive patient spreads the disease to 15 to 20 persons per year. Every year approx. 20 lakhs people develop TB and 5 lakhs die from it.1 India is the highest TB burden country accounting more than one third of the global incidence. Tuberculosis has been one of the contagious diseases in human communities during the past 50 years. World Health Organization (WHO) has been reported that one

third of world population infected with Mycobacterium tuberculosis .The high occurrence of infection has caused a large number of morbidity and mortality which is partly due to serious adverse reactions induced by Anti TB drugs. The detection of adverse drug reactions (ADRs) has become increasingly significant because of introduction of a large number of potent toxic chemicals as drugs in the last two or five decades.

World Health organisation (WHO) Defines Pharmacovigilance "as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem"

World Health Organization (**WHO**) – Adverse Drug Reaction is defined as "Any response to a drug which is noxious and unintended, and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function".

The goal of current study is to reduce mortality and morbidity due to TB and the study focuses in assessing the rate of adverse drug reactions (ADRs) induced by anti-tubercular drugs and to detect serious and preventable recognized ADRs as the primary objectives.

Material and methods

Study site

The study entitled "A Pharmacovigilance Study in the Department of Chest & Tuberculosis on Anti Tubercular Therapy in a Tertiary Care Teaching Hospital of South India" was carried out in a 600 bedded tertiary care teaching hospital located at Nellore, Andhra Pradesh, India.

Study duration: 06 months (July 2021 to December 2021).

Study sample: 50 patients.

Inclusion criteria: All patients who were getting admitted to the study site during study period with pulmonary TB.

Exclusion criteria: Patients with chronic hepatitis illness such as cirrhosis, chronic hepatitis and acute viral hepatitis were excluded. The patients who all are unwilling to participate in the study and terminally ill will not include in the study.

Plan of study: Study procedure was categorized to three phases (I, II & III) respectively.

Phase I:

1. Submission of protocol and obtaining consent from hospital authority.

2. Literature survey

3. Designing of: Data entry format, Patient Information & consent form.

Data entry form for incorporating inpatient details were designed and the format contains provision to enter the details such as name, age, sex, height, weight, IP. No, date of admission, date of discharge, vital signs, reason for admission, past medical history, past medication history, and any predisposing factors. Provision was given in the Format for entry of details like Blood sugar levels, blood counts, Liver function test, Renal function test, Electrolytes, Urine examination, Lipid profile, Diagnosis, Drug chart, ADR monitoring chart and Drug interaction chart and dose and any interventions.

Phase II

1. Data collection through standard data entry format.

2. Literature survey.

3. Data analysis

- To assess the rate of adverse drug reactions (ADRs) induced by anti-tubercular drugs in the department of Chest & Tuberculosis.

- To detect serious and preventable recognized ADRs.

Phase III

1. Literature survey.

2. Data analysis

The obtained data will be thoroughly analysed to evaluate the appropriateness of anti-tubercular drug use.

3. Preparation and submission of reports.

Results

During the 06 months study period 50 patients were diagnosed with positive TB. These patients were put on routine treatment protocol. Of these patients, 23 (23%) developed at least one adverse drug reaction. Total number of 47 adverse drug reactions detected in this study. The 23 patients with ADR consisted of 09 females and 14 males. Occurrence of adverse reactions led to prolongation in hospital stay for 21 (19%) patients. The rate of adverse reactions was various in different age groups. It does appear that with Anti-TB drugs used in this study the rate of ADRs increases with increased age reported in Table I (Anti-TB induced adverse drug reactions in different age groups).

Anti-TB induced adverse drug reactions in different age groups

S.N	Age	Patient	Patient with ADR
1	0-10 years	00	00
2	11-20 years	02	01
3	21-30 years	04	02
4	31-40 years	08	04
5	41-50 years	13	06
6	51-60 years	21	08
7	>60 years	04	02

Drugs used in the treatment of tuberculosis

According to their clinical utility the anti -TB drugs can be divided into:

First line: These Drugs have high anti tubercular efficacy as well as low toxicity are used routinely.

Second line: These drugs have either low anti tubercular efficacy or higher toxicity under used when first line cannot be used, or to supplement them.

First line drugs:

1. Isoniazid.
2. Rifampicin.
3. Ethambutol.
4. Pyrazinamide.
5. Streptomycin.

Second line drugs:

Fluoroquinolone:

1. Ofloxacin
2. Levofloxacin
3. Moxifloxacin
4. Ciprofloxacin

Other oral drugs:

1. 1.Ethionamide
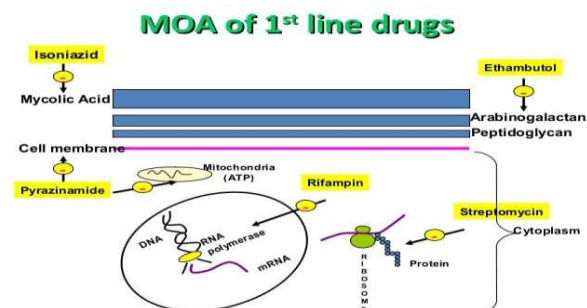2. Para amino-salicylic acid (PAS)
3. Rifabuti

Injectable drugs:

1. 1.Kanamycin
2. Amikacin

Table No. 02: Causality of ADRs induced by Anti-TB drugs according:

S.no	Scale	%	Frequency
1	Probable	21.33	20
2	Possible	20.34	19
3	Certain	8.22	08
	Total	50	47

Fig 01: Mechanism of action of first line drugs in the body

The most serious adverse reaction induced by Anti- TB therapy was reported in Table II, in which hepatitis was (11.56%), leading to death in two patients. In this study, increase in plasma uric acid was observed in 2 patients (2.43%) due to pyrazinamide. These reactions occurred in average 26.7 days after the beginning of treatment and followed by arthritis. After discontinuing of Pyrazinamide, the level of uric acid returned to normal range within 10 days. Isoniazid caused reactions such as constipation (6.33%), and peripheral neuropathy (4.24%) rifampicin was the major cause of headache (4.36%), rash and pruritus (3.12%) and diarrhoea (2.06%). The only adverse reaction suspected to be induced by Ethambutol was vision abnormality such as blurred vision and burning eyes in two patients (1.06%). The main action taken in patients with detected ADR was discontinuation of drug regimen (35.05%). The action mainly was taken when hepatotoxicity was detected the ADRs induced were given in the table.03. There was no specific treatment for alleviating the adverse reactions, other than headache and constipation. The causality assessment of ADRs revealed that 08(8) cases were detected as certain, 20(20.43) as possible and 21(21.36) probable reactions in the table 2.

Table No. 03: Type of detected ADRs induced by Anti-TB drugs:

S.no	Reaction	Frequency	%
1	Hepatitis	11	11.56
2	Constipation	6	6.33
3	Increased liver transaminases	5	5.43
4	Headache	4	4.36

5	Hyperglycaemia	5	5.64
6	Peripheral neuropathy	4	4.24
7	Rash	3	3.12
8	Dysuria	3	3.56
9	Increased uric acid	2	2.43
10	Diarrhoea	2	2.06
11	Prolonged PT	1	1.07
12	Vision abnormality	1	1.06
	Total	47	50

Discussion

In this study of pharmacovilance of anti – TB drugs, 23 (23%) patients were exposed to at least on adverse reaction. This type of high percentage of incidence of adverse reactions significates that there is a need for more evaluation of acceptability of patients for developing Anti-TB induced ADRs. In this study it is confirmed that the rate of ADRs will increases with increase in age. In our study Hepatitis was observed in 11 (11.56%) patients, leading to the death of 3 patients. Some evidence initially suggested that continuous use of INH and rifampicin might lead to a greater risk of hepatotoxicity. It is believed that Rifampicin can induce the metabolism of INH to hepatotoxins. In this study the patients were showed constipation is 6 (6.33), and increased plasma uric acid concentration is observed in 2(2.43%), rashes in 3 (3.12) patients. The multi drug regimen (more than 3 drug s) will shows higher incidence of adverse drug reactions (ADRs).

However, caution should be taken in high risk individuals such as elderly, alcoholics, those taking additional hepatotoxic agents and those with pre-existing liver diseases. Rifampicin usually causes cholestasis, which results in high concentrations of alkaline phosphatase and bilirubin. Liver toxicities can be the major side effect of all three main anti-TB drugs, Isoniazid, Rifampicin and Pyrazinamide. This shows that there were many adverse reactions (ADRs) are induced in the patients who were involved in Anti-tubercular treatment. In this treatment few of the patients were died.

Conclusion

After this study the conclusion is that, Anti-TB drugs used in the tubercular treatment will result in significant adverse reactions (ADRs) both in quantity and severity.

People may develop more frequently severe adverse reactions, such as hepatitis, constipation, liver toxicity. This may lead the patients to be hospitalized and even to dead of the patients. To confirm this hypothesis many more studies with large population is needed.

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