International Journal of Pharmacological Research
ISSN: 2277-3312
www.ssjournals.com
Journal DOI:10.7439/ijpr

Adverse Drug Reactions to First Line Anti-Tubercular Drugs - A Pharmacovigilance Study

Dr. Umeshchandra C Honnaddi[1*], Dr. Madhushalini U Honnaddi[2], Dr. Tharangini SR[3], Dr. Taher Hossain[4], Dr. Roopali Somani[5]

[1]*Department of Pharmacology, M. R. Medical College, Sedam Road, Gulbarga, Karnataka, India*
[2]*Vydehi Institute of Medical Sciences & Research Centre (VIMS), Bangalore, Karnataka, India*
[3, 4, 5] *Department of Pharmacology, M. R. Medical College, Sedam Road, Gulbarga, Karnataka, India*

Corresponding author*

Dr. Umeshchandra C Honnaddi
S/o Chandrashekhar S Honnaddi
III Year Postgraduate Resident,
Department of Pharmacology,
M. R. Medical College, Gulbarga, India
E-mail: honnaddiumeshchandra@gmail.com

Abstract

Introduction: Tuberculosis is one of the major health problems in India and developing countries. It is the second leading infectious cause of morbidity and mortality in the world.

Objective: The present study was undertaken to study the Adverse Drug Reactions (ADRs) to first line Anti-tubercular drugs (ATTs) prescribed to tuberculosis patients admitted to Medicine Department, BTGH, attached to M.R. Medical College, Gulbarga.

Materials and Methods: A Prospective Observational study was carried among tuberculosis patients on Directly Observed Short Course Chemotherapy (DOTS), admitted to Medicine Department, BTGH, attached to M.R. Medical College; Gulbarga.120 Patients were included during the study period of 9 months from 1st October 2014 to 30th June 2015. The data was collected in a Proforma which included questionnaire.

Results: A total of 120 tuberculosis patients on DOTS were enrolled for the study. Out of 107 patients, 63 patients (58.87%) developed ADRs. Out of 63 patients, 32 patients (51%) developed Gastro-intestinal problems, 14 patients developed CNS problems (22%), 11 patients (18%) developed Hepatitis, 4 patients (6%) developed Fever and 2 patients (3%) developed Pancreatitis. The most serious ADR was Hepatitis.

Conclusion: Results of the study reveals that about 58.87% of patients developed ADRs during the study period. These ADRs will lead to stoppage of drugs, development of Drug resistance and Therapeutic Failure. If a proper Pharmacovigilance system is implemented in the hospital, most of the patients may report their ADRs and thereby we can improve the patient adherence and treatment outcome.

Keywords: Tuberculosis, First-line-Anti-tubercular drugs, Adverse drug reactions.

1. Introduction

Tuberculosis (TB) is a chronic granulomatous infectious disease caused by Mycobacterium tuberculosis bacteria and has become now as the second leading infectious cause of death in the world [1]. It is one of the major health problems in India and developing countries. In India alone about 1.8 to 2.0 million people develop tuberculosis every year [2]. It accounts up to 20% of total yearly cases in the world and about 0.4 million die every year from it [2]. The World Health Organization (WHO) declared TB as a global health emergency in 1996 [3]. According to the latest Global Tuberculosis Control report 2014 of WHO, 9 million developed TB and 1.5 million died from the same [4]. The primary strategy in the treatment of TB is to use multiple drug regimens to prevent the emergence of resistance and eradicate the disease.

Anti-tubercular regimens have been in use for more than 30 years, and include use of multiple drugs for long term, depending on the category of the disease. The first line drugs used in the treatment of TB are Isoniazid (H), Rifampicin (R), Pyrazinamide (Z) and Ethambutol (E). However the frequency of occurrence of ADRs to them is not well known, probably due to lack of awareness, detection and under reporting [5]. ADRs lead to decrease in patient compliance and adherence, thereby leading to stoppage of the drugs by the patient which ultimately leads to treatment failure and development of resistance.

1.1 Objective

The present study was undertaken to study the ADRs to first line Anti-tubercular drugs prescribed to tuberculosis patients admitted to Medicine Department, BTGH, attached to M.R. Medical College, Gulbarga.

2. Materials and Methods

2.1 Type of Study: Prospective Observational Study.

2.2 Place of Study: Department of Medicine, BTGH, attached to M.R. Medical College, Gulbarga in tuberculosis patients who were on Directly Observed Short Course Chemotherapy (DOTS).

2.3 Duration of Study: 9 months from 1st October 2014 to 30th June 2015.

All the participants were explained about the type and purpose of the study and informed that participation is voluntary and written informed consent was obtained.

2.4 Inclusion criteria

- Patients on First-line Anti-tubercular Drugs.

2.5 Exclusion criteria

- Patients on Anti-Retroviral Therapy.
- Patients on Second-line Anti-tubercular Drugs.
- Patients on Other Medications.

2.6 Sample size

- 120 patients were enrolled in the study after applying inclusion & exclusion criteria
- **Ethical approval:** Ethics committee approval was obtained from the Institutional Ethics Committee.
- **Data Analysis:** Analyzed and presented as percentages using descriptive statistics.

3. Results

A total of 120 tuberculosis patients on DOTS were enrolled for the study.

Figure 1: Showing Gender distribution of disease in the Study

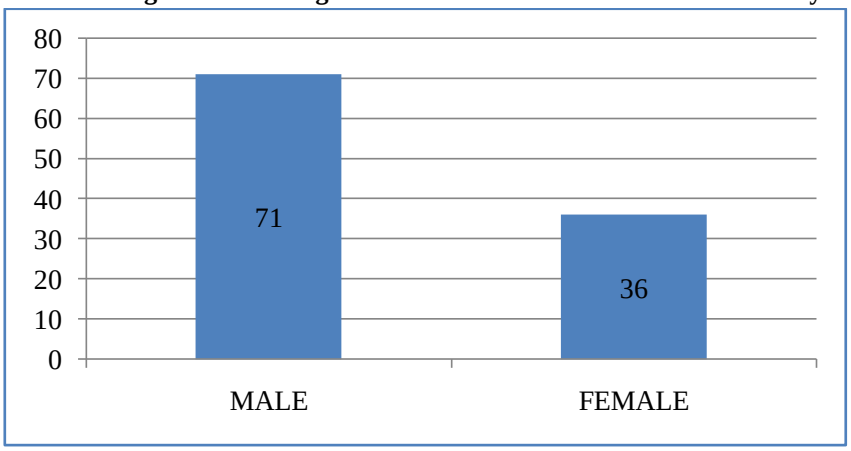
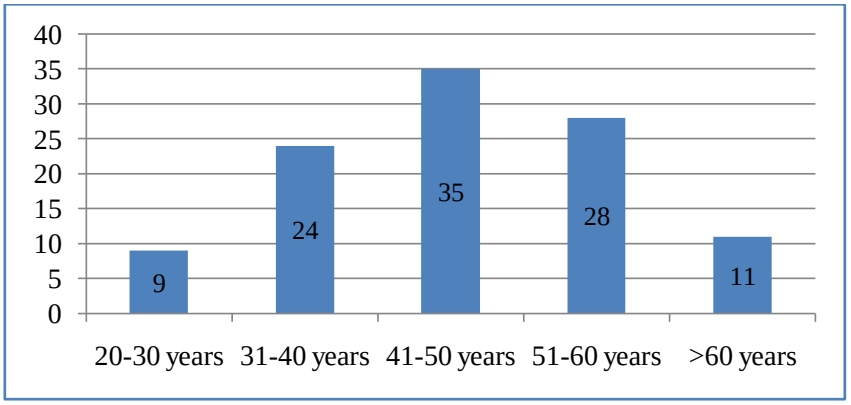


Figure 2: Showing Age distribution of disease in the Study



Out of 107 patients, 63 patients (58.87%) developed ADRs. Out of 63 patients, 32 patients (51%) developed Gastro-intestinal problems, 14 patients developed CNS problems (22%), 11 patients (18%) developed Hepatitis, 4 patients (6%) developed Fever and 2 patients (3%) developed Pancreatitis. The most serious ADR was Hepatitis.

Figure 3: System wise Distribution of ADRs

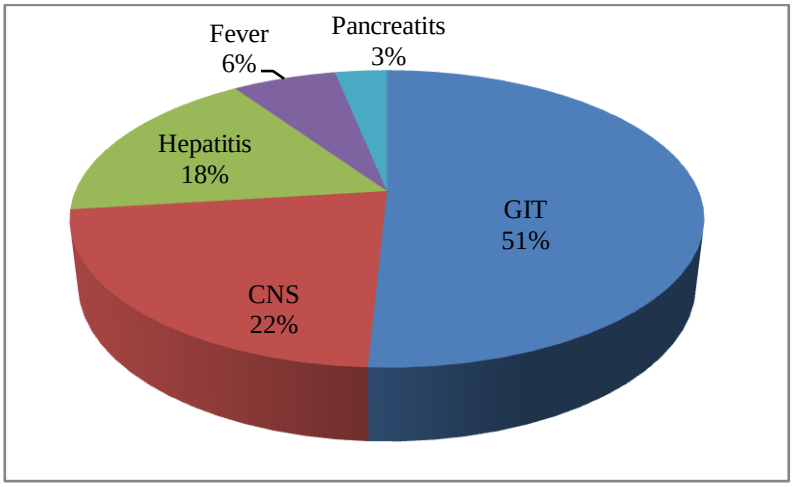
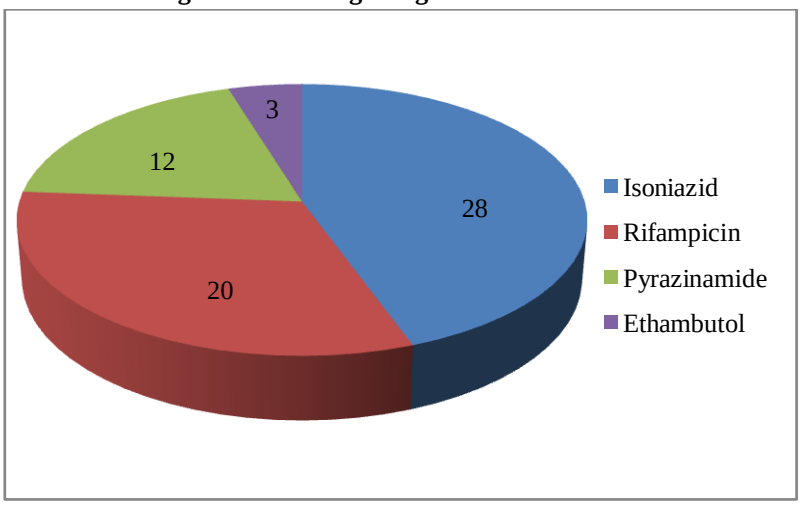


Table 1: Showing Drugs Involved in ADRs

Name of Drug	Number of Patients	Percentage (%)
Isoniazid	28	44
Rifampicin	20	32
Pyrazinamide	12	19
Ethambutol	3	5
Total	63	100

Figure 4: Showing Drugs Involved in ADRs



4. Discussion

First line Anti-Tubercular Drugs are highly efficacious & potent hence are the preferred agents for the treatment unless there is resistance to them. Isoniazid (H), Rifampicin (R), Pyrazinamide (Z) and Ethambutol (E) are the first line Anti-Tubercular Drugs used in the treatment of TB. WHO recommends DOTS regimen, where the Anti-Tubercular Drugs are given under the supervision of medical professional three days a week, usually given for 6 months, with 4 drugs in intensive phase for 2 months and 2 drugs in continuation phase for 4 months. Adverse Drug reactions (ADRs) can be defined as noxious, undesired (or) unintended effect of a drug, which may occur at doses normally used for prophylactic, therapeutic and diagnostic (or) the modification of a physiological state [6]. According to WHO, Pharmacovigilance is defined as "science and activities relating to the Detection, Assessment, Understanding and Prevention of adverse effect (or) any other drug related problems[6]. The Ministry of Health and Family Welfare, Government of India has set up National Pharmacovigilance Programme in 2004 [6].

Table 2: Showing MOA & ADRs of 1st Line ATTs

Drugs	Mechanism of Action	Major ADRs noted in our Study
Isoniazid 5 mg/kg/day	Inhibits the synthesis of mycolic acid	Peripheral neuritis Hepatitis Hypersensitivity reactions
Rifampicin 8-10 mg/kg/day	Inhibits the DNA dependent RNA polymerase	GIT disturbances Flu like syndrome Hypersensitivity reactions
Pyrazinamide 15-30mg/kg/day	Inhibits the synthesis of mycolic acid	Hepatitis Hyperuricemia
Ethambutol 15 mg/kg/day	Inhibits Arabinosyl Transferase	Optic Neuritis Hyperuricemia

Among 63 patients who reported adverse drug reactions, the highest numbers of ADRs were observed in males 41 (65%) and the remaining 22 (35%) were observed in females. Incidences of ADRs in our study were: GIT (51%), CNS (22%), Hepatitis (18%), Fever (6%) and Pancreatitis (3%). Most of the GIT ADRs occurred during first week of therapy, whereas others systems were involved during the later weeks of therapy. Causality Assessment was done according to Naranjo's Scale; the score in our study ranged from 5-8, therefore majority of ADRs in our study were Probable.

5. Conclusion

Results of the study reveal that about 58.87% of patients developed ADRs during the study period. Most of the ADRs were due to Isoniazid & Rifampicin. Most common systems involved in ADRs were GIT, CNS, Biliary. Most serious adverse effect was Hepatitis. ADRs will lead to Stoppage of Drugs by the patients, Development of Drug Resistance, Amplified Healthcare Cost and Therapeutic Failure. If a proper Pharmacovigilance system is implemented in the hospital, patients can report their ADRs and thereby, Patient Adherence and Therapeutic Outcome can be improved.

References

[1] Dale DC. Infectious Disease: The Clinician's Guide to Diagnosis, Treatment and Prevention. In. New York: WebMD Inc; 2003.
[2] Srivastava S K, A Complete Textbook of Medical Pharmacology, 1st edition; Chapter 56: 888.
[3] WHO report 2009 Global tuberculosis control- Epidemiology, Strategy, Financing. Geneva: World Health Organization; 2009.
[4] Global Tuberculosis Control report 2014 of WHO.
[5] Bulletin On Adverse Drug Reactions, April 2012/Vol: 2/Issue: 1. Available from URL: http://www.ltmgh.com/Common/Uploads/pdf/BulletinonAdverseDrugReactions%20April2012Vol2Isu1.pdf
[6] Srivastava S K, A Complete Textbook of Medical Pharmacology, 1st edition; Chapter 4: 81-90.