



PHARMACOVIGILANCE STUDY: DRUGS USED IN THE TREATMENT OF TUBERCULOSIS AT CIVIL HOSPITAL ROHRU (SHIMLA), HIMACHAL PRADESH.

¹Shiv Kumar Kushawaha*, ¹Amit Sharma*, ²Arti Ralta, ²Ruchika Sharma, ³Dev Raj

¹Department of Pharmacology, ³Department of Pharmaceutics,
²Laureate Institute of Pharmacy, Himachal Pradesh, India.

Corresponding Author:-**Amit Sharma**
E-mail: amit.clinical@yahoo.com

<p>Article Info</p> <p>Received 25/05/2014 Revised 19/06/2014 Accepted 22/06/2014</p> <p>Key words: Pharmacovigilance, Tuberculosis, ADR, DOTS.</p>	<p>ABSTRACT</p> <p>Pharmacovigilance is the “science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem. Pharmacovigilance is an arm of patient care and surveillance. It aims at getting the best outcome from treatment with medicines. Good pharmacovigilance will identify the risks within the shortest possible time after the medicine has been marketed and will help to establish or identify risk factors. When communicated effectively, this information allows for intelligent, evidence-based prescribing with the potential for preventing many ADRs. Such information will ultimately help each patient to receive optimum therapy at a lower cost to the health system. In TB treatment programmes, this would include reporting any ADR of concern, all suspected serious reactions, and persistent ADRs that can threaten adherence. It is important that the WHO continues to drive home the importance of the Pharmacovigilance and DOTS strategy, in order that today’s drugs are used wisely and effectively. Furthermore, the infrastructure for delivering the Pharmacovigilance and DOTS strategy will ensure that new tools and rational drugs are used correctly.</p>
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INTRODUCTION

Tuberculosis is the leading infectious disease killer among adults and youth, with one-third of the world’s population infected with *M. tuberculosis*. The World Health Organization (WHO) estimates that active cases of tuberculosis afflict seven to eight million people annually, and lead up to three million deaths per year. Furthermore, a person infected with human immunodeficiency virus (HIV) is ten times more likely to develop tuberculosis than an HIV-negative individual; consequently, the spread of HIV is accelerating the rise in tuberculosis case rates. Yet despite these global health conditions, there has been virtually no novel antituberculosis drug development in over twenty-five years [1]. Tuberculosis or TB is an infectious bacterial disease caused by mycobacterium tuberculosis, which most commonly affects the lungs. It is transmitted from person to

person by droplet infection. It also affects the central system, bone joint and skin. Other bacteria which cause tuberculosis: *Mycobacterium bovis*, *M. africanum*, *M. microti* but these are less common [2]. Currently WHO promotes the five-component DOTS strategy as the best approach toward treatment and global tuberculosis control. If DOTS is not adhered to properly, the risk of multi-drug resistance increases. As more multi-drug resistant strains of *M. tuberculosis* are transmitted across populations, drugs currently in our possession become impotent for effective treatment and control. Ultimately, without the advent of improved tools, the longer-term outlook for global tuberculosis control appears grim. Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem (WHO).



Laboratory and Diagnostic Studies

Radiology (chest x-rays), A tuberculin skin test, Mantoux test, Blood test, DNA diagnosis, Microscopic examination, Microbiological culture of body fluids. Active tuberculosis may be considered as a possible diagnosis when findings on a chest radiograph of a patient being evaluated for respiratory symptoms are abnormal, as occurs in most patients with pulmonary tuberculosis. The radiographs may show the characteristic findings of infiltrates with capitation in the upper and middle lobes of the lungs [3].

Approach to Pharmacovigilance

As with other branches of surveillance, in pharmacovigilance there are three main streams.

1. Spontaneous reporting

Spontaneous (or voluntary) reporting means that no active measures are taken to look for adverse effects other than the encouragement of health professionals and others to report safety concerns. Reporting is entirely dependent on the initiative and motivation of the potential reporters. This is the most common form of pharmacovigilance, sometimes termed passive reporting. In some countries this form of reporting is mandatory. Clinicians, pharmacists and community members should be trained on how, when, what and where to report.

2. Targeted spontaneous reporting (TSR)

TSR is a variant of spontaneous reporting. It focuses on capturing ADRs in a well-defined group of patients on treatment. Health professionals in charge of the patients are sensitized to report specific safety concerns. TSR is intended to ensure that patients are monitored and that ADRs are reported as a normal component of routine patient monitoring and to achieve the requisite standard of care. This focused approach has the same objectives and flow of information as for spontaneous reporting. The reporting requires no active measures to look for the particular syndromes. Its construct would thus differ from cohort event monitoring (CEM) explained below.

3. Active surveillance

Active (or proactive) safety surveillance means that active measures are taken to detect adverse events. This is achieved by active follow-up after treatment and the events may be detected by asking patients directly or screening patient records. It is best done prospectively. Active pharmacovigilance is sometimes very descriptively referred to as "hot pursuit". The most comprehensive method is CEM. It is an adaptable and powerful method of getting good comprehensive data. Other methods of active monitoring include the use of registers, record linkage and screening of laboratory results in medical laboratories. The critical stages of causality assessment and signal identification are applicable to all three methods of

surveillance and will be covered in detail after the individual methods have been discussed.

Pharmacovigilance for anti-TB medicines

Most of the medicines used to treat tuberculosis (TB) today have been on the market for several decades. Clinicians treating TB patients around the world know these medicines well, and are usually well aware of their associated adverse drug reactions (ADRs). The occurrence of these reactions is known to be frequent. The TB patient on treatment is taking more than one anti-TB medicine simultaneously and regimens last from many months to 2 years or more. This increases the likelihood of ADRs, some of which are severe. Most patients on treatment for drug-resistant TB experience at least one side-effect, and a recent study has shown that two thirds of such patients have had at least one medicine stopped temporarily or permanently as a result of ADRs. These events may damage public confidence in any national treatment programme and affect patient adherence.

Patients who stop taking anti-TB medicines pose a risk to themselves and to others. The generation of drug resistance is a very real risk [4].

So why should TB practitioners today reflect on a more systematic approach to surveillance of drug-related problems, which is at the heart of pharmacovigilance. Firstly, while national TB programmes are generally well structured to monitor patients and have a long tradition of following up care using standardized indicators, they do not collect information on ADRs directly. It is therefore difficult to assess precisely the net benefit of a treatment programme if adversities related to the medicines used are not factored in. The contribution of ADRs to death, treatment default and failure can therefore only be conjectured. Secondly, the widespread recognition by health workers that anti-TB medicines often cause ADRs is poorly reflected in the published information on the subject. There is a dearth of published literature about anti-TB drug-induced mortality, morbidity and reduced quality of life, particularly in low-resource settings. The overall burden of adversity directly attributable to anti-TB medicines is poorly quantified and it is not usually well profiled in individual TB control programmes. Thirdly, with the increasing use worldwide of more extensive regimens for drug-resistant TB, the added use of antiretrovirals (ARVs) in patients with HIV-associated TB, and the imminent advent of new classes of medicines to treat TB, the case for improved pharmacovigilance becomes even stronger. Pharmacovigilance needs to be an integral accompaniment to treatment programmes as they expand their geographical coverage, given that the frequency and expression of ADRs may be influenced by factors linked to the demographic, genetic and nutritional patterns, and to the background co-morbidity (e.g. TB/HIV) in a population [5].



Objectives

1. To document the cases admitted to Civil Hospital Rohru (Shimla) due to Tuberculosis.
2. To list the symptoms of Tuberculosis.
3. To list the type of drugs and combinations used for the treatment of Tuberculosis.

The aim is to improve patient care and safety in relation to the use of medicines and all medical and paramedical interventions, by collecting good information on the effects of medicines and providing early warning and communication of problems which might affect the success of the programme. It will thus support the safe, rational and more effective (and more cost-effective) use of medicines. Rapid identification of events that are likely to affect adherence to treatment and determination of their rates, and identification of the risk factors that make these events more likely, with the aim of reducing their occurrence. Measurement and evaluation of the outcome of the response or of action taken (e.g. reduction in risk, improved medicine use, or improved outcome for patients experiencing a particular ADR) [6].

METHODOLOGY

The present study was carried out in the in-patient and out-patients Medicine Department of Civil Hospital Rohru (Shimla) after obtaining the ethical committee clearance from the Institutional Ethical Review Board of the hospital. Informed consent was obtained from the conscious patients or from their relatives if the patients were unconscious.

The study was conducted for a period of one year.

STUDY CRITERIA

Inclusion Criteria

- All in-patients admitted and out-patients due to Tuberculosis in Civil Hospital Rohru (Shimla) and who were willing to participate in the study.

Exclusion Criteria

- All out-patients.
- Patients who were not willing to participate in the study.

Source of Data

Data was collected from case sheets, lab reports and prescriptions of Tuberculosis patients admitted in Civil Hospital Rohru (Shimla), H.P.

Method

The students of Pharmacy 4th year participated in the ward rounds identified the Tuberculosis cases and collected the data. A visit to hospital was given to check for any new cases.

Details of each Tuberculosis case was recorded in the data collection form which included details of age, gender, region, literacy levels, occupation, marital status, habits, past history, month & time of exposure to infection,

signs & symptoms, treatment given, current treatment including DOTS, lab reports, length of hospital stay and patient status after treatment.

RESULTS

The study was conducted in the Civil Hospital Rohru (Shimla) for the period of one year (2013-14). The patient's data was collected from the case report and in the in-patient and out-patient department of the same. In this study we found that the age of patients ranged from 12 to 84 yrs. Majority of the patients belonged to the age group of 19-30 years. Among the 44 patients who got admitted due to tuberculosis, male (24) were slightly more than female (20) patients. Majority of the patients were from urban region (40) followed by rural region (4). Number of patients with primary education and more (Literate) constituted 20 % whereas 80 % were illiterates. Maximum number of the patients were businessmen (20) followed by students (10), and housewives (14). Majority of the patients were married followed by single and widowed patients. The number of patients who were alcoholic was 22.72%, out of which 93.1% were male and 6.89% were female. Smokers were 64.54% patients, out of whom 89.47% were male and 10.52% were female. 14.74% patients were neither smokers nor alcoholic, out of which 28.57% were male and 71.42% were female. 34.54% patients were both smokers and alcoholic out of whom 86.47% were male and 10.52% were female.

Although 73 % of the patients were admitted due to tuberculosis for the 1st time, 19% of the cases were due to 2nd attempt and 5.5 % cases were third time (relapsed cases). During the study we found that the maximum numbers of admissions were in the month of December followed by January, July and August. Out of 44 cases, CNS symptoms were seen in 52.2 % cases, GI symptoms were seen in 61.81 % cases, CVS symptoms were seen in 31 % of cases, respiratory symptoms were seen in 78.18 % cases and 7.27 % cases presented with allergy and hypersensitivity reactions. The specific drugs that were used were HRZE (54.27%) TID/ week, followed by HRZES- TID/Week (45.73%) of the cases.

TREATMENT GIVEN

1. First line Anti-tubercular drugs (Standard drugs):

Isoniazid (H), Rifampicin (R), Pyrazinamide (Z), Ethambutol (E), Streptomycin (S).

2. Second line Anti-tubercular drugs (reserve drugs):

Ciprofloxacin, Moxifloxacin, Rifabutin, Azithromycine, Rifapentine

3. MDRS:

For H Resistance – RZE given for 12th months is recommended.

For H+R Resistance – ZE+S/ Kmc/ Am/Cpr+Cipro/ofl ± Etm could be used. The actual regimen is devised according to the features of the individual patient.



Table 1. Concurrent Medications Prescribed for Treatment

Concurrent Medication	Number of Patients out of 44
Analgesics	12
Antibiotics	44
Antiemetics	15
Antiulcers	03
CNS depressants	05
Diuretics	00
Nutritional supplements	40
Anti-Histaminic	15
Supportive therapy	07

Table 2. Lab parameter

Lab parameter	Number of patients
Decrease in Blood count	30
Increase in ESR	33
Normal lab reports	01
Sputam Test(Speciman) Visual Apprance	Postive- 40 Negative- 04
Grade	A-20B-13C- 11

The duration of stay in the hospital varied from seven to twenty days depending on severity of infection. Hospitalization days ranged from 4 to 20 days with a mean of 10-15 days. Out of 44 cases, 33 patients recovered partially and 11 patients relapsed with the positive sign of tuberculosis.

CONCLUSION

Tuberculosis is a major problem in urban as well as rural setting leading to hospitalization and even death of individuals.

- Maximum incidence of tuberculosis was seen in patients from urban region in the age group of 19-30 yrs.
- Majority of the patients were literates with businessmen, followed by students and housewives.
- Most of the patients were alcoholics.

As per the study the recommended treatment for the tuberculosis was found to be

First line Anti-tubercular drugs (Standard drugs):

- Isoniazid (H), Rifampicin (R), Pyrazinamide (Z), Ethambutol (E), Streptomycin (S).

Second line Anti-tubercular drugs (reserve drugs):

- Ciprofloxacin, Moxifloxacin, Rifabutin,

Azithromycine, Rifapentine

MDRS

- For H Resistance – RZE given for 12th months is recommended.
- For H+R Resistance – ZE+S/ Kmc/ Am/Cpr+Cipro/ofl ± EtmCoud be used.
- The actual regimen is devised according to the features of the individual patient.
- Having information about the commonly drugs used for tuberculosis and updated guidelines for the management of the same would be helpful to the clinicians as a quick reference before treating the patients.

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