DOI: 10.21276/sajp.2016.5.6.5

Scholars Academic Journal of Pharmacy (SAJP) **ISSN 2320-4206 (Online)**
Sch. Acad. J. Pharm., 2016; 5(6): 251-255 **ISSN 2347-9531 (Print)**
©Scholars Academic and Scientific Publisher
(An International Publisher for Academic and Scientific Resources)
www.saspublisher.com

Research Article

Event Monitoring in Patients Prescribed with Anti-tubercular Therapy

Vaishnavi Prasannan*[1], Dr. K.K Shyamala[2], Binai K Sankar[3], Saumya Sabu[1], Khalid P K[4]. Legimol Sunny[4]
[1]Pharm. D Intern, Department of Pharmacy Practice, Acharya & B. M Reddy College of Pharmacy, Bangalore, Karnataka, India
[2]Assistant professor, Department of Pulmonology, Dr. B R Ambedkar Medical College and Hospital, Bangalore, Karnataka, India
[3]Assistant Professor, Department of Pharmacy Practice, Acharya & B. M Reddy College of Pharmacy, Bangalore, Karnataka, India
[4]Third year Pharm.D student, Department of Pharmacy Practice, Acharya & B. M Reddy College of Pharmacy, Bangalore, Karnataka, India

***Corresponding author**
Vaishnavi Prasannan
Email: girijatampi@gmail.com

Abstract: Tuberculosis is a chronic, granulomatous infectious disease caused by Mycobacterium tuberculosis. Multi-drug resistance is a chronic problem associated with treatment of tuberculosis where a substantial proportion of tuberculosis cases reported in India are multi-drug resistant. Poor patient compliance plays a major role in development of resistance. The main objective of the study was to monitor the events associated with ATT in pulmonary and extra-pulmonary tuberculosis patients and to achieve better patient outcomes by regular monitoring. This was a prospective observational study which analysed patients diagnosed with pulmonary and extra-pulmonary kochs', attending inpatient and out-patient departments as well as registered under the RNTCP at Dr. B.R Ambedkar Medical College and Hospital for a period of 1 year for any events associated with ATT. Routine investigations which are carried out by the patient at the treatment initiation and whenever required were monitored. A total of 175 patients were monitored in the study out of which majority were males. Most patients were category 1 patients. More than one-third of the patient population reported an adverse event. Most ADRs were related to the GI system, followed by Skin Allergy. Most of the events (72%) were patient reported during physician visit while 26% were reported on investigation. The study found that ADRs has led to medication incompliance which leads them to discontinue the medication for a short duration. Close monitoring of these events from the treatment initiation should be emphasized to prevent medication in adherence. It is suggested that the establishment of pharmacovigilance programs in DOTS centres is essential.
Keywords: ATT, Anti-tubercular Therapy, Tuberculosis, Adverse Events.

INTRODUCTION

Tuberculosis is a chronic granulomatous infectious disease caused by a bacterium, *Mycobacterium tuberculosis*. India accounts for two-third of the world tuberculosis burden. A percentage of Indian population is diagnosed with tuberculosis in which a substantial percentage is multi drug resistant (MDR-TB) cases [1]. Tuberculosis (TB) remains a leading infectious killer globally. Left untreated or improperly treated, tuberculosis causes progressive tissue destruction and eventually, death [2]. Active disease is characterized by fever, chills, night sweats, weight loss, and changes on chest radiography. Several risk factors for tuberculosis have been identified, including immune suppression, exposure to close contacts, and smoking [3].

Drug treatment is the cornerstone for management of tuberculosis patients. In a patient with active tuberculosis, the overall treatment goals are to cure the individual patient and to minimize the transmission of *M. Tuberculosis* [2].The primary goals of chemotherapy are rapid bacterial killing, prevention of emergence of drug resistance, and elimination of persistent tubercle bacilli to prevent relapse. Effective treatment of tuberculosis requires a substantial period (minimum 6 months) of intensive drug therapy with at least two active bactericidal drugs [3].

The currently recommended anti-tuberculosis regimen /DOTS ($2H_3R_3Z3E_3+4H_3R_3$) is usually well tolerated. However, some patients may experience problems, usually due to the bulk of the medicines with a single day's dose consisting of 6-7 tablets [4]. Treatment-related side effects can be minor or major.

Therefore, rather than concentrating only on the treatment, the adverse effects of the drugs should also be looked upon for achieving better patient compliance. The first line drugs prescribed under Directly Observed treatment Short Course (DOTS) regimen are Isoniazid (H), Rifampicin(R), Pyrazinamide (Z), and Ethambutol (E) [5]. The commonly reported adverse effects during DOTS therapy are vomiting, peripheral neuropathy, nausea, hepatotoxicity, urine discolouration. Drug adverse effects leads to loss of patient compliance, thereby causing disease progression, transmission of infection and repeated default of treatment which results in development of MDR-TB and XDR-TB, decreased quality of life and decreased life expectancy. Patient compliance which is an important factor for better treatment outcome can also be lost due to pill burden and social stigma [1].

The DOTS strategy contains elements of adherence and compliance. The term "adherence" (or patient-centred compliance) refers to the extent to which patients follow a prescribed regimen. It implies a more active and collaborative involvement of patients working with health-care providers in managing their treatment. "Adherence" is currently preferred to "compliance" in medical literature as it portrays a more respectful and active role of the patient in disease management [6].

The World Health Organization defines a tubercular treatment defaulter as a patient whose treatment was interrupted for two consecutive months or more. As with HIV treatment, tubercular therapy requires high (> 90%) compliance to facilitate cure [7]. Good adherence results in high compliance and absence of treatment default2. Default rate is a crude approach to adherence monitoring, since it does not really reveal why the patient interrupted treatment for 2 or more consecutive months [6].

The side-effects profile of anti-tubercular therapy is more magnified in patients with concurrent HIV treatment and/or prior history of hepatitis, and those being treated with second-line drugs for multidrug-resistant tuberculosis, during which as many as 86% of patents may develop medication side-effects [8]. To minimize the adverse impact of medication side-effects in tuberculosis treatment adherence, it is important that tuberculosis health staff is adequately trained on their recognition and management. Such training should include how to provide concise pre-treatment counselling to patients on possible side-effects of treatment [9]. It is also important that medications for managing side-effects should be ordered concurrently with the ordering of anti-tubercular therapy to facilitate timely and adequate treatment of such side-effects [10].

MATERIALS AND METHODS

Ethical approval: The study was approved by the Ethics committee of Dr. B.R Ambedkar Medical College and Hospital, Bangalore.

Study Setting: The study was carried out in both inpatient and outpatient departments as well as in co-ordination with the RNTCP and DOTS centre of Dr. B.R Ambedkar Medical College and Hospital.

Inclusion and exclusion criteria: All tuberculosis patients who were above the age of 18 were included in the study. Pulmonary as well as extra-pulmonary tuberculosis patients of category I & II were included in the study. Patients who are willing to appear for an interview and laboratory investigations are included in the study. All the tuberculosis patients from both inpatient and out-patient wards who are less than 18 years of age are excluded from the study. Old tuberculosis cases who completed the treatment are excluded from the study.

Data collection

The relevant data required for the study were collected using self-designed patient profile forms. The data was collected by directly asking the patient, patient medication records, from nurses, physician and patients' bystanders followed by the written consent of the patient or the bystander after describing about the study. Data was collected regarding the socio-demographic profile of the patient, history of diabetes, hepatitis, chronic renal failure and alcohol consumption, course of treatment, height, weight, and HIV status in addition to of pregnancy or postpartum. The diagnosis was made either histologically or microbiologically, or improvements in the clinical status of the patients after completing a full course of treatment for tuberculosis as evaluated by their physician were also noted. Haematological tests were carried out at pathological laboratories. The side effects were recorded in the files of the patients. Basal levels of transaminases and bilirubin and a complete blood count were ordered for all tuberculosis patients prior to the onset of the anti-tubercular therapy in our hospital. Regular ward visits were carried out for the collection of data. DOTS centre was visited thrice in a week on alternate days for the relevant data and information. The data collected were documented in excel sheet.

RESULT

A total of 175 patients were included in the study, out of which 115 were category 1 tuberculosis patients and 60 were category II tuberculosis patients. Out of 175 patients, 66 (37%) patients were observed to have various adverse effects of ATT (Table No.1).

Table-1: Number of patients with ADRs

Total no. of patients	No. of patients		Percentage (%)
175	With ADRs	66	37.28
	Without ADRs	109	62.38

Majority of patients included were from IP department (108, 62%) and 67 (38%) were from OP department. (Table No.2)

Table-2: Distribution of patients in IP and OP departments

Department	No. of patients	Percentage (%)
IP	108	61.714
OP	67	34.85

In IP department, out of 108 patients, only 12 (11%) patients were reported to have ADRs. (Table No. 3)

Table-3: Number of Inpatients with ADR

IP	No. of patients	Percentage (%)
Patients with ADR	12	11.1
Patients without ADR	96	88.8

While 54(81%) patients out of 67 patients from OP department were found to have ADRs. (Table No.4)

Table-4: Number of Outpatients with ADR

OP	No. of patients	Percentage (%)
Patients with ADR	54	80.59
Patients without ADR	13	19.4

In category 1, out of 115 patients, 46 (40%) patients were observed to have ADRs. While out of 60 category II patients, 16 (27%) patients were observed to have various ADRs. (Table No.5)

Table-5: Distribution of Category 1 and Category II patients

Category	No. of patients	%	No. of patients with ADR	%	No. of patients without ADR	(%)
CAT 1	115	65.71	46	40	69	26.66
CAT II	60	34.28	16	60	44	73.33

In this study, it was found that most ADRs were related to the GI system(45%), followed by Skin Allergy(33%), generalised weakness(31%), arthralgia/ bone pain (24%), CNS disorders(21%), visual disturbances (15%), fever (10%), urine discoloration (8%), liver disorders (3%) and auditory disturbances(<1%). (Table No.6)

The majority of the patients were in 1-10 days of hospital stay (24). While least number of patients were in 111-140 (1) days. (Table No.7)

Table-6: Incidence of various ADRs

Disorders	No. of incidence	Percentage (%)
GI system	30	45.45455
Skin Allergy	22	33.33
Generalised weakness	21	31.81818
Arthralgia/bone pain	16	24.24242
CNS disorders	14	21.21212
Visual disturbances	10	15.15152
Fever	7	10.60606
Urine discoloration	5	7.575758
Liver disorders	2	3.030303
Auditory disturbances	1	-1.51515

Table-7: Distribution of hospital stay

Duration of hospital stay (days)	No. of patients
0-10	24
11-20	19
21-30	9
31-40	14
41-50	18
51-60	5
61-70	9
71-80	7
81-90	2
91-100	0
101-110	2
111-120	1
121-130	0

131-140	1

The majority of ADRs were in 1-10 days of hospital stay whereas no ADRs were found after 81 days of hospital stay. (Table No.8).

From this study, we observed that the patients werenon-compliant to their regular anti-tubercular medications due to the occurrence of adverse events.

It has also observed that the majority of ADRs (47, 71%) were reported during regular visits by asking to the patient. While 18(27%) were reported by the patients themselves. (Table No.9)

Table-8: Relationship between hospital stay and incidence of ADRs

Duration of hospital stay (days)	No. of ADRs
0-10	3
11-20	2
21-30	1
31-40	1
41-50	3
51-60	0
61-70	1
71-80	2
81-90	0
91-100	0
101-110	0
111-120	0
121-130	0
131-140	0

Table-9: Mode of ADR reporting

Reporting	No. of patients	Percentage (%)
Self-reported	18	27.27
Others	47	71.21

In our study we found that 2 patients had encountered with Type 1 hypersensitivity reaction one during the initiation of category 1 treatment and other during the initiation of category II treatment.

DISCUSSION

According to the recent statistics available, In India today, 2 deaths occur every 3 minutes from tuberculosis. Side effects associated with anti-tubercular drugs were encountered with different frequencies especially among patients hospitalized for pulmonary tuberculosis, and these patients should be followed up by closer monitoring for the related side effects for better treatment outcome. About 37% of our study population has been observed to have events of adverse reactions compared to the study conducted by Tak DK *et al.* [11] and the study conducted by Banu Eris-Gu¨lbay *et al.* [11,12]. The patients who were non-compliant to the medication were restarted on their treatment following their visits to the physician or during the regular visits of ward by the physician. Majority of the ADR occurred are associated with the GI system followed by skin allergy compared to the study conducted by Kumarjit Sinha, *et al.* [4]. It has been advised to include an awareness session regarding the disease condition, course of treatment, duration of treatment, medications and its adverse effects, life style modifications which helps the patient to recover in a better way and improve the treatment outcome. One-fourth of the patient population in the study has been reported with the incidence of arthralgia/bonepain during the initial intensive phase of treatment. It has been suggested to include uric acid level examination in the routine haematological examination since pyrazinamide can cause non-gouty arthralgia during the initial intensive phase of treatment. Spontaneous reporting of the adverse events of anti-tuberculosis drugs can reduce the severity of the condition and helps in better recovery of the patient. It is also observed that Type 1 hypersensitivity reactions can be encountered at any time during the treatment course. The main limitation of our study is that it is a single centred study. In contrast to multiple published studies [12-14], there was no increased risk of hepatotoxicity among elderly patients in this present study.

CONCLUSION

In our study we found that the patient reported adverse events were less than during the physician visit which is considered as an important factor contributing to the in adherence to the treatment. Most of the adverse events reported during the intensive phase are frequent arthralgic symptoms. So it is also suggested for uric acid examination in the intensive phase. It is

recommended that pharmacovigilance should be established at DOTS centres. The author also recommends a checklist with various adverse events should be should be provided and educated to each and every patient for better treatment outcome and should be implemented in RNTCP program.

REFERENCES

1. Surendra KS, Alladi M; Tuberculosis.Second edition.new Delhi:Jaypee publishers, 2009.
2. Dipiro TJ, Talbert LR, Yee CG, Matzke RG, Wells GB, Posey ML; Pharmacotherapy a pathophysiologic approach. Seventh edition.United States. The McGraw-Hill Companies, 2008.
3. Alldredge KB, Corelli LR, Ernst EM, Guglielmo JB, Jacobson AP, Kradjan AW et al.; Applied Therapeutics clinical use of drugs. Tenth edition. Philadelphia. Lippincitt Williams & Wilkins, 2013.
4. Singh KA, Pant N; Adverse effects of first line antitubercular medicines on patients taking directly observed treatment short course: A hospital based study. International Journal of Medicine and Public Health; 2014; 4(4):354-358.
5. Sivaraj R, Umarani S, Parasuraman S, Muralidhar P; Revised National Tuberculosis Control Program regimens with and without directly observed treatment, short-course: A comparative study of therapeutic cure rate and adverse reactions. Perspectives In Clinical Research, 2014; 5(1):16-19.
6. Awofeso N; Anti-tuberculosis medication side-effects constitute major factor for poor adherence to tuberculosis treatment. Bulletin of the World Health Organization, 2008; 83(3): B-D.
7. Sri Sathya; Textbook of Pulmonary and Extrapulmonary Tuberculosis. Fourth edition. New Delhi: Mehta Publishers; revised, 2001
8. Sinha K, MarakR TI, Singh AW; Adverse drug reactions in tuberculosis patients due to directly observed treatment strategy therapy: Experience at an outpatient clinic of a teaching hospital in the city of Imphal, Manipur, India. The Journal of Association of Chest Physicians, 2013; 1(2):50-53.
9. Kashyap KA, Whig J, Gupta D, Joshi S; Clinical Outcome Of Patients Of Tuberculosis Under Directly Observed Treatment Short Course In A Tertiary Care Centre In Ludhiana India. CHEST Journal, 2009; 136(4).
10. Verma R, Mahor Gr, Shrivastava KA, Pathak P; Adverse drug reactions associated with first-line anti-tubercular drugs in a tertiary care hospital of central India: a study of clinical presentations, causality, and severity. Asian Journal of Pharmaceutical and Clinical Research, 2014; 7(5):
11. Tak DK, Acharya LD, Gowrinath K, Rao PGM, Subish P; Safety Evaluation of Antitubercular Therapy under Revised National Tuberculosis Control Programme in India. Journal of Clinical and Diagnostic Research, 2009; 3:1395-1401.
12. Gu¨lbay EB, Gu¨rkan UO, Yıldız AO, O¨nen PZ, Erkekol OF, AyseBac-c-ıog˘lu, Acıcan T; Side effects due to primary antituberculosis drugs during the initial phase of therapy in 1149 hospitalized patients for tuberculosis. Respiratory Medicine, 2006; 100:1834–1842.
13. Athira B, Manju CS, Jyothi E; A study on adverse drug reactions to first line antitubercular drugs in DOTS therapy. International Journal of Pharmacology and Clinical Sciences, 2015; 4(1): 7-11.
14. YEW WW, Leung ACC; Antituberculosis drugs and hepatotoxicity. Respirology, 2006; 11: 699–707.