Adverse drug reactions impact on DOTS therapy courses in tuberculosis patients at bidar institute of medical sciences

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Abstract

Introduction: ADRs are one of the major causative factors for increased morbidity and mortality rate in human healthcare. Monitoring adverse drug reaction in tuberculosis patients is not done properly by the healthcare professionals owing to lack of awareness.

Materials and Methods: About 100 TB diagnosed patients were selected for the study at Bidar Institute of Medical sciences. Based on the prospective observational study method the cases were divided into before and after anti-TB therapy under DOTS course. Several lab examinations were conducted for the patients after the treatment. The severity of ADRs were recorded.

Results: After the study we observed about 57% of mild ADR, 31% of moderate ADR and 12% severe ADRs were noted in the patients who are under DOTS therapy in RNTCP unit. The results obtained from this study showed that when compared to female patients, ADRs faced by male patients are of high percentage.

Conclusions: There is increasing evidence from preclinical and clinical studies supporting the adverse effects of anti-TB therapy, but further mechanistic and experimental studies are required to establish the dose–response relationships and safety profiles of these kind of therapeutic medicines.

Keywords: Adverse drug reactions, DOTS, Tuberculosis, Pharmacovigilance.

Introduction

Adverse Drug Reactions (ADRs), the major worldwide clinical and public health problem reporting to regulatory authorities to activate drug safety surveillance and regulation. This paper provides the reports about ADRs of DOTS therapy in Tuberculosis (TB) patients.[1]

TB (Tuberculosis) is the most lethal communicable disease caused by the bacterium *Mycobacterium tuberculosis*. TB affects primarily the lungs which is termed as pulmonary tuberculosis [PTB] and secondarily it also affects other body sites which termed as extra- pulmonary tuberculosis [EPTB].[2] This accounts for leading cause of worldwide deaths and concerns a major global health problem. In 2017 Global TB report evidenced that 10.4 million TB incident cases and 1.4 million global deaths were reported. In India 28,00,000 TB incidents were recorded which accounts for increased morbidity and mortality rates in 2017.[3]

The major aims of treatment tragedy which includes patient cure ensure adequate life style and efficiency in order to prevent death from active TB or its delayed lethal effects, relapse prevention, transmission diminution and prevention of drug resistance development and transmission.[3] The first line drugs were used currently for the treatment of newly diagnosed TB cases which includes isoniazid (H), rifampicin (R), ethambutol (E) and pyrazinamide (Z) for 6-9 months. DOTS (Directly Observed Treatment Short course) was launched by WHO in 1995, which is a combination of drugs such as H, R, E and Z were required to take by the patients continuously throughout the designated period based on their body weight, India also practiced the same. Anti-TB drugs were supplied as separate drug regimen or fixed dose combination (FDC) in India.[4]

Even though multidrug regimens have positive therapeutic action, various findings suggest that the consumption of these drugs can cause adverse drug reactions (ADRs). ADRs contribute drastic changes in the drug regimen resulted in declining activity of drug which is used for treatment and occasionally more toxic, significant increase in cost of treatment and substantial raise in home visit numbers, outpatient visits as well as hospitalization. The patient may interrupt or abandon the treatment, resulting in increased rate of treatment failure as well as acquired resistance and increased TB cases very rarely deaths.[5] From the above literature review, the present study was aimed to find out the summary of ADRs at Bidar Institute of Medical Sciences due to DOTS therapy.

Materials and Methods

Participants in the Observational Analysis

Prospective observational analysis was carried out at RNTCP unit, in Bidar Institute of Medical Sciences in the year 2019. After getting approval from institutional ethical committee, about 100 successive diagnosed TB patients were selected for this study. Selection based on irrespective of age, sex as well as race of the patients. Patient who receive treatment for other illness and HIV positive cases were excluded from our study. Culture, sputum test and chest X-rays were performed periodically for the assessment of treatment tragedy. Moreover, adverse drug reactions (ADRs) were monitored and promptly managed during the entire path of the treatment.

Data Collection and Study Variables

Patients were divided into before and after anti-TB therapy under DOTS course. Several lab examinations were

conducted for the patients after the treatment. Participants recruited completes the baseline questionnaire before Anti-Tb treatment and undergo various laboratory assessments which includes routine blood test (CBC), routine urine test (pH value, uric acid and protein content, WBC, RBC), renal and liver function test and HBsAg test. Same parameters were measured again after two months in the follow up period after initiation of Anti-TB treatment. If TB patients had any discomfort or adverse effects during treatment period, ADRS severity was noted and reported to the medical college outpatient clinic. Based on the seriousness of the ADR in patients, adjust their DOTS and/or receive symptomatic therapies.

Morimoto and co-workers[6] classified the ADRs severity which ranges from mild, moderate and severe. Mild ADRs is a self-limiting mild reactions which are able to resolve at certain time without treatment and did not contribute to prolongation length of stay, moderate ADRs requires therapeutic intervention and hospitalization prolonged by 1 day but resolved in <24 h or change in drug therapy or specific treatment to prevent a further outcome and severe ADRs were life-threatening, producing disability and prolonged hospital stay or led to hospitalization, required intensive medical care, or led to the death of the patients.[7]

Statistics
The clinical data were collected through questionnaires and medical records by trained health workers. For assessing the associated factors in the development of ADRS among patients and TB treatment outcomes in patients who developed ADRS, the Chi-squared test was used. Significance level was set as $p<0.05$ for all statistical tests performed.

Results
Demographic and Clinical Characteristics of Patients
Totally 100 patients were diagnosed TB newly at Bidar Institute of Medical Sciences. Based on the exclusion criteria 62 male and 38 female cases were enrolled in the current study.

Demographic and clinical variables of cases were comparable between before and after anti-TB treatment were depicted in figure1. All patients were ranged from age of 15-65 years. Most cases of this study (35.1%) were the range of 31-40 years of age, whereas 21.27% of cases range from 41-50 years of age, 51-60 years aged cases contributes 15.95%, 12.76% of patients were in range of 21-30 years, 8.5% of cases were reported to above the age of 60 years, whereas >20 years age group contributes 6.38% in total cases. This differences of ADRs in different age groups were statistically significant (P < 0.001). When compared to female cases (38%), male patients (62%) have majorly experienced the ADRs which is statistically significant at p< 0.001.

Types and incidence of ADRs detected and represented in table 1. At least one ADR was experienced by total of 100 patients. Most commonly encountered ADR was gastrointestinal problems (28.0%), generalised weakness

(24%), liver dysfunction (12%), allergic reactions (11%), neurological symptoms (5%) and fever (20%).

Mild ADRs which includes gastrointestinal symptoms, general weakness, neurologic symptomswere detected for 57% of the patients, moderate ADRs which includes (allergy and fever) were detected for 31% of the patient, severe ADRs includes liver dysfunction were detected for 12%, the result were shown in Fig. 2.
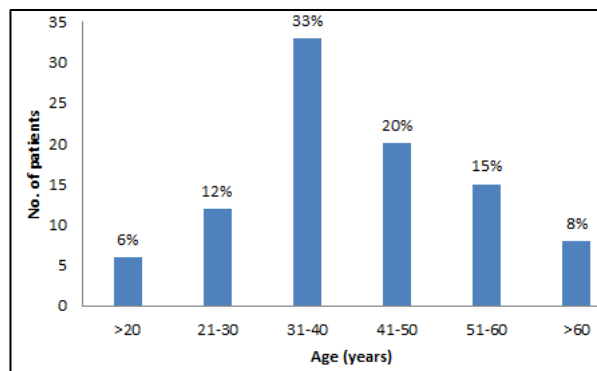

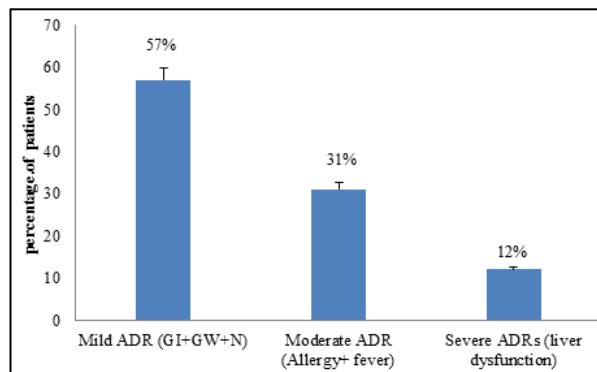**Fig. 1:** Age wise distribution of TB patients

Fig. 2: This figure depicts the ADRs incidence in TB patients after DOTS course

Table 1: ADRs of anti-TB therapy

ADRs	Number of patients
GI related ADRs (anorexia, vomiting, nausea)	28
Generalised weakness	24
Liver dysfunction	12
Allergic reactions	11
Neurological symptoms	5
Fever	20

Discussion
Tuberculosis (TB) is a most important public health problem and the incidence was raised continuously through the world. Currently treatment with the drug is the only effective treatment tragedy but medication adherence was affected by ADRs. In order to explore the risk factors associated with the increased development of ADEs/ADRs and to diminish their incidence, the number of drug-resistant TB patients and anti-TB drugs has increased.[8]

The present study was designed to find out the anti-TB drug ADRs in TB patients at BIDAR hospital upon DOTS therapy. The findings from the study suggest that males constitute the major population than females. Drug addiction, alcoholism and smoking are the major causative factors in males to get TB compared to females and also males have more social activities and visit public places more often. Due to involvement of bad activities such as smoking, use of tobacco products, high alcohol intake, 31-40 years and 21-30 years aged group cases have been found increased prevalence of TB, because these activities deteriorate the immune system.[9]

Anti-TB therapy consist regimen of isoniazid, rifampicin, ethambutol and pyrazinamide for active tuberculosis. This treatment tragedy coupled with significant ADRs which can make the successful treatment of active TB in patients with drug-sensitive disease a challenge[9].Common ADRs reported from field trials of first-line anti-tuberculosis drugs include skin rash, hepatitis, nausea/vomiting, thrombo-cytopenia, influenza-like illness, arthralgia and neuro-psychiatric symptoms.[8]An ADR can result in significant morbidity, leading to the withdrawal of first-line medication and its substitution with a less effective and often more poorly tolerated second-line medication.[10]

Only those ADRs that were considered to be major events were included in the data analysis defined as a moderate or severe reaction that was definitely, probably or possibly associated with the TB medications according to the criteria. ADR remains problematic during the DOTS treatment course of TB patients[11]. Neuropsychiatric reactions, as expected, were representative of adverse effects of anti-TB drugs, since its central active mechanism as a partial NMDA-agonist and high brain–blood barrier permeability.[12] TB patients treated with pyrazinamide commonly affected by gastrointestinal symptoms like nausea, vomiting and anorexia. Anti-TB drugs cause hepatitis, this might be due to liver hypersensitive mechanism to drugs that are intrinsically hepatotoxic or liver might not able to metabolize the toxic substances produced by the drug.[13]

PZA, RFP and INH are the commonly used anti-TB drugs, which responsible for GI discomfort in most of the cases. Above 73.24% of the ADRs were reported to produce only mild reaction, whereas severe reactions like hepatic tissue dysfunction were caused by 15.49%. the results obtained from the present investigation we found that, about 57% mild ADRs were recorded in 31-40 years age group cases, 13% of moderate ADRs were found in 21-30 years age group patients and severe ADRs (12%) were recorded in other age groups.

Conclusion

Awareness needs to be created among the medical doctor's treating the TB patients for timely recognition and treatment of ADR with minimum modification of treatment regimen.

Equal attention should be showed during DOTS therapy without ADR cases to raise over all cure rate.

Conflict of Interest: None.

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