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Original Research Article

Incidence of adverse drug reactions in patients taking anti-tuberculosis treatment

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ABSTRACT

Background: High incidence of infection has caused a large number of morbidity and mortality which is partly due to serious adverse reactions induced by Anti-Tuberculosis (Anti-TB) drugs. In present prospective study an attempt is made to estimate the incidence and risk factor for ADRs among patients treated for tuberculosis.
Methods: All the new patients starting their treatment with selected six DOT center were enrolled in study. All patient's complete clinical history was recorded. They were followed regularly for occurrence of ADR till end of their treatment.
Results: Total of 108 patients (67 male and 41 female) had taken and completed their treatment during the study period (March 2007 - April 2008) and were observed for occurrence of ADR during their treatment period. Out of total108, 28 patients (25.9%) experienced one of the ADR, out of 28 patients, 12 (42.85%) patients developed GIT intolerance, and hepatitis was seen in 8 (28.57%) patients, while 4 (14.48%) patients developed skin reactions. Only 3 (7.14%) patient developed dizziness and loss of balance, which was relieved by reduction of dose of streptomycin.
Conclusions: With close monitoring and on time action, RNTCP DOTs regimens can be safely and successfully administrated.

Keywords: Adverse drug reaction, Directly observed treatment, Revised National Tuberculosis Control Program, Tuberculosis

INTRODUCTION

Tuberculosis has been one of the common diseases in human communities during the past 40 years. High incidence of infection has caused a large number of morbidity and mortality which is partly due to serious adverse reactions induced by Anti-Tuberculosis (Anti-TB) drugs.[1,2]

The frequency and nature of Anti-TB drugs induced adverse drug reactions (ADRs) have been the matter of concern in many communities. One of the serious ADR detected in these studies is hepatotoxicity. There are differences in reported rate of hepatotoxicity induced by Anti-TB drugs in different studies.[3-5] This reaction could be affected by the genotype of patients receiving these drugs e.g. rapid-acetylator patients are more susceptible for isoniazid induced hepatotoxicity. Studies show that the risk of hepatotoxicity in patients from India is higher than those reported in West (11.5% versus 4.3%).[6] Regarding the difference reported between Asian and Western people in developing Anti-TB induced hepatotoxicity, it is necessary to detect the rate of Anti-TB drugs induced ADRs with emphasis on hepatotoxic reactions in patients, since it could be helpful to revise the therapeutic protocols.

In present prospective study an attempt is made to estimate the incidence and risk factor for ADRs among patients treated for tuberculosis.

METHODS

It was cohort study conducted between periods of 1st march 2007 to 30th April 2008 in Jamnagar district of Gujarat state covering urban population of Jamnagar city, all enrolled patient were followed up every 15 days by investigator from start to end of their Tuberculosis treatment for actively recording occurrence of any adverse drug reaction. All incidence adverse drug reaction was recorded in case record form adopted from WHO Adverse drug reaction monitoring form

Study Population: Total population of Jamnagar city is 5, 29,308 at the time of study, city has one TB control unit (TU) ,20 designated Microscopic Centres(DMC) and 2 general hospital out of which one attached with medical college. Total number of new patients registered during study period was 1027 in TB control unit of city

Sampling method: For achieving ideal sample of population representing all geographic and socioeconomic class city was divided in 6 major region and 6 DOT Provider with highest turnover in that region was selected. All new patients starting treatment for tuberculosis and assigned to these 6 DOT providers were enrolled in the study. Total of 119 patient were registered for study from start of their treatment. Out of which 108 patients completed the treatment in study period with study criteria

Each patient's complete clinical history was recorded. They were followed regularly for occurrence of ADR till end of their treatment. All suspected ADRs were initially assessed by the consultants and subsequently the information was analysed by pharmacologists. Detailed clinical and drug history and relevant information about the suspected reaction, its onset, duration, temporal association with drug intake if any, concomitant drug therapy, past history ,history of other risk factors, reports of relevant laboratory investigations undertaken to arrive at the clinical diagnosis were recorded in an ADR reporting form . The reactions were later categorized, and causality assessment was done according to WHO criteria for causality assessment of adverse drug reaction.[7]

Inclusion criteria

- All new patients starting their treatment with selected 6 DOT centers.
- Patients of all age and sex.
- Patients of any of three tuberculosis category.
- Patients with known risk factor like alcoholism or past history of liver disease.

Exclusion criteria

- Those patients who migrate from selected DOT center to another center.
- Patient not completing treatment till the end of study.
- Patients leaving treatment in between for a reason other than ADR.
- Patients not attending follow up visit regularly.

Statistical analysis

Data generated was entered in MS-Excel spreadsheet, incidence rate was analysed in MS-Excel and the correlation between BMI and the ADR occurrence was analysed using Fisher's exact test in Epi info version 3.5.1.

RESULTS

A total of 108 patients have taken and completed their treatment during the study period (March 2007 - October 2008) and were observed for occurrence of ADR during their treatment period. Demographic and other characteristics of the enrolled patients (Table 1).

Table 1: Demographic data of the patients.

	Total no of patients	No of patients with ADR
Age (years)		
11-20	8	1
21-30	44	15
31-40	37	5
41-50	15	5
>50	4	2
Sex		
Male	67	19
Female	41	9
BMI		
≤18.5	77	26
18.6 - 24.9	30	2
≥25	1	0
Category		
I	58	13
II	28	10
III	22	5

Summary of adverse drug reactions to patients on anti-TB drugs is shown in (Table 2). Out of 8 serious ADR only 3 required hospitalization and none of them required change in regimen (Table 2).

In present study malnutrition was the most common risk factor present. The occurrence of ADR was more in the malnourished group (BMI <18.5) and it was statistically significant (Fisher's exact test) (Table 3).

Alcoholism was present in 10.18% patients. In present study, majority of ADR cases 13 (46.42%) were noted in category I, followed by category II (35.71%) and category III (17.85%). 13 (22.41%) patients out of 58 under category I in study developed ADR, while 10 (35.71%) out of 28 patients under category II developed

ADR and only 5 (22.72%) patients from 22 patients under category III developed ADR.

Table 2: Types and number of patients with adverse drug reactions.

ADR incidence		no of patient with ADR
	Present	28
	Absent	80
Type of ADRs		
	GIT intolerance	12
	hepatitis	8
	skin	4
	peripheral neuropathy	1
	Vestibular	3
Time of appearance of ADR		
(Days)	0 - 10	12
	11 - 20	6
	21-30	4
	31-40	1
	41-50	2
	51-60	1
	61-70	
	71-80	1
	81-90	1
	>91	
Severity		
	Trivial	20
	Serious	8
Causality*		
	Definitive	3
	probable	9
	possible	16

*According to WHO Causality assessment[7]

Table 3: BMI and Incidence of ADRs.

Body Mass Index	Adverse reaction present	Adverse reaction absent	Total
BMI ≤18.5	26*	49	77
BMI ≥18.5	2*	29	31
Total	28	80	108

*Fisher exact test p=0.0031(95% CI)

Out of 8 patients of hepatitis, 5 patients were alcoholic, and one patient had viral hepatitis, 1 patient with peripheral neuropathy was alcoholic.

DISCUSSION

In present study, incidence of total adverse drug reaction was 25.93% as compared to 53% and 11% in two previous studies.[8,9]

Most common adverse effect observed was GIT intolerance, same was observed in one of the previous study.[8] Incidence of hepatitis observed among total adverse reaction was 28.57% in present study where as it was 25.9% and 27% in previous studies.[8,9] Although 3.5% had peripheral neuropathy in present study. This is comparable to 6.2% in previous study.[8] Frequency of dizziness and loss of balance (Vestibular type of ADR) was found in 7.14% of patients with ADR as compared to 8% in previous study.[8]

In present study only 12.5% patients from 11-20 years age group developed ADR to treatment regimen compared to 45% in reference study.[8] While 34.09% patients from 21-30 years age group developed ADR as compared to 29% in previous study.[8] 13.51% patients from 31-40 years age group developed ADR in present study as compared to 30% in reference study.[8] In present study 33.33% patients from 41-50 years age group developed ADR as compared to 48% in reference study, while all (50%) patients above 50 years of age developed ADR as compared to 80% in reference study.[8]

In present study 21.95% female patients and 20.35% male patients developed ADR as compared to 23% females and 21% males in reference study.[8]

Majority (42.85%) of ADR were detected in first 10 days of treatment, which is comparable to 69.6% in reference study.[8] Incidence of ADRs was highest in first 10 days of drug therapy and lowest in continuation phase of drug therapy.

Most important coexisting risk factor for ADRs was malnutrition (71.29%), which was not compared in previous studies. Other risk factors where alcohol (10%) and age>50 (3.7%) as compared to 17% and 20% in previous study.[9]

In present study 10.71% ADR was reported definite, about 32% were probable and 57% were possible according to WHO scale. In past study done by Gholami in Iran in 2006 had found rates of 8.6%, 48.2%, and 43.2% of definite, probable and possible respectively. That study had used naranjo's probability scale. But this scale lacks validity in assessment of adverse reaction leading to liver injury.[10]

CONCLUSION

Most of the patients were from socioeconomically productive age group and most had undernourished status by body mass index (BMI) parameter. Prevalence of malnutrition in studied group was high independently it had significant ADR precipitating effect. Patients with risk factors, like malnutrition should be under strict supervision for ADR. Most ADR occurred in initial treatment phase, so intensive periodical follow-up of all patients during intensive phase will facilitate early reorganization of ADR and their appropriate

management, which enhances patient-compliance and faith in revised national tuberculosis control programme (RNTCP) and thereby overall acceptance and success of RNTCP.

With close monitoring and on time action, RNTCP DOTs regimens can be safely and successfully administrated.

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REFERENCES

1. Burman WJ, Reves RR. Hepatotoxicity from rifampin plus pyrazinamide: lessons for policymakers and messages for care providers. Am J Respiratory Crit Care Med. 2001 Oct 1;164(7):1112-3.
2. Kopanoff DE, Snider Jr DE, Caras GJ. Isoniazid-related hepatitis: a US Public Health Service cooperative surveillance study. Am Rev Respiratory Dis. 1978 Jun;117(6):991-1001.
3. British T. Short-course chemotherapy in pulmonary tuberculosis. Lancet. 1975:119-24.
4. Taneja DP, Kaur D. Study on hepatotoxicity and other side-effects of antituberculosis drugs. J Ind Medica Assoc. 1990 Oct;88(10):278-80.
5. Snider JD, Long MW, Cross FS, Farer LS. Six-months isoniazid-rifampin therapy for pulmonary tuberculosis. Report of a United States Public Health Service Cooperative Trial. Am Rev Respiratory Dis. 1984 Apr;129(4):573-9.
6. Sharma SK, Balamurugan A, Saha PK, Pandey RM, Mehra NK. Evaluation of clinical and immunogenetic risk factors for the development of hepatotoxicity during antituberculosis treatment. Am J Respiratory Crit Care Med. 2002 Oct 1;166(7):916-9.
7. Causality Assessment Scale of Suspected Adverse Reactions. Available at: https://www.who.int areas. Accessed on 18th November 2019.
8. Gholami K, Kamali E, Hajiabdolbaghi M, Shalviri G. Evaluation of anti-tuberculosis induced adverse reactions in hospitalized patients. Pharma Prac. 2006 Jul;4(3):134-8.
9. Yee D, Valiquette C, Pelletier M, Parisien I, Rocher I, Menzies D. Incidence of serious side effects from first-line antituberculosis drugs among patients treated for active tuberculosis. Am J Respiratory Crit Care Med. 2003 Jun 1;167(11):1472-7.
10. Garcia-Cortes M, Lucena MI, Pachkoria K, Borraz Y, Hidalgo R, Andrade RJ, et al. Evaluation of naranjo adverse drug reactions probability scale in causality assessment of drug-induced liver injury. Alimentary pharmacol ther. 2008 May;27(9):780-9.

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