ORIGINAL RESEARCH PAPER | MEDICAL SCIENCE | Volume : 6 | Issue : 7 | July 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

Incidence of Adverse Drug Reaction Among the Tuberculosis Patients Treated Under Directly Observed Treatment Short course (DOTS) Regimen in North India

KEYWORDS: Adverse Drug Reaction, Antituberculous Drug, DOTS

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ABSTRACT *Objective: Adverse drug reactions (ADR) in anti-tuberculous drugs act as an important factor for treatment failure. The present observational study was undertaken to demonstrate the extent of adverse effects of anti-tuberculosis drug used in category 1st category 2nd and category 3rd, treatment regimens under DOTS and impact of these adverse drug reaction on the clinical outcome of treatment.*

Materials and Methods: A total of 196 patients between with tuberculosis (TB), who were treated under DOTS in category 1st, 2nd, and 3rd were included in the study. Two consecutive sputum smear examination and culture were performed for the diagnosis of pulmonary TB. Further investigation like X-ray chest PA view was also done for the confirmation of pulmonary TB.

Result: Out of 196 patients 82(42%) were developed ADR. In females higher incidence (47.5%) of adverse drug reactions were observed. Among different categories the higher number of adverse drug reactions were observed in category 2. In all the categories the maximum numbers of incidence of ADR were noted in gastro intestinal tract (GIT)

Conclusion: Female as well as patient with category two is more prone to develop ADR. So physician should take proper care while treating these patients to prevent gastrointestinal discomfort which is more common.

Introduction

Tuberculosis remains a major social and economical burden in the developing country like India. According to the World Health Organization (WHO), one–third of the world's population have been exposed to the tuberculosis pathogen.[1] Treated tuberculosis has a mortality rate of less than 5% in developing countries.[2] Adverse Drug Reactions (ADR) have potential to further complicate the issue of poor treatment compliance. To overcome these issues, Government of India in association with WHO and Swedish International Development Agency (SIDA), launched Revised National Tuberculosis Control Programme (RNTCP).[3]

This is well known that all drugs are able to produce adverse drug reactions and when we prescribe drugs to the patient, we take a risk of inducing adverse drug reactions. The incidence of developing adverse drug reactions is 10-25% documented in different clinical settings and they are more common with multiple drug therapy for a long duration. The present observational study was undertaken to demonstrate the extent of adverse effects of anti-tuberculosis drug used in category 1st category 2nd and category 3rd, treatment regimens under Directly Observed Treatment Short-Course(DOTS) and impact of these adverse drug reaction on the outcome of treatment.

Materials and Method

Patients and Settings:

The present study was carried out at the Department of Pharmacology and the Microbiology cum DOTS centre in a North Indian teaching hospital for the period of 2 years. After obtaining the permission from the ethical committee 196 patient between the ages of 5 and 80 years with tuberculosis, who were treated under DOTS in category 1st, 2nd, and 3rd were included in the study. Individuals with multi drug resistant tuberculosis (MDR) and extended drug resistant tuberculosis (XDR), previously existing severe disease, history of recurrent psychotic or major affective disorder, alcohol or drug abuse within the previous year or current cardiac, renal or hepatic dysfunction, women who were pregnant, lactating, or planning to become pregnant were excluded from study.

Clinical Details:

Identification and Isolation of Patient

Two consecutive sputum smear examination and culture were performed for the diagnosis of pulmonary tuberculosis. Further investigation like X-ray chest PA view was also done for the confirmation of pulmonary tuberculosis.

The clinical details of the patient were documented in a standard performa. Duration of treatment was categorised as per following groups; 6 months for category 1st and 3rd and 8 months for category 2nd. Patients were clinically evaluated and examined for their response on every month and advised to visit any time if develops any severe problems during treatment were documented. The presence of symptoms suggestive of adverse drug reactions and as well as their severity like mild, moderate and severe were documented.

Statistical Analysis

Statistical analysis was based on intent to treat (ITT) population, which included all patients who received various regimens of DOTS under RNTCP. Study variables were summarized by descriptive statistics. Proportions were ex-

Volume : 6 | Issue : 7 | July 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

pressed as percentages; for continuous variables. Ranges were used with means and standard deviations as appropriate. Chi-square test was used to compare categorical data.

Result

A total of 196 patients with tuberculosis were examined to assess the development of ADRS after the treatment. Out of 196 patients 117 were come under category 1, 36 in category 2 and 43 in category 3. Of the 196 patient 133 were male while 63 were females with the age group of 05-20= 49, 20-35= 82, 35-50= 40 and 50-80= 25. Under category1; 84(63.16%) were male and 33(52.38%) were female. Under category 2; 23(17.29%) were male and 13(20.63%) were female and under category 3; 26(19.55%) were male and 17(26.98%) were female. In category 1; maximum number of patients were 48 (41%) with age group 20-35 years, followed by 28(24%) with age group 05-20years, 26(22%) with age group 35-50 years and 15(13%) with age group 50-80 years respectively. In category 2 maximum number of patients were 17 (47%) with age group 20-35 years, followed by 07(19%) with age group 50-80 years, 06 (16%) with age group 35-50 years and 06 (16 %) with age group 05-20 years respectively. In category 3 maximum number of patients were 17 (39%) with age group 20-35 years, followed by 15(35%) with age group 05-20 years, 08 (18%) with age group 35-50 years and 03 (07 %) with age group 50-80 years respectively. Out of 196 patients 82(42%) were developed ADR. In females higher incidence (47.5%) of adverse drug reactions were observed. Among different categories the higher number of adverse drug reactions were observed in category 2. The details of adverse drug reactions among the different age groups, time periods of the treatment and patient's socioeconomically group are summarized in table 1.

Category of Patients	Patients with ADRS (N=82)
Category I (n= 117)	44 (37.5%)
Category II (n= 36)	23 (64%)
Category III (n= 43)	15 (35%)
Sex	
Male (n= 133)	52 (39%)
Female (n= 63)	30 (47.5%)
Age Group	
05 – 20 (n= 49)	46 (94%)
20 – 35 (n= 82)	37(45%)
35 – 50 (n= 40)	14(35%)
50 – 80 (n=25)	15 (60%)
Time Period	
1ST month (n= 196)	43 (21%)
2nd month (n= 196)	20 (10%)
3rd month (n= 196)	09 (4.5%)
4th month (n= 196)	07 (3.5%)
5th month (n= 196)	03 (1.5%)
Socioeconomic Groups	
I (n= 21)	08 (38.1%)
II (n=32)	12 (37.5%)
III (n=29)	10 (34.4%)
IV (n=53)	22 (41.5%)
V (n=61)	30 (49.1%)

In all the categories the maximum numbers of incidence of ADR were noted in Gastro Intestinal Tract (GIT). Different types of ADRs developed among the categories are summarized in table 2.

Type of ADRs	Cat.1st (117)	%	Cat. 2nd (36)	%	Cat. 3rd (43)	%
Mild gastritis	37	31.62	9	25.00	7	16.27
Sever gastritis	13	11.11	5	13.89	4	9.30
CNS	6	5.12	4	11.11	2	4.65
PNS	6	5.12	3	8.33	1	2.32
Hepatitis	9	7.69	2	5.55	3	6.93
Renal	1	0.86	2	5.55	0	0
Itching	4	3.41	1	2.76	3	6.93
Otologic	1	0.86	3	8.33	1	2.32
Occular	2	1.76	1	2.76	1	2.32
Joint pain	7	5.98	2	5.55	4	9.30
Psychiatric	5	4.27	2	5.55	1	2.32

On analysis of the outcome of the patient, we found 40 (25%) patients with ADRs were recovered with proper antibiotic therapy however the mortality rate was significantly low (1.53%). Details of the outcome of the treatment among the patient with ADRs are summarized in table 3

Outcome of treatment	Patients with ADRs	%
Improved	40	20.40
Treatment continue	12	6.12
Treatment failure	1	0.51
Lost to follow up	11	5.61
Alteration in therapy	9	4.59
Stop therapy	6	3.06
Expired	3	1.53
Total	82	41.83

Discussion

Compliance with anti-TB medication is essential to effective management. Two strategies to en-sure compliance are DOTS and fixed dose combination (FDC)[4]. Our study fully applied on DOTS strategy. Generally these drugs are well tolerated[5], may be associated with unwanted effects of different origin.

In our study, the incidence of ADRs was 41.83%. However several studies from other part of the world reported higher incidence of ADR among their study population.[6, 7] In contradiction to those findings, our study reported a lower rate of ADRs, However lower incidence of ADRs also reported from different part of the world [8, 9] which is lesser than our findings. This discrepancy may be due to geographical and physical factor of the population.

We are not the first to observe that females are at higher risk of developing ADRs. Several other studies also reported the higher prevalence of ADR among the female patient.[10, 11] The reason behind that they pass through different life stages like pregnancy, menarche etc., which modify the drug response.[12] Based on those findings we can suggest that female patients need special precautions while prescribing antituberculous drugs.

In the present study the incidence of ADR were significantly higher in gastrointestinal tract however incidence of ADR were low in excretory tract which indicates that gastrointestinal tract is more affected due to ADR in compare to other system.[13]

We also observed 1 in 4 patients with ADR were recovered with proper antibiotic treatment however mortality rate was significantly lower in the study population.On analysis of

Volume : 6 | Issue : 7 | July 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

the category based distribution we observed in category 1, 1 in 3 patients were female, in category 2, 1 in 2 patients were female and in category 3, 1 in 2 patients were female.

On category based distribution we also observed in category 1, 1 in 4 patients were with age group 05-20 years, 1 in 2 with age group 20-35 years, 1 in 4 patients with age group 35-50 years and 1 in 8 with age group 50-80 years. In category 2, 1 in 6 patients were with age group 05-20 years, 1 in 2 with age group 20-35years, 1 in 6 patients with age group 35-50 years and 1 in 5 with age group 50-80 years. In category 3, 1 in 3 patients were with age group 05-20 years, 1 in 2 with age group 20-35 years, 1 in 5 patients with age group 35-50 years and 1 in 14 with age group 50-80 years.

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