ORIGINAL RESEARCH PAPER

Pharmacology

PATTERN OF ADVERSE DRUG REACTIONS OF ANTI-TUBERCULAR DRUGS IN TERTIARY CARE HOSPITAL

KEY WORDS: Adverse drug reactions, anti-tubercular drugs, pyrazinamide, tuberculosis.

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ABSTRACT

Aim: The aim of this study was to analyze the pattern of adverse drug reactions (ADRs) of anti-tubercular drugs
Materials and Methods: A prospective, observational study was carried out in 650 patients for period of eighteen months at nodal RNTCP center. Details of adverse drug events were recorded and severity was assessed.
Results: 32.62% patients presented with ADRs. Most ADRs (79.25%) were mild in nature and among it gastrointestinal disturbances were most common. However, 67.38% patients did not present with any ADRs.
Conclusion: Need of intensive monitoring of ADRs due to anti-tubercular therapy is mandatory to maintain compliance.

INTRODUCTION

Tuberculosis is one of the leading cause of morbidity and mortality in developing countries.[1] Around 11,83,371 new cases had detected in India in year 2012. This figure represent the burden of this disease on developing countries.[2]

Directly observed treatment, short course(DOTS) was introduced in India in 1993 which contains standard anti-tubercular therapy that requires continually taking drug combinations of Isoniazid(H), Rifampicin(R), Pyrazinamide(Z), Ethambutol(E) and Streptomycin (S) for 6-9 months.[3] However, tuberculosis is still a threat with high mortality rate in spite of high success rate of anti-tubercular treatment. One of the reasons is non-compliance due to development of adverse drug reactions(ADRs).[4] This non-compliance can lead to relapse or development of multi drug resistance tuberculosis(MDR-TB). Therefore, monitoring of ADRs due to anti-tubercular treatment is very necessary to prevent this non-compliance. So, the present study was conducted to see the pattern and prevalence of ADRs with anti-tubercular treatment.

MATERIALS AND METHODS

A prospective, observational study was carried out for a period of eighteen months (June 2016-December 2017) at nodal RNTCP center. Institutional ethics committee approval was taken before initiation of the study. Written informed consent was taken from patients before inclusion in the study. All diagnosed patients of tuberculosis of either sex aged 18 years or above receiving anti-tubercular treatment were included in the study. Patients with other co-morbidities, pregnant and lactating females, patients receiving other drugs concomitantly were excluded from the study. Data regarding patient demographics and clinical information were recorded on a pre-structured proforma. ADRs were diagnosed on basis of patient complaints and physician diagnosis. ADRs reported were categorized according to Hartwig et al.,[5] as: 1) mild reaction that were self-limiting and resolve without treatment, 2) moderate reactions required therapeutic intervention and hospitalization prolonged by one day but resolved in less than 24 hours, and 3) severe reactions were life threatening producing disability or death of patient.

RESULTS

A total number of 650 patients were screened out of which 56.92% (n=370) were male and 43.08% (n=280) were females. Out of total 650 patients, 32.62% (n=212) patients show ADRs in which 15.09% (n=98) were males and 17.53% (n=114) were females. Maximum number of ADR was presented in age group of 31-40 years followed by age group of 18-30 years. Females show much more frequency of ADRs in comparison to males. [Table I]

Out of 212 ADRs reported, maximum number of ADRs was in mild category followed by moderate then severe. Assessment of total ADR profile revealed, gastrointestinal disorders accounting for maximum number of ADRs although they were mild in nature. Among gastrointestinal disorders, majority presents with complaint of anorexia and burning epigastrium. Among moderate ADRs, patients present with complaints of fever and allergy. In severe ADR, liver dysfunction was there for which hospitalization or discontinuation of drug regimen was needed. [Table II]

Severity of ADRs was assessed on Hartwig et al.,[5] scale. According to it, 79.25% (n=168) ADRs were mild, 13.68% (n=29) were moderate and 07.07% (n=15) were severe in nature. [Table III]

DISCUSSION

The present study was done to find out the frequency and pattern of ADRs of anti-tubercular drugs among tuberculosis patients at tertiary care center. Out of total patients, majority were males (56.92%) followed by females (43.08%). Sinha K et al., also found higher incidence of tuberculosis in male (76.47%) against female (23.63%). [6] It may be due to high risk factors in males like smoking, drug addiction etc.

It was observed that tuberculosis was more prevalent in age group 31-40 years followed by 21-30 years. Sinha K et al., found the same result [6] while Adoh and Ejei also found higher incidence in age group 21-40 years. [7]

In terms of development of ADRs, female shows much more frequency (17.53%) in comparison to male (15.09%). Thus, females are more prone to develop ADRs.[8] Yee D et al., also found similar results. [9] The reason may be due to alteration of drug response because of pregnancy, menarche etc. [10]

The most common ADRs were mild in nature (79.25%) and related to gastrointestinal system. Similar findings were in Sinha K et al., study [6] while Gillani et al., study shows skin reactions more common followed by gastrointestinal disorders.[11]

Liver dysfunction, although less in frequency, was a serious problem. American Thoracic Society (ATS) also issued statement about hepatotoxicity due to anti-tubercular drogs in 2006. [12] Most common offending drug is pyrazinamide. [13] Similar studies show same results. [14,15,16] Also anti-tubercular drug induced hepatotoxicity shows more frequency in elderly patients. [17]

This study has certain limitations. As it was single center study with small sample size, the data may not represent national statistics. Despite it, the strength of this study was that ADR analysis done prospectively with minimal loss of data.

CONCLUSION

This study was done to obtain information on pattern of ADRs during anti-tubercular therapy. Need of intensive monitoring for ADRs is mandatory and patient education should be important to maintain compliance and reduce drop outs.

TABLE I: Distribution of patients according to age, gender and occurrence of ADRs

Age group (in years)	Patients screened						Patients presented with ADRs						Patients not developed ADRs					
	Total		Male		Female		Total		Male		Female		Total		Male		Female	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
18-30	178	27.39	95	14.62	83	12.77	56	08.61	29	04.46	27	04.15	122	18.77	66	10.16	56	08.61
31-40	250	38.46	149	22.92	101	15.54	95	14.62	39	06.01	56	08.61	155	23.85	110	16.92	45	06.93
41-50	170	26.15	94	14.46	76	11.69	41	06.31	20	03.08	21	13.23	129	19.84	74	11.39	55	08.45
51-60	42	06.46	24	03.69	18	02.77	18	02.77	10	01.54	08	01.23	24	03.69	14	02.15	10	01.54
More than 60	10	01.54	08	01.23	02	00.31	02	00.31	00	00.00	02	00.31	08	01.23	08	01.23	00	00.00
Total	650	100	370	56.92	280	43.08	212	32.62	98	15.09	114	17.53	438	67.38	272	41.85	166	25.53

TABLE II: Distribution and Severity of ADRs in Tuberculosis patients

Adverse drug reactions		Total number of patients		Total number of males		Total number of females	
		No.	%	No.	%	No.	%
Mild	Anorexia	40	18.89	11	05.18	29	13.68
	Burning epigastrium	29	13.68	16	07.55	13	06.13
	Nausea	20	09.43	12	05.66	08	03.77
	Vomiting	10	04.72	06	02.83	04	01.89
	Joint pain	38	17.92	15	07.08	23	10.85
	Generalized weakness	31	14.61	15	07.08	16	07.55
Moderate	Allergic skin disorders	15	07.07	09	04.25	06	02.83
	Fever	14	06.60	06	02.83	08	03.77
Severe	Liver dysfunction	15	07.08	08	03.77	07	03.30
Total ADRs		212	100.00	98	46.23	114	53.77

TABLE III: Frequency of severity of ADRs in tuberculosis patients

Patients showing Adverse drug reactions	Mild	Moderate	Severe	Total
Total number	168	29	15	212
%	79.25	13.68	07.07	100.00

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