



Epidemiological Study of Adverse Drug Reactions of Antitubercular Drugs Used in Dots Therapy

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ABSTRACT

The Adverse Drug Reactions (ADRs) to the drugs used is one of the major reasons for the patient default for treatment. A general knowledge of the various ADRs and their management is essential for the effective management of Tuberculosis. This study was planned for detection, assessment, classification and causality analysis of ADRs to Anti-tubercular drugs used in DOTS therapy in Hamidia Hospital, Bhopal and T.B. Hospital Idgah Hills, Bhopal. Information of the ADRs is data based collected from DOTS center with the help of treating physician and other health care professionals in a specialized Performa and the assessment of ADRs done with the help of various scales and investigations. Maximum numbers of ADR were reported among male population within 4 week of starting DOTS therapy. The causality assessment was found to 50% possible and 30.64% probable. Gastrointestinal system (Gastritis) was the most common system affected followed by Skin (Rashes). Majority of ADRs 53.22% were moderate, and 46.77% were mild. No severe life threatening ADRs were observed during the study period. We found DOTS therapy safer, but regular monitoring is required for ADRs, so as to prevent the ADRs at the initial stage.

Keywords: Adverse Drug Reactions (ADRs), Antitubercular drugs, DOTS therapy.

INTRODUCTION

According to WHO an ADR is any response to a drug that is noxious and unintended, that occurs at doses normally used in humans for prophylaxis, diagnosis and therapy of diseases or for the modification of physiological function. Adverse Drug Reactions (ADRs) are common occurrence in hospital settings and more so in the community and is attributed to the severity and complexity of the disease process, use of multiple drugs, drug interactions.¹

The World Health Organization (WHO) declared tuberculosis (TB) as a global emergency in 1993.² The WHO estimated that globally 9.27 million new cases of TB occurred in 2007 (139/100,000 population). India, China, Indonesia, Nigeria and South Africa ranks first to fifth in the total number of incident cases. MDR-TB and XDR-TB are strong indicators of TB control programme failures due to multi drug therapy and their ADR. The global estimates of the burden of MDR-TB (511,000 incident cases, 150,000 deaths) and XDR-TB, cases (50,000 cases, 30,000 deaths).³

Antitubercular drugs, just like other drugs used in clinical practice, are not free from ADRs. The added problem is that combinations of drugs are always used for prolonged periods of time therefore; it is likely that the adverse reactions of one drug may be potentiated by the companion drugs used. Moreover, the Adverse Drug Reactions (ADRs) to the drugs used is one of the major reasons for the patient default for treatment. A general knowledge of the various ADRs and their management is essential for the effective management of TB.⁴

Aims and Objectives

1. To detect adverse drug reactions (ADRs) to Antitubercular Agents used in patients of DOTS center Hamidia Hospital (Gandhi Medical College) Bhopal and TB hospital Idgah hills Bhopal.
2. To assess probable correlation of ADRs to age & sex of patients.
3. To do causality analysis of ADRs.
4. To assess and analyze the ADRs According to their demographic distribution, onset, reporting and presentations.
5. To classify the severity of ADRs to anti-tubercular Agents in to mild, moderate and severe based on the clinical feature and investigations.

MATERIALS AND METHODS

The present study was conducted in the department of Pharmacology Gandhi Medical College Bhopal and TB Hospital Idgah hills Bhopal from 15 April 2010 to 15 Dec. 2010. The cases were included all the patients visiting the DOTS Center and those admitted in the medical wards in Hamidia Hospital and TB Hospital Idgah hills Bhopal with suspected ADRs due to antitubercular drugs.

- Information of the ADRs is data based collected from DOTS center with the help of treating physician and other health care professionals in a specialized Performa.



- The assessment of ADRs done with the help of following scales and investigations.

Assessment scale

- WHO assessment scale⁵
- Naranjo scale⁶
- European A.B.O scale⁷

Investigations

- Liver Function Test.
- Routine haemogram
- Peripheral Blood smear
- Stool for occult blood,
- Urine routine and microscopy examination,
- Blood urea,
- Serum creatinine and
- Upper gastrointestinal endoscopy (in necessary cases).

Inclusion Criteria

1. Patients of all the categories of TB with ADRs to Anti-tubercular agents visiting in the DOTS center.
2. Patients with ADRs to Anti-tubercular Agents in wards.
3. Patients above 12 years of Age.
4. Patients receiving minimum one Anti-tubercular Agents.

Exclusion Criteria

1. Patients below 12 years of age.
2. Patients who were HIV Positive.
3. Pregnancy.
4. Patients known case of Diabetes Mellitus.
5. Patients of MDR-TB and XDR-TB.

Observations

Total 820 patients who were taking DOTS therapy, included in this study out of which 720 patients from OPD and 100 patients from IPD. The most common age of patient was 21-30 years followed by 31-40 years. Total 62 ADRs detected in 62 patients, 2 patients were dropped out from DOTS therapy due to ADR (Table 1 & 2).

The majority of ADR were moderate 33 (53%) and mild 29 (47%) and no severe ADR were reported, the mild ADRs required no treatment or simply modification in the doses of suspected drug while moderate ADRs were required discontinuation of suspected drug and switch over to other antitubercular drug or symptomatic treatment of ADRs (Table 4).

Maximum number of ADRs detected were gastritis 28 (45%) followed by 12 (19%) of rash, 6 (10%) of arthralgia, 4 (6%) of hepatitis, 2 (3%) of peripheral neuropathy, 2 (3%) of flu like syndrome, 6 (10%) of vertigo, 2 (3%) were of psychosis (Table 5).

Table 1: Patients treated with antitubercular drugs

Age Group	Male	Female	Total	Percentage
12-20	85	65	140	17%
21-30	90	70	160	19%
31-40	90	80	170	21%
41-50	90	80	170	21%
51-60	85	65	150	18%
> 60	20	10	30	4%
Total	460 (56%)	360 (46%)	820	100 %

Table 2: Age and sex wise distribution of ADRs

Age Group	Male	Female	Total	Percentage
12-20	6	5	11	17.74%
21-30	10	7	17	27.41%
31-40	8	7	15	24.19%
41-50	10	4	14	22.58%
51-60	4	1	5	8.06%
> 60	0	0	0	0
Total	38 (61%)	24 (39%)	62	100 %

Table 3: OPD and IPD Wise Distributions of ADRs

ADRs	OPD	IPD	Total
GIT	24	4	28
Skin	10	2	12
Musculo	4	2	6
Hepatobiliary	2	2	4
CNS	3	1	4
Other	5	3	8
Total	48 (77.41%)	14 (22.58%)	62 (100%)

Table 4: Severity of ADR in different age groups

Age Group	Mild	Moderate	Severe	Total	Percentage
12-20	8	3	0	11	18%
21-30	8	9	0	17	27%
31-40	7	8	0	15	24%
41-50	5	9	0	14	23%
51-60	1	4	0	5	8%
Total	29 (46.77%)	33 (53.22%)	0	62	100 %

Causality assessment using standard method is probably the best way to establish the causal relationship between a drug and its effects. In our study we found a majority of the ADRs to be "possible". The causal link between the ADRs and the suspected anti-tubercular drug by Who

scale, certain relationship was established between the anti-tubercular drug and ADRs in 12 (19.35%) patients while 19 (30.64%) probable and 31 (50%) ADRs were categorized as possible (Table 6).

Our study revealed 46.77% mild and 53.22% moderate ADRs, there was 56% of type A reaction and 44% of type B reaction (Table 7).

Table 5: Severity of ADR involvement of different system

ADR	Mild	Mod.	Severe	Total	Percentage
GIT(GASTRITIS)					
Vomiting	2	8		10	16.12%
Abdominal cramps	4	10	0	14	22.58%
Diarrhea	2	2		4	6.45%
Skin					
Itching	6	2		8	12.90%
Rashes	3	1	0	4	6.45%
Musculoskeletal					
Arthralgia	3	3	0	6	9.67%
Ototoxicity					
Vestibular Symptoms	1	3	0	4	6.45%
Auditory Symptoms	1	1		2	3.22%
Hepatobiliary Hepatitis	3	1	0	4	6.45%
CNS					
Periph. Neuropathy		2	0	2	3.22%
Psychosis	2			2	3.22%
Others flu like syndrome	2		0		
Total	29 (47%)	33 (53%)	0	62	100%

Table 6: Causality assessment (WHO Scale) of ADR

Drug Anti-Tubercular	No. of ADR	Certain	Probable	Possible
H	22	4	7	11
R	16	2	5	9
Z	10	3	2	5
E	7	0	2	5
S	7	3	3	1
Total	62	12 (19%)	19 (31%)	31 (50%)

Table 7: Types of ADR

Anti-Tubercular Drugs	No. Of ADR	Type-A	Type-B
H	22	8	14
R	16	11	5
Z	10	5	5
E	7	5	2
S	7	6	1
Total	62	35 (56%)	27 (44%)

Table 8: Total numbers of ADR for Individual anti-tubercular drugs

ADRs	H	R	Z	E	S	Total	Percentage
GIT							
Vomiting	4	4		2		10	16.12%
Abdomen cramps	4	4	4	2		14	22.58%
Diarrhea		2	1	1		4	6.45%
Skin							
Itching	4	2		1	1	8	12.9%
Rash	2	1		1		4	6.45%
Musculoskeletal							
Arthralgia	1		5			6	9.67%
CNS							
P.N.	2					2	3.22%
Psychosis	2					2	3.22%
Hepatobiliary Hepatitis	3	1				4	6.45%
Others							
Ototoxicity					6	6	9.67%
Flu syndrom		2				2	3.22%
Total	22(35%)	16(26%)	10(16%)	7(11%)	7(11%)	62	100%

Prevalence of ADRs in our study was 7.56% and the incidence of ADRs 7.75% per month.

If we see the individual drug, total 22 patients reported ADRs to H (Isoniazid), 16 patients reported to R (Rifampicin), 10 patients reported to Z (Pyrazinamide) and 7 patients reported to each drug E (Ethambutal) & S (Streptomycin) (Table 7 & 8).

CONCLUSION

Since there can be no hope of eliminating all the adverse effects of drugs it is necessary to evaluate pattern of adverse reactions.⁸ There is a special need for systemic collection of information on ADRs in India due to wide variation in genetic, nutritional, environmental and disease patterns.⁹ Therefore, better approaches must be devised for reporting assessment and management of individuals who present with drug induced disease.¹⁰

This study was planned for detection, assessment, classification and causality analysis of ADRs to Anti-tubercular drugs used in DOTS therapy in Hamidia Hospital, Bhopal and T.B. Hospital Idgah Hills, Bhopal.

Maximum numbers of ADR were reported among male population with in 4 week of starting DOTS therapy.

The causality assessment was found to 50% possible and 30.64% probable. Gastrointestinal system (Gastritis) was the most common system affected followed by Skin (Rashes).

Majority of ADRs 53.22% were moderate, and 46.77% were mild. No severe life threatening ADRs were observed during the study period. We found DOTS therapy safer, but regular monitoring is required for ADRs, so as to prevent the ADRs at the initial stage.

Thus, this study was performed with the ultimate aim of generation of information about ADRs to antitubercular drugs of DOTS center in Hamidia Hospital and TB Hospital Idgah Hills, Bhopal to add knowledge about the safety of medicines and prevention of ADRs.

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