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ADVERSE DRUG REACTIONS DUE TO ANTI-TUBERCULAR DRUGS IN PATIENTS OF MULTIDRUG RESISTANT TUBERCULOSIS IN RAJINDRA HOSPITAL PATIALA

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ABSTRACT

Patients with MDR-TB may be more likely to have had problems with non adherence in the past. In addition, adherence with MDR-TB therapy is made more difficult by its prolonged treatment regimens, with larger numbers of drugs that have more serious adverse effects. These adverse effects lead to non- adherence to the regimen, improper and inadequate drug intake by the patient and may lead to the further emergence of resistance. Therefore this study was done to know the Spectrum of adverse drug reactions caused by ATT. **METHOD:** 100 patients who were diagnosed as MDR-TB by Department of Chest and Tuberculosis Diseases, Government Medical College, Patiala were enrolled in the study over a period of December 2014 to march 2016. Detection and monitoring of ADR was done by interviewing patient and reviewing laboratory tests on monthly basis till their ATT continued. Patients were instructed to report any sign and symptoms they come across during the treatment period. **RESULTS:** Most of the patients were in age group 21-40 years. Male: Female patients were 75:25 patients with a ratio of 3:1. Most patients were in the weight range of 31-45 kgs. 30% patients had gastrointestinal symptoms as the common ADR, 18% with Sleep Disturbances, 15% with hearing loss,10% with joint pains, 7% with Allergic reactions. Out of 100, 11% patients were admitted only due to ADR's caused by Drugs. **CONCLUSION:** All patients

undergoing treatment for the disease should be closely assessed during initial periods after starting MDR regimen or at least monthly to identify and address potential adverse reactions. The reactions may range from inconsequential to severe and may be caused by medications other than those prescribed for TB drugs.

KEYWORDS: ATT, ADR, DOTS PLUS.

INTRODUCTION

Tuberculosis, caused by the infectious agent Mycobacterium tuberculosis, has plagued the humankind since the beginning of recorded history. TB is world's 7th leading cause of death.[1] In 2012 there were estimated 8.6 million incident cases of TB (range 8.3 to 9 million) globally, equivalent to 122 cases per 1 lack population.[2] India has been called the TB capital of world as we have highest population based prevalence. With about a sixth of world's population, we have nearly a third of global TB cases.[3]

Multidrug resistant tuberculosis (MDR-TB), defined as TB with isolates showing in vitro resistance to at least isoniazid and rifampicin, contributes to rising TB morbidity and mortality on a global level.[4] DOTS stands for directly observed treatment short course DOTS is a methodology for making sure that every patient starting TB treatment gets best chance of being cured.[5] MDR treatment programs have achieved cure rates of greater than 80% even in resource poor setting.[6]

Patients with MDR-TB may be more likely to have had problems with non adherence in the past. In addition, adherence with MDR-TB therapy is made more difficult by its prolonged treatment regimens, with larger numbers of drugs that have more serious adverse effects. Thus, MDR-TB patients are at risk of not being able to adhere to treatment, an essential element to prevent the generation of pan-resistant strains with the potential for communitywide spread and virtually no chance of cure for the patient.[7]

RISK FACTORS FOR ADVERSE DRUG REACTION

Many factors can increase the likelihood of an adverse drug reaction. This includes the simultaneous use of several drugs, very young or old age, pregnancy, and breastfeeding. Hereditary factors also make some people more susceptible to the toxic effects of certain drugs. Certain diseases can alter drug absorption, metabolism, and elimination and the body's response to drugs. Taking several drugs, whether prescription or over-the-counter, contributes

to the risk of having an adverse drug reaction. The number and severity of adverse drug reactions increase disproportionately as the number of drugs taken increases. The use of alcohol, which is technically a drug, also increases the risk.[8] Sex is also an important determinant of drug use and drug response. Women tend to have a higher risk of adverse drug reactions with a 1.5 to 1.7 fold greater risk than men. Older age and female gender are significantly associated with ADR related hospital admission.[9] Minor adverse reactions are extremely common in MDR TB treatment, and should be expected and built into patient counselling from the beginning; most such side effects are manageable with re reassurance and symptomatic treatment. Patients experiencing higher rates of adverse drug reactions may be at increased risk of non-adherence. Therefore, early and effective management of adverse drug reactions should be part of adherence-promotion strategies in the management of MDR-TB. In most cases, management of the adverse effects can be accomplished using relatively simple and low cost interventions without compromising the integrity of the regimen.[10]

This Study was conducted with following Aim and Objective:-

1. To study the pattern of Adverse Drug Reactions in patients of MDR-TB in Rajindra Hospital, Patiala.

MATERIAL AND METHODS

A total of 100 patients attending Department of Chest and Tuberculosis, Government Medical College, Patiala who were diagnosed as MDR-TB were enrolled in the study after obtaining the approval from institutional ethics and research review board. Written informed consent was taken from each patient enrolled in this study. Detection and monitoring of ADR was done by interviewing patient and reviewing laboratory tests accordingly. Patients were instructed to report any sign and symptoms they come across during the treatment period. Patients were encouraged to return at any time if new symptom or problem arises during therapy. Adverse effects, their timing of appearance during treatment, as well as subsequent modification in regimen were noted.

INCLUSION CRITERIA

1. Diagnosed case of MDR-TB.
2. Willing to join the study and signing the informed consent by himself or surrogate.

EXCLUSION CRITERIA

1. Patient having known hypersensitivity to any drug.

RESULTS

In this study, most patients were in the age group of 21-40 years(62%), followed by 41-60 years age group(17%), followed by less than 20 years age group(13%) followed by more than 60 years age group(8%).

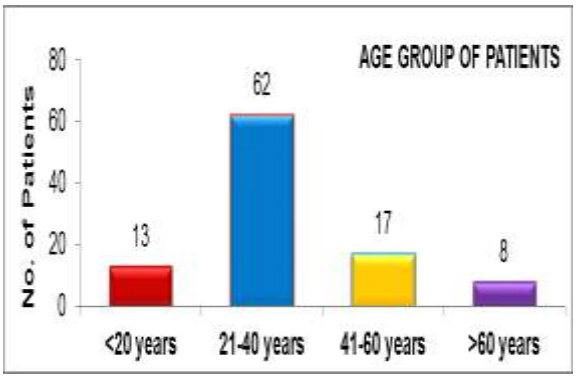

Fig. 1.

In this study, out of 100 patients enrolled, 75% were male patients and 25% were female patients with Male: Female ratio of 3:1, female were having earlier onset of disease as compared to male patients.

Table 1: Gender wise distribution of patients.

Gender	No. of patients	Percentage
Male	75	75.0%
Female	25	25.0%
Total	100	100%

In this study 22% patients had the history of ATT taken earlier of Category1 and 78% patients had history of ATT taken of Category 2.

Table 2: Distribution of Patients based on History of ATT.

History of ATT	Number	Percentage
CATEGORY1	22	22.0%
CATEGORY2	78	78.0%
Total	100	100%

In this study, 63% patients had weight range of 31-45 kgs, followed by 29% patients in the range of 46-60 kgs, and 8% patients had their weight in the range of 15-30 kgs.

Table 3: Weight wise distribution of patients.

Weight in kgs	Number	Percentage
15-30	08	8.0%
31-45	63	63.0%
46-60	29	29.0%
Total	100	100%

Out of total 100 patients, most patients 30.0% patients had gastrointestinal symptoms followed by Sleep disturbances in 18% patients, Hearing loss in 15% patients, 10% patients had joint Pains, 7% had allergic reactions, 4% patients had seizure as ADR and 3% patients suffered from depression and 2% patients had dizziness as the Adverse event of drug treatment.

Table 4: ADR wise distribution of patients.

ADR	Number of patients	Percentage
GI symptoms	30	30%
Depression	3	3%
Allergic reactions	7	7%
Dizziness	2	2%
Hearing loss	15	15%
Joint pains	10	10%
Seizure	4	4%
Sleep disturbance	18	18%
Total	89	89%

In this study out of 100 patients 11% patients needed admission to the hospital due to ADR's only. These were Hepatitis and Hearing loss in 3% patients each, followed by nephrotoxicity in 2% patients, and Depression, psychosis and Visual blurring in 1% patients each.

Table 5: Distribution of patients needing admission due To Adverse Effects.

Reason	No. of patients	Percentage
Depression	1	1.0%
Hepatitis	3	3.0%
Hearing loss	3	3.0%
Psychosis	1	1.0%
Nephrotoxicity	2	2.0%
Visual blurring	1	1.0%
Total	11	11.0%

Out of 89 patients, Pyrazinamide was stopped in 1 out of 30 patients of GIT Symptoms, 3 out of 7 patients of allergic reactions, 5 out of 10 patients of joint pains and these patients were given Para amino salicylic acid as replacement and symptomatic treatment, Kanamycin was

stopped in 10 out of 15 patients of Hearing Loss and they were given Pas as replacement + symptomatic treatment, and Cycloserine was stopped in 1 out of 3 patients of depression, 4 out of 4 patients of Seizures, and 1 out of 1 patient of Psychosis and were given Pas as replacement + symptomatic treatment, 18 patients of sleep disturbance and 1 patients of Dizziness were continued on same treatment+ Counselling of patient.

Table 6: Outcome/ any substitution in treatment in patients having ADR's.

Type of ADR	No. of Patients	YES	NO	Stopped drug	Treatment/ Substituted Drug
GI symptoms	30	1	29	Pyrazinamide	Para amino salicylic acid(Pas)
Depression	3	1	2	Cycloserine	Pas
Allergic reactions	7	3	4	Pyrazinamide	Pas
Hearing loss	15	10	5	Kanamycin	Pas
Joint pains	10	5	5	Pyrazinamide	Pas
Seizure	4	4	0	Cycloserine	Pas
Psychosis	1	1	0	Cycloserine	Pas
Sleep Disturbance	18	0	18	-	Patient Counselling
Dizziness	1	0	1	-	Patient Counselling
Total	89	25	64	-	-

DISCUSSION

Most patients were in the age group of 21-40 years(62%),75% were male patients and 25% were female patients with Male: Female ratio of 3:1. 58% patients had symptoms of less than 3 months duration and 42% patients had symptoms more than 3 months duration. In this study, 63% patients had weight range of 31-45 kgs, followed by 29% patients in the range of 46-60 kgs, and 8% patients had their weight in the range of 15-30 kgs, which is similar to the study conducted by Vishakha K.et al in.[11] In this study 30.0% patients had gastrointestinal symptoms followed by sleep disturbances in 18% patients, hearing loss in 15% patients, 10% patients had joint Pains, 7% had allergic reactions, 4% patients had seizure as ADR and 3% patients suffered from depression and 2% patients had dizziness as the ADR of drug treatment, similar to study conducted by Wai Yew W. et al[12] which showed Gastro intestinal 20% along with Central nervous symptoms in 17.46% patients. Evans et al also showed the prevalence of gastrointestinal tract adverse events (abdominal pains, constipation, diarrhea, nausea and vomiting) was 64%.[13] Akshata et al showed the most common of adverse drug reactions was related to gastrointestinal system. 435(71.7%) patients of 607 complained of mild gastritis, nausea, vomiting. Other five commonly occurring adverse reactions were athralgia (14%), depression (13%), diarrhoea (8.6%), peripheral neuropathy (5.8%) and skin

rash (4.3%). The least occurring were nephrotoxicity (0.5%) which shows variation in less number of GIT adverse events in our study compared to this study.[14]

CONCLUSION

All patients undergoing treatment for the disease should be closely assessed during initial periods after starting MDR regimen or at least monthly to identify and address potential adverse reactions. The reactions may range from inconsequential to severe and may be caused by medications other than those prescribed for TB drugs. So, to have the highest likelihood of success, chemotherapy must be provided within a clinical and social framework based on individual patients needs. Training of all the health staffs will be done to identify and manage ADRs. Close monitoring of patients is necessary to ensure that the adverse effects of the drugs are recognized quickly by health-care personnel. Timely and intensive monitoring for identifying and management of adverse reactions are essential. It will help to improve patient adherence to treatment, reduce mortality and obtain better treatment outcomes. Ancillary drugs for the management of adverse reaction should be made available to the patient free of cost.

ABBREVIATIONS

ADR- Adverse Drug Reaction.

ATT- Anti-tubercular treatment.

DOTS- Directly observed treatment short course.

MDR-TB - Multi drug resistant Tuberculosis.

Pas- Para amino salicylic acid.

REFERENCES

1. Qayyum A, Shafiq M, Farogh A. Prevalence of Pulmonary Tuberculosis Among Diabetics. Biomedical, 2004; 20: 73-78.
2. GlobalTuberculosisReport2013;11-19.Available at http://www.who.int/tb/publications/global_report/gtbr13_main_text.pdf.
3. John TJ, Vashishtha VM, John SM, Sudarsanam TD. Tuberculosis control must be scientifically defined and soundly designed. Indian J Med Res., 2010; 132: 4-8.
4. Shin SS, Pasechnikov AD, Gelmanova IY, Peremitin GG, Strelis AK, Mishustin S et al. Adverse reactions among patients being treated for MDR-TB in Tomsk, Russia. Int J Tuberc Lung Dis., 2007; 11(12): 1314-20.

5. WHO: An expanded DOTS framework for effective tuberculosis control Stop TB communicable diseases. WHO/CDS/TB/2002.297.
6. Park SK, Kim CT, Song SD. Outcome of chemotherapy in 107 patients with pulmonary tuberculosis resistant to isoniazid and rifampicin. Int J Tuberc Lung Dis., 1998; 2: 877–84.
7. Adverse Reaction. In Guidelines on Programmatic Management of Drug Resistant TB (PMDT) in India. Revised National Tuberculosis Control Programme, 2012; 59-61.
8. Haregewoin Bezu, Daniel Seifu, Getnet Yimer, Tesfamariam Mebrhatu[3]et al. Journal of Tuberculosis Research Prevalence and Risk Factors of Adverse Drug Reactions Associated Multidrug Resistant Tuberculosis Treatments in Selected Treatment Centers in Addis Ababa Ethiopia., 2014; 2(3).
9. Eline M Rodenburg, Bruno H Ch Stricker, and Loes E Visser et al. Sex-related differences in hospital admissions attributed to adverse drug reactions in the Netherlands. Br J Clin Pharmacol., 2011 Jan; 71(1): 95–104.
10. Treatment Delivery and Adherence. In Guidelines on Programmatic Management of Drug Resistant TB (PMDT) in India. Revised National Tuberculosis Control Programme, 2012; 63.
11. Dr. Kapadia Vishakha K. Dr. Tripathi Sanjay B.*Analysis of 63 patients of MDR TB on DOTS plus regimen: An LG hospital, TB Unit, Ahmedabad experience. GUJARAT MEDICAL JOURNAL / DECEMBER – 2013.
12. Yew WW, Chan CK, Chau CH, Tam CM, Leung CC, Wong PC, Lee J.et al. Outcomes of patients with multidrug-resistant pulmonary tuberculosis treated with ofloxacin/levofloxacin-containing regimens. Chest., 2000 Mar; 117(3): 744-51.
13. Sagwa E, Mantel-Teeuwisse A, Ruswa N, Musasa JP, Pal S, Dhliwayo P, van Wyk B. The burden of adverse events during treatment of drug-resistant tuberculosis in Namibia. Southern Med Review, 2012; 5(1): 6-13.
14. J. S. Akshata, Anushree Chakrabarthy, R. Swapna, Shashidhar Buggi, Somashekar et al. Adverse Drug Reactions in Management of Multi Drug Resistant Tuberculosis, in Tertiary Chest Institute. Journal of Tuberculosis Research, 2015; 3: 27-33.