



OCCURRENCE AND PROPORTIONAL ANALYSIS OF ADVERSE DRUG REACTIONS IN DOTS PLUS

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<p>Article history Received 03/6/2014 Available online 15/07/2014</p> <p>Keywords: Adverse Drug Reactions, Antitubercular drugs, DOTS plus, Tuberculosis</p>	<p>ABSTRACT</p> <p>To evaluate the adverse drug reactions (ADRs) induced by antitubercular drugs used in Directly Observed Treatment Short Course Plus (DOTS plus) from previously reported articles from referred sources. The occurrence rate of each type of ADR from entire ADRs were analyzed and compared. The total 2992 patients from 17 studies were analyzed. 2042 (68.24%) patients showed at least one type of adverse drug reaction. The majority of ADRs were related to nervous system, which were occurred in 2,013 (48.37%) patients. 1024 (25.52%) patients suffered with ADRs related to digestive system. Major ADRs were occurred related to GIT system such as liver disorders and hepatocellular injury etc. 502 (12.6%) patients showed ADRs related to sense organs. 134 (3.22%) patients showed ADRs such as insomnia, fatigue, headache, anemia, electrolyte disturbance and hypokalemia etc. Various types of adverse drug reactions related with different systems of body were observed in the study. ADRs were needed to be monitored during DOTS plus therapy.</p>
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INTRODUCTION

Anti-tuberculosis (TB) drug resistance is a major public health problem that threatens progress made in TB care and control worldwide. Drug resistance arises due to improper use of antibiotics in chemotherapy of drug-susceptible TB patients^[1].

Multi-drug-resistant tuberculosis (MDR-TB) is defined as tuberculosis that is resistant to at least isoniazid (INH) and rifampicin (RMP), the two most powerful first-line anti-TB drugs. Isolates that multiply resistant to any other combination of anti-TB drugs but not to INH and RMP are not classed as MDR-TB.

As of 2013, 3.7% of new tuberculosis cases have MDR-TB. Levels are much higher in those previously treated for tuberculosis - about 20%. WHO estimates that there were about 0.5 million new MDR-TB cases in the world in 2011. About 60% of these cases occurred in Brazil, China, India, The Russian Federation and South Africa alone. In Moldova, the crumbling health system has led to the rise of MDR-TB. In 2013, the Mexico–United States border was noted to be "a very hot region for drug resistant TB", though the number of cases remained small^[2].

Community-based treatment programs such as DOTS-Plus, a MDR-TB-specialized treatment using the popular Directly Observed Therapy – Short Course (DOTS) initiative, have shown considerable success in the treatment of MDR-TB in some parts of the world. These programs have proven to be a good option for proper treatment of MDR-TB in poor, rural areas. A successful example has been in Lima, Peru, where the program had seen cure rates of over 80%.

Adverse drug reactions are frequently serious enough to result in admission to hospital. It is well recognized that adverse drug reactions place a significant burden on the health service^[3].

ADR is a persistent problem along with the DOTS plus treatment. We studied with an objective to evaluate incidence and pattern of adverse drug reactions in the MDR TB population undergoing DOTS plus treatment.

METHODOLOGY

We evaluated 35 articles from various sources like print journals, online journals and databases like science direct, Medline etc. As per study criteria, we shortlisted 18 articles from referred sources and

informed all authors via emails. Evaluation of articles had been done thoroughly. We assessed incidence rate of adverse drug reactions in MDR TB treatment and classified adverse drug reactions into 9 segments which are as follows :-

Digestive System, Renal System, Skeleton System, Muscular System, Nervous System, Endocrine System, Reproductive System, Sense Organ and Others again they are sub-divided as follows :-

Such as, Digestive system covers GIT (Dyspepsia, Diarrhoea, Constipation, Abdominal Pain, Epigastric Disorder, Irritable Bowel Diseases, Gastritis, Loss of Appetite, Gastrointestinal Disturbance) and Liver (Hepatotoxicity, Hepatitis, Jaundice, Liver Dysfunction, Liver Cirrhosis, Hepatocellular Injury.)

Nervous System covers (Nausea, Depression, Psychosis, Behaviour (Violent & Altered), Giddiness, Dizziness (Vertigo), Mental Problem, Seizures, Myxoedema Coma, Neurological Disorders, Neuropathy, Peripheral Neuritis, Anxiety, Ataxia, CNS Complications, Vomiting, Confusion).

Renal system covers (Renal Dysfunction, Nephrotoxicity And Decreased Urine).

Skeletal system covers (Arthritis (Gout Arthritis), Arthralgias).

Muscular system covers (Tendonitis, Convulsion, and Musculoskeletal disorder).

Endocrine system covers (Hypothyroidism, Dysglycemia, Gynecomastia).

Reproductive system covers (Impotence, Loss of Libido.)

Sense Organs covers Ear (Hearing Loss, Tinnitus, Ototoxicity), Eye (Visual Blurring), Skin (Skin Reaction, Rash, Abscess at injection site/swelling, Cutaneous, Itching) and Oral (Loss of Taste).

Other covers (Insomnia, Fatigue, Headache, Anemia, Electrolytic Disturbance and Hypokalemia).

RESULT

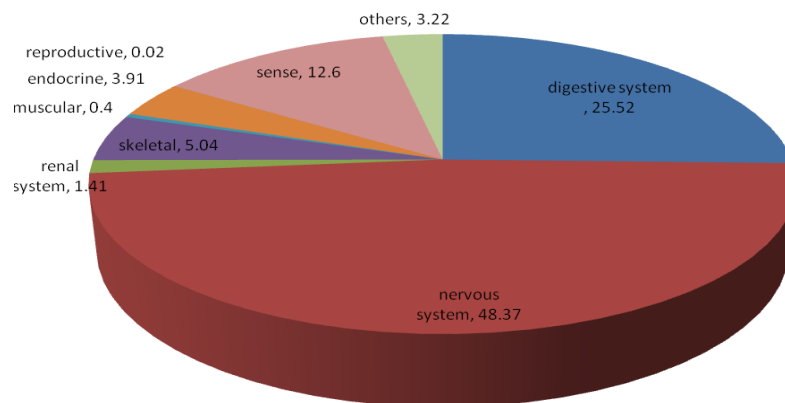
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Table No. 1. ADR distribution in MDR TB treatment

Name of System	Percentage (%)
Digestive system	25.52
Nervous system	48.37
Renal system	1.41
Skeletal	5.04
Muscular	0.4
Endocrine	3.91
Reproductive	0.02
Sense	12.6
Others	3.22

Table No. 2. Incidence rate of ADR in MDR TB treatment

Total no. of patients	No. of ADR's	Percentage (%)
2992	2042	68.24

**Fig. 1. ADR distribution in MDR TB treatment**

DISCUSSION

The most common ADR was related to nervous system which may be due to Cycloserine. ADR's related to the GI system were seen due to use of drugs like Ofloxacin, Ciprofloxacin, Levofloxacin, Ethionamide and Para-Aminosalicylic acid (PAS) in the treatment. ADR's of the renal system were due to Amikacin, Kanamycin, and Capreomycin. Skin reactions were occurred because of Clofazimine.

Drugs show ADR's as follows: Cycloserine shows ADR's such as psychosis, convulsions, depression, headache, rash. Drugs like Ofloxacin, Ciprofloxacin and Levofloxacin show ADR's like Gastrointestinal (GI)upset, dizziness, hypersensitivity, headaches, restlessness. Drugs like Amikacin, Kanamycin, and Capreomycin show ADR's such as toxicity, auditory, vestibular, renal, chemical imbalance, dizziness. Drugs like Ethionamide, Para-Aminosalicylic acid (PAS) show GI upset, hepatotoxicity, hypersensitivity, metallic taste, sodium load. Clofazimine shows ADR's such as GI upset, discoloration of skin, severe abdominal pain and organ damage due to crystal deposition. Nervous system disorders were commonly observed ADR in DOTS plus treatment^[6].

The spread of MDR-TB can only be prevented by rapid identification and treatment with a combination of effective drugs.

The study illustrate that there is a need to monitor DOTS Plus therapy in concern with ADR. Proper monitoring system for ADR's can improve patient's compliance as well as patients cure rate.

CONCLUSION

Various types of adverse drug reactions related with different systems of body were observed in the study. ADRs were needed to be monitored during DOTS plus therapy for the prevention of serious harmful effects like death.

The very low rate of defaulted patients in this cohort manage the adverse effects may reduce the incidence of rejection of therapy and increase rates of cure.

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