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Side Effects of Antitubercular Drugs on Directly Observed Treatment Strategy Underrevised National Tuberculosis Control Programme in a Teaching Hospital

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Abstract: Tuberculosis (TB)is one of the oldest infectious diseases whose complications had caused tremendous impact on human population for times. According to World Health Organization (WHO) tuberculosis is a global emergency. In order to exaggerate the efforts to control TB, the Government of India introduced the Revised National Tuberculosis Control Programme (RNTCP). The present study is aimed to evaluate the side effects of antitubercular drugs on out patients under directly observed treatment strategy (DOTS) in RNTCP. Fifty Patients of both genders aged between 18 to 65 years who were previously diagnosed with pulmonary tuberculosis attending the outpatient department of Tuberculosis and Chest disease were recruited for the study. Patients from hepatic, cardiac, renal and patients who had any previous multiple drug resistance were exempted from the study. Demographic details, types of TB and side effectsproduced by each category regimen was recorded on monthly basis and whenever required follow-up was conducted till the regimen period is over. The results revealed that 92.5% of patients experienced various side effects of therapy. Ten different types ofside effects were reported. Anorexia/nausea/ vomiting were the highest among the complaints. However 7.5% patients had no complaints during their therapy. We conclude DOTS therapy to be harmless. However, further taxation is required to minimize the side effects and ADRs.

Key words: Tuberculosis · WHO · DOTS · RNTCP · ADR

INTRODUCTION

Tuberculosis is one of the world's alarming disasters that requireprime attention even in India and worldwide, after the incidence of acquired immunodeficiency syndrome (AIDS).A large number of morbidity and mortality have been reported due to tuberculosis. The global rate of tuberculosis is growing at approximately 1.1% per year [1]. The World Health Organization (WHO) professed tuberculosis as a universalcrisis. DOTS is an amenity to guarantee that each individual under TB treatment benefits the maximum fromit.In early stage, before the initiation of the DOTS programme, India had a National TB Programme to combat theproblem of TB. India's National Tuberculosis Programme (NTP) was initiated as a truly integrated programme, instigated through District Tuberculosis Centers (DTCs). After fewdecades, the NTP made prominent, but not remarkable progress [2].

In order to exaggerate the efforts to control TB, the Government of India progressively replaced NTP by the DOTS strategy/programme in 1993 and it is now recognized as the RevisedNational Tuberculosis Programme (RNTCP). The objective of RNTCP is to accomplish a cure rate of 85% for infectionsand seriouslyill patientsthrough sporadic (three days a week) overseen short course chemotherapy or the directly observed treatment, short course (DOTS). Under RNTCP, the doses of first lineanti-TB drugs (Isoniazid, Rifampicin, Pyrazinamide, Streptomycin and Ethambutol) were consistenton the basis of body weight and were given in different regimens. All regimens have an initial intensive

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phase lasting 2-3 months,aimed to rapidly kill the TB bacilli, bring about sputum conversion and to afford symptomatic relief. This is followed by a continuation phase lasting 4-6 months,during which the remaining bacilli are eliminated so that relapse does not occur [3, 4].

The currently indorsed anti-tuberculosis regimens are usually well abided. However some patients may experience problems, usually due to the bulk of the drugs, a single day's dose consisting of more than five drugs. Drug related side effects might be minor or major [5]. In general, a patient who has minor side effects should be encouraged to continue the treatment with symptomatic measures such as antacids, antihistamines, antiemetics, or analgesic. If major side effects occur, the regimen, or the offending drug, if identified, must be stopped. Further management depends on the nature of side effects and may have to be done in a hospital [6]. Antitubercular drugs, just like other drugs used in clinical practice, are not free from side effects. The added problem is that combinations of drugs are always used for prolonged periods of time [7] and therefore, it is likely that the adverse reactions of one drug may bepotentiated by the companion drugs used. Hence, there is a need to monitor the side effects of antitubercular drugs in a hospital set up.

MATERIAL AND METHODS

Study Design: Prospective observational study.

Study Site: The study was conducted in SRM medical college hospital and research center, SRM University, Kattankulathur, Chennai, Tamilnadu, India.

Ethical Committee Approval: The study was approved by institutional ethical committee (IEC). Ethics clearance number: 148/IEC/2011.

Study Duration: Eight months (August 2010 to March 2011).

Operational Modality: The study was conducted in fifty patients aged between 15 to 65years who had been previously diagnosed with pulmonary tuberculosis. Patients of both genders were included. The Exclusion criteria were hepatic, cardiac, renal, HIV infections and patients who had any previous multiple drug resistance (MDR-TB). The profile of all the patients was maintained after obtaining consent form. On a monthly basis the side effect produced by each drug is recorded and whenever required follow-up was conducted till the regimen period is over.

Table 1: Demographic details of the patients receiving DOTS

Demographic variables		n	%
Age	<20	6	12
	20-29	15	30
	30-39	5	10
	40-49	9	18
	50-59	10	20
	60+	5	10
Sex	Male	21	42
	Female	29	58
Smoking	No smoking	37	74
	Smoking	13	26
Alcohol	No alcohol	37	74
	Alcohol	13	26
Diet	Vegetarian	10	20
	Mixed diet	40	80
Smear	Negative	26	52
	Positive	24	48
Site of the disease	Pulmonary	23	46
	Extra pulmonary	27	54

RESULTS AND DISCUSSION

A total of fifty patients were included in the study. The demographic details of the patients receiving DOTS are shown in Table 1. From the table it is clear that 6 (12%) of patients were less than twenty. 15 (30%) individuals age in between 20 to 29, 5 (10%) individuals age in between 30 to 39, 9 (18.%) individuals age in between 40 to 49, 10 (20%) individuals age in between 50 to 59 and 5 (10%) individuals age was 60 and above. The study showed that 92.5% of the patients experienced side effects, among which 40% of the patients had multiple side effects. Out of fifty patients, 42% were male and 58% were female category.

Table 2 shows the frequency distribution of different categories of drug and its side effects. Among category I drug users 5 (17.9%) persons got anorexia/ vomiting/ nausea; 4 (14.3%) persons got cough; 3 (10.7%) persons got dermatological manifestation; 3 (10.7%) persons got fever; 3 (10.7%) persons got cold; 3 (10.7%) persons got tiredness; 2 (7.2%) persons got joint pain; 1 (3.6%) person got abdominal pain; 1 (3.6%) got burning sensation; 1 (3.6%) person got head ache. 2 (7.2%) persons have no side effect.

Among category II drug users 3 (20%) persons got anorexia/vomiting/nausea; 2 (13.3%) persons got abdominal pain; 2 (13.3%) persons got dermatological manifestation; 2(13.3%) got cough; 2 (13.3%) got burning sensation; 1 (6.7%) person got fever; 1 (6.7%) got joint pain; 1 (6.7%) got cold. One person (6.7%) has no side effect. Among category III drug users 7 (18.9%) persons

Table 2: Frequency distribution of different categories of drug and its side effects

	CAT I		CAT II		CAT III		Total	
Different side effects	No	%	No	%	No	%	No	%
Anorexia/Vomiting/Nausea	5	17.9	3	20.0	2	5.4	10	12.5
Abdominal pain	1	3.6	2	13.3	7	18.9	10	12.5
Dermatological manifestation	3	10.7	2	13.3	1	2.7	6	7.5
Fever	3	10.7	1	6.7	3	8.1	7	8.8
Cough	4	14.3	2	13.3	2	5.4	8	10.0
Tingling and burning sensation in hands and feet	1	3.6	2	13.3	4	10.8	7	8.8
Joint pain	2	7.2	1	6.7	5	13.5	8	10.0
Cold	3	10.7	1	6.7	4	10.8	8	10.0
Tiredness	3	10.7	0	0	4	10.8	7	8.8
Head ache	1	3.6	0	0	2	5.4	3	3.8
No side effect	2	7.2	1	6.7	3	8.1	6	7.5

got abdominal pain; 5 (13.5%) persons got joint pain; 4 (10.8%) persons got burning sensation; 4 (10.8%) persons got cold; 4 (10.8%) persons got tiredness; 3 (8.1%) persons got fever; 2 (5.4%) persons got anorexia/vomiting/nausea 2 (5.4%) persons got cough; 2 (5.4%) persons got head ache and one person got dermatological manifestation. 3 (8.1%) persons have no side effect.

The frequency distribution of different categories of antitubercular drugs for tuberculosis patients on DOTS therapy under RNTCP in this study provided an insight into the various side effects experienced by patients during their therapy in SRM Medical College hospital and Research Center. The data revealed that among fifty patients were included in study and ten different side effects were reported by the patients.

The present study is in accordance with WHO guidelines [2] which state that extra pulmonary tuberculosis are accountable for 20-25% of reported cases. In the present study extra pulmonary tuberculosis patients (54%) reported more side effects than pulmonary tuberculosis patients (48%). It was observed in present study that majority of the side effects were reported by female. It is in accordance with most of other literature [8-11] that female gender is a pre disposing factors for side effects. A study conducted by Daphne *et al*. [11] reported that most of the side effects were occur in patients above the age group of 60 years. But in the current study, the above concept was not in accord which may be due to less number of patients above sixty years. Anorexia/nausea/vomiting were the most common among the complaints. From the present study it is clear that there is no life threatening side effects to patients, however patients must be recognized on time and should be managed in order to reduce the inconvenience and to make the patient comfortable. Proper sample size calculation, rechallenge and dechallenge could be done by doing causality assessment. Our future plan of this study is to perform pre and post treatment of various bio chemical tests and clinical examination during DOTS therapy and to assess the incidence and pattern of ADRs.

CONCLUSION

Anorexia/vomiting/nausea was commonly observed side effects during the study period. We conclude that in spite of safer regimen in DOTS therapy, regular monitoring is warranted so as to prevent in initial stage and to make the patients more comfortable.

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