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IMPACT OF ADVERSE DRUG REACTIONS (ADR'S) OF FIRST LINE ATT (HRZE) ON SPUTUM CONVERSION IN NEWLY DIAGNOSED SPUTUM POSITIVE PULMONARY TB PATIENTS

Pharmacology

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ABSTRACT

INTRODUCTION: Pulmonary TB (PTB) is one of the leading causes of death due to infectious agent above HIV/AIDS. Sputum smear microscopy is the primary diagnostic tool to detect PTB. Smear positive PTB patients have to be paid more attention as they are more likely to spread the disease in the community, as compared to patients with Extra Pulmonary Tuberculosis. Various factors which may delay the time to sputum conversion have been demonstrated, but there are very few studies which have demonstrated the impact of various ADR's of anti-TB drugs on sputum conversion.

MATERIAL AND METHOD: Open, prospective, observational, non-comparative study of 18 months duration was conducted on 100 sputum positive PTB patients of either sex, in age group of 14 to 65 years, who were on DOTS category I, and sputum conversion rate (SCR) were assessed at the end of 1st and 2nd month.

RESULTS: Incidence of TB is more common in the younger age group (14-25 years) followed by elderly. Out of 100 patients, 69 became sputum negative at the end of 1st month of treatment and 81 at the end of 2nd month of treatment with Category I anti-TB drugs. SCR at end of 2 months of treatment in patients with ADR's and without ADR's was 79.77% and 87.5% respectively but the difference between two groups was not statistically significant (p-value: 0.474).

KEYWORDS

PTB, SCR, DOTS category 1

INTRODUCTION:

Pulmonary tuberculosis (PTB) is the most common form of Tuberculosis (TB) and is transmitted from person to person by droplet infection. TB is caused by the bacillus Mycobacterium tuberculosis bacilli (Mtb) which was discovered by Robert Koch in 1882(1). TB is one of the leading cause of death due to infectious agent (above HIV/AIDS).(2) Millions of people continue to fall sick with TB each year. According to WHO global TB report 2018, globally 10.0 million people (range, 9.0–11.1 million) developed TB disease in 2017. Among them 5.8 million were men, 3.2 million women and 1.0 million children. TB infection occurs more in young and adults (aged ≥15 years) with two thirds of the TB cases seen in these eight countries: India (27%), China (9%), Indonesia (8%), the Philippines (6%), Pakistan (5%), Nigeria (4%), Bangladesh (4%) and South Africa (3%).(2)

The estimated incidence of TB in India was approximately 28,00,000 which accounts for about a quarter of the world's TB cases .(3) The National Strategic Plan (NSP) proposes various strategies to rapidly decline TB incidence and mortality in India by 2025, and its goal is to attain the vision of a TB-free India.**(4)**

Diagnosis of smear- positive PTB patient is done primarily by direct sputum smear microscopy after staining with Ziehl-Neelsen.—(5) One specimen positive out of the two is enough to declare a patient as smear-positive PTB, which is further classified as a new or re-treatment case based on their previous treatment history, and there after an appropriate therapy is prescribed. In addition to test's high specificity, the use of two samples ensure that the diagnostic procedure has a high (>99%) sensitivity also. The additional advantages of this test includes simple, inexpensive, requires minimum training, high specificity, high reliability with low inter-reader variation, can be used for diagnosis, monitoring and defining cure, and results are available quickly.(6) More recently, the diagnostic algorithm has been modified wherein Cartridge Based Nucleic Acid Amplification Test (CBNAAT) is offered to cases who are smear negative but have an X ray suggestive of TB, as well as for new TB cases."(7)

Patients who are smear positive PTB have to be paid more attention as they are more likely to spread the disease in the community, as compared to people with Extra pulmonary tuberculosis (EPTB) and it has been seen that one untreated infectious tuberculosis patient is likely to infect 10-15 persons annually.(8)

Smear conversion is defined as new smear-positive PTB cases who became smear negative after a period of anti-TB treatment and are therefore no longer infectious (confirmed by at least two consecutive negative sputum acid fast bacillus (AFB).(9) It has been found out that 80-90% of patients become smear negative after 2 or 3 months of treatment (10) and there are various factors which has been identified that may delay the sputum conversion.(11)

With this background it was essential to know the impact of ADR,s of anti-TB drugs on sputum conversion rate (SCR) .

MATERIAL AND METHODS:

Open, prospective, observational, non-comparative study which was conducted in the Department of Pharmacology in collaboration with Department of Tuberculosis and Chest Diseases, Government Medical College, Amritsar for the duration of 18 months (March 2015 to September 2016). One hundred newly diagnosed sputum positive patients of pulmonary tuberculosis on DOTS category I, of either sex, in age group of 14 to 65 years, were included in present study and their sputum examination were followed up at the end of 1st and 2nd month.

The approval of Institutional Ethics Committee was taken before the start of study. Written informed consent was taken from patients in their vernacular language. The study subjects were put on DOTS Category I regimen comprising of 600mg Isoniazid(H), 450mg Rifampicin(R), 1200 mg Ethambutol (E) and 1500 mg Pyrazinamide (Z).

Patients with age less than 18 years, extra-pulmonary TB, cardiac, hepatic, renal diseases, HIV, diabetes, pregnant, lactating females and patients on any other drugs were excluded from the study.

Sputum conversion rate (SCR) was assessed and data was analyzed using Relative Risk.

RESULTS:

TABLE 1: INCIDENCE OF TB IN VARIOUS AGE GROUPS (N=100)

Age (years)	Incidence of TB n(%)
14-25	24 (24.00%)
26-35	16 (16.00%)
36-45	19 (19.00%)
46-55	21 (21.00%)
56-65	20 (20.00%)

Above table shows that incidence of TB is more common in the younger age group (14-25) followed by elderly age group.

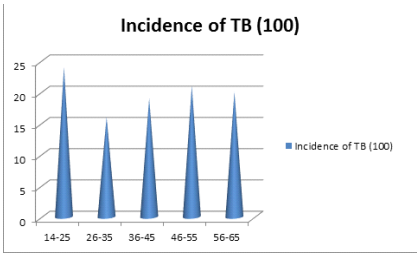

FIGURE 1: INCIDENCE OF TB IN VARIOUS AGE GROUPS

TABLE 2: PERCENTAGE OF PATIENTS WHOSE SPUTUM BECAME NEGATIVE AT THE END OF 1ST AND 2ND MONTH (n=100)

	Baseline	AT 1st month	At 2nd month
Sputum negative	-	69 (69%)	81 (81%)

In present study we observed that out of 100 patients, 69 became sputum negative at the end of 1st month of treatment with Category I anti-TB drugs.

Eighty one patients were found to be sputum negative at the end of 2nd month of treatment with Category I anti-TB drugs (also include patients who became sputum negative at the end of 1st month).

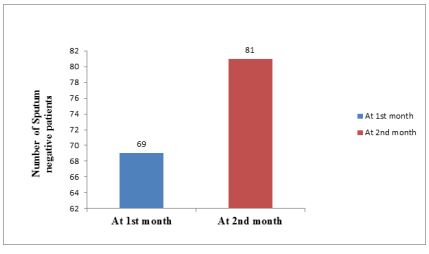

FIGURE 2: NUMBER OF PATIENTS CONVERTED TO SPUTUM NEGATIVE AT THE END OF 1ST AND 2ND MONTH

TABLE 3: IMPACT OF ADR's ON SPUTUM CONVERSION RATE (SCR) AT THE END OF INTENSIVE PHASE

Category	Patients with ADR's	Patients without ADR's	RR	p- value
Smear results at the end of intensive phase				
Positive	17	2	1.08	0.474
Negative	67	14		
SCR*	79.77%	87.5%		

*SCR: Sputum Conversion Rate

SCR at end of two months of treatment in the patients with ADR's and without ADR's was 79.77% and 87.5% respectively. The difference between two groups was not statistically significant (p-value: 0.474).

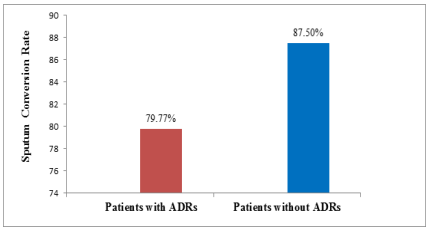

FIGURE 3: SPUTUM CONVERSION RATE IN PATIENTS WITH ADR's AND WITHOUT ADR's AT THE END OF INTENSIVE PHASE

DISCUSSION:

INCIDENCE:

The current study demonstrated that incidence of TB is more in the younger age group i.e 14-25years age group patients are affected most.(Table:1) This was similar to the study conducted by Sintayehu et al. [8] and Mekonnen [11] in Ethiopia which also concluded that smear positive cases were high in age groups below 45 years, but is in contrast to the study done by Adesse et al. [10], where more AFB positive cases were seen at age group above 45 years, this may be due to differences in prevalence of TB among two population.

SPUTUM CONVERSION AND SPUTUM CONVERSION RATE

The best way to monitor the treatment results of a pulmonary smear positive case is to check for the conversion of sputum from smear positive to smear negative(12)(13)(14)(15)(16). In the present study, among 100 cases of sputum positive pulmonary tuberculosis (category-I) patients, 69 (69%) patients become smear negative at the end of 1st month, 81 (81%) patients become sputum smear negative at the end of 2nd month and 19 patients remained sputum positive even after the end of 2nd month. (Table:2)

The present study match with the study of Baruwa et al.(17) conducted in Indian patients, which showed sputum conversion of 68% at the end of 1st month. The study done by Baurawa et al.(17) had also taken same four drug in fixed dose combination in sputum positive patients.

Study by Bawri et al. (18) at DOTS centre, Guwahati Medical College and Hospital also showed similar results, with 71% patients becoming smear negative at the end of 1st month. Like our study, this study had also enrolled 100 cases of new smear positive pulmonary tuberculosis on DOTS category I.

Sputum Conversion Rate (SCR) in patients with ADR's was 79.77% and in patients without ADR's was 87.5% (Table:3) but there was no significant difference in sputum conversion rates (p-value: 0.47) in both groups. The reason could be active surveillance of ADR's in our study settings at 30, 60 days with timely referral and management of patients.

CONCLUSION:

Tuberculosis is the most common infective disease which is responsible for high mortality in developing nations, especially India. The anti-tubercular drugs are highly efficacious in relieving symptoms of disease with early sputum conversion, thereby leading to non-infectivity.

In our study we found out that TB is badly affecting the most productive age groups (ie 14-25 years age group), whereas in low prevalence countries like United States, TB is now becoming a serious health issue of elderly persons. This may be due to differences in awareness among the two populations and lack of proper preventive measures in high prevalence countries.

After completion of one month of DOTS therapy 69% of the patients become sputum negative and further after the completion of 2nd month of treatment total 81% of the patients become sputum negative, which means even after completion of 2 months of DOTS therapy we are still left with sputum positive patients, which can further infect much other population also. So it is the need of an hour to find out various reasons behind such non conversion in sputum positive patients so that active measures can be taken to have 100% SCR.

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