Original Article

Evaluation of Efficacy of Present Fixed Dose Combinations for Daily Antitubercular Treatment Under Revised National Tuberculosis Control Programme [RNTCP]

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Abstract

Introduction: Tuberculosis [TB] still accounts for millions of cases of active disease and deaths worldwide. The disease mainly affects the developing countries. Modern Anti-tubercular treatment can cure virtually all patients provided correct combination treatment is taken in amount and duration. Treatment of TB has been shifted towards daily regimen with administration of daily fixed dose combination of first-line anti Tuberculosis drugs [ATD] as per appropriate weight bands.

Objectives: To study efficacy of RNTCP recommended Anti TB FDCs [Fix drug combination' in different weight ranges of weight Bands.

Materials and Methods: A Prospective cohort study was conducted involving a total of 830 patients presenting to Department of Respiratory Medicine, Lokmanya Tilak Municipal Medical College and General Hospital, Sion, Mumbai with diagnosed tuberculosis and Registered for category I[CATI] and category II [CATII] anti tuberculosis treatment [ATT].Duration of study was 21 months. Follow up was done at the end of intensive phase (2 months) [at the end of maximum 3 months in extrapulmonary TB] and at the end of continuation phase (6 months for Cat I and 8 months for Cat II patients). Outcome of ATT was studied in different weight bands asper RNTCP. (Cure, Failure and treatment completed). Data was analyzed using SPSS version 22.0.

Result: Among treatment categories, most patients (78.6%) were registered under Category I (new patients) as compared to retreatment cases (Category II and Category I Retreatment). Among PTB patients cure rate was 78.2%, while among EPTB patients treatment completion rate was 85.2%. Compliance of patients was better with FDCs due to reduced pill load, single dose administration, can be conveniently given to patients of all weights as per their weight bands.

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Conclusion: Among PTB patients cure rate was 78.2%, while among EPTB patients treatment completion rate was 85.2%.

Key words: Efficacy, FDC, RNTCP.

Introduction

Tuberculosis (TB) is one of the major causes of death from a curable infectious disease.[1] The disease mainly affects the developing countries. Modern Anti-tubercular treatment can cure virtually all patients provided correct combination treatment is taken in amount and duration. In India, the standard short-course therapy for all categories of drug-sensitive TB is a 6-month regimen that includes a 2-month intensive phase of four medications (HRZE), namely isoniazid (H), rifampicin (R), pyrazinamide (Z), and ethambutol (E), at doses of 75/150/400/275 mg, and a 4-month continuation phase of three medications, namely HRE at doses of 75/150/275 mg.[2]

Despite the availability of effective anti-TB drugs, poor drug adherence may lead to treatment failure and may promote drug resistance. Additionally, inadequate doses may also lead to treatment failure and to the emergence of drug resistance.[3] In high-burden countries, lowering non-adherence to ATT may have a greater epidemiological impact on TB incidence than reducing loss to follow-up during treatment.[4] Treatment of TB has been shifted towards daily regimen with administration of daily fixed dose combination of first-line ATD as per appropriate weight bands. The use of fixed-dose combinations (FDCs) of anti-TB drugs and a directly observed treatment short-course strategy (DOTS), as recommended by the World Health Organization (WHO) and other organizations, helps to ensure adequate treatment.[5] Due to various concerns of the patient and healthcare system burden, in 2014, India's National TB Elimination Program (NTEP) adopted daily medication dosing in India replacing the previous thrice-weekly dosing protocol.[6]

Various advantages of FDC include

1. improvements in adherence and ease of drug administration,
2. improvements in drug supply logistics
3. prevention of drug resistance, and
4. reductions in prescription errors
5. reduction in cost &
6. simple treatment plan.
7. With this background present study was conducted to assess efficacy of daily FDC treatment.

OBJECTIVES

1. To study efficacy of RNTCP recommended Anti TB FDCs in different weight ranges of weight bands in terms of a) cures and treatment failures in case of pulmonary TB. b) treatment completed and treatment not completed in case of extrapulmonary Tb and sputum negative TB.

Material and Methods

Prospective study was conducted involving total of 830 patients presenting to Department of Respiratory Medicine, Lokmanya Tilak Municipal Medical College and General Hospital, Sion, Mumbai with diagnosed tuberculosis and Registered for CAT I and CAT II ATT were enrolled into the study. All previously treated patients were registered under Category I Retreatment from 1stJanuary 2019. (As per New RNTCP guidelines from 1stJanuary2019).

INCLUSION CRITERIA

All patients of tuberculosis (pulmonary and extrapulmonary) registered for CatIand CatII ATT

And CatI Retreatment (from 1stJanuary 2019). aged above 12 year of age and above 25 kg in weight.

EXCLUSION CRITERIA

1. Patients not giving consent
2. Patients already taking ATT at time of enrollment
3. Medically Unstable patients (Admitted and serious patients.)
4. Multi Drug Resistant [MDR] & Extensive Drug Resistant [XDR] TB patients.
5. Patient who lost to follow up.

Statistical Methods and Data Analysis:

Data was entered into Microsoft Excel and analyses were done using the Statistical Package for

Social Sciences (SPSS) for Windows software (version 22.0; SPSS Inc, Chicago).

Descriptive Analysis:

Descriptive statistics such as mean and standard deviation (SD) for continuous variables, frequencies and percentages were calculated for categorical Variables were determined. Association between Variables was analyzed by using Chi-Square test for categorical Variables. Pie charts were used for visual representation of the analyzed data. Level of significance was set at 0.05.

Methodology

All patients presenting to Department of Respiratory Medicine, Lokmanya Tilak Municipal Medical College and General Hospital, Sion, Mumbai with diagnosed tuberculosis and Registered for CAT I and CAT IIATT were enrolled in to the study. Cat I ATT was including patients who have never taken ATT or taken ATT less than 4 weeks. Cat II ATT (Retreatment category) was including patients who has previously taken ATT for more than 4 weeks (will include relapses, treatment failures and defaulters). All previously treated patients were registered under Category I Retreatment. (As per New RNTCP guidelines from 1st January 2019).Informed written consent was taken from all patients. Selected Patients were given anti-tubercular treatment in RNTCP on the basis of their different weight bands. History of patients was taken in terms of chief complains (like fever, cough, weight loss, etc in cases of pulmonary TB and abdominal pain, backache /joint pain, seizures, nodulars welling, urinary complains, etc in cases of extrapulmonary TB). Follow up was done with sputum examination, weight recording, and specific radiological imaging (in case of extrapulmonary TB based on baseline investigations that was done) (e.g. USG in lymph node TB, genitourinary TB, CT (computed Tomography scan) in abdominal TB,MRI (Magnetic Resonance Imaging) in spine TB and CNS (central nervous system) TB, X ray chest in cases of pleural effusion, etc) and systemic examination of system involved.

Findings:

Table 1: Sociodemographic characteristics of study participants (n=830)

Sr No.	Characteristics	Number of participants	Percentage
1	**Age(in Years)**		
	13-20	138	16.63
	21-30	290	34.94
	31-40	144	17.35
	41-50	138	16.63
	51-60	67	8.07
	>60	53	6.39
	Total	830	100.00
2	**Gender**		
	Male	452	54.46
	Female	378	45.54
	Total	830	100.00
3	**Weight Bands**		
	25-39kg	182	21.93
	40-54kg	481	57.95
	55-69kg	163	19.64
	>70kg	4	0.48
	Total	830	100.00
4	**Type of TB**		
	PTB (Pulmonary TB)	458	55.2
	EPTB (Extra Pulmonary TB)	372	44.8
	Total	830	100.00
5	**Number of family members**		
	Lungs	458	55.18
	Lymph Nodes	162	19.52
	Pleural Effusion	158	19.04
	Abdomen	52	6.26
	Total	830	100.00

Out of total of 830 patients participated in the study majority were in the age a group of 21-30 years. Total 710 (85.5%) patients were between age group of 13-50 years. Among the study participants 452(54.5%) were males and 378 (45.5%) were females, 458 (55.2%) were suffering from PTB and 372 patients (44.8%) were suffering from EPTB.

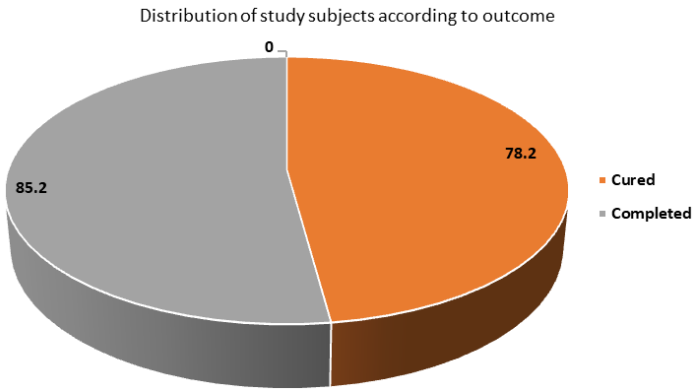

Figure 1: Distribution of study subjects according to outcome

Out of 458 PTB patients 358(78.2) were cured and out of 372 patients 317(85.2) patients completed treatment.

Table 2: Association between Age Group and Outcome (N=830)

Age (in Years)	PTB	Cured	EPTB	Completed
13-20	56	47(83.9)	82	71(86.6)
21-30	154	118(76.6)	136	115(84.6)
31-40	80	68(85.0)	64	52(81.3)
41-50	84	64(76.2)	54	48(88.9)
51-60	46	36(78.3)	21	18(85.7)
>60	38	25(65.8)	15	13(86.7)
Total	458		372	
PValue		0.213		0.904

The cure rate in PTB and Completed rate in EPTB has no significant correlation with age of patient.

Table 3: Association between gender and Outcome (N=830)

Gender	PTB	Cured	EPTB	Completed
Male	277	207(74.7)	175	149(85.1)
Female	181	151(83.4)	197	168(85.2)
P Value		0.027*		0.846
Chi-Square Test, P Value *Significant				

Cure rate was significantly better in females than males. Among EPTB patients, out of 175 male patients, 149 (85.1) have completed treatment and out of 197 female patients, 168 (85.2) have completed treatment. Difference was statistically not significant in treatment completion rate of EPTB in males and females.

Table 4: Association between type of TB and Outcome (N=830)

PTB/EPTB	N	Cured	Completed
Pulmonary TB	458	358(78.2)	
Extra-Pulmonary TB	372		317(85.2)
P Value		<0.001*	<0.001*
Chi-Square Test, P Value *Significant			

The cure rate for PTB and Completion rate for EPTB were 78.2% & 85.2% respectively.

Table 5: Association between type of TB and Outcome (N=830)

Site	Number	Cured	Completed
Lungs	458	358(78.2)	
Lymph Nodes	162		139(85.8)
Pleural Effusion	158		146(92.4)
Abdomen	52		32(61.5)
P Value		<0.001*	<0.001*

Treatment completion rates were best seen with pleural effusion (92. 4%) cases followed by lymphnode cases (85.8%) of TB, Pulmonary cases (78.2%)(cured) and least with Abdominal TB (61.5%) {reason for low treatment completion rate in abdomen TB were persistence of radiological lesions, despite of symptomatic improvement occurred in most patients}

Table 6: Association between Treatment Category and Outcome (N=830)

Treatment Category	Total	N	Cured	n	Completed
I	652	349	287(82.2)	303	266(87.8)
II	82	40	25(62.5)	42	29(69.0)
IR	96	69	46(74.2)	27	22(81.5)
P value:	0.001				
Chi-Square Test, P Value * Significant					

Cure and Completion rates were lesser in retreatment cases than new cases. However, this data cannot be compared as Cat II was abolished from 1stJanuary 2019. So, number of patients on Cat II and IR were farless.

Table 7: Association between weight band and Outcome (N=830)

Weight Band	Total	N	Cured	n	Completed
25-39kg	182	76	57(75.0)	106	89(84.0)
40-54kg	481	278	225(80.9)	203	173(85.2)
55-69kg	163	101	74(73.3)	62	54(87.1)
>70kg	4	3	2(66.7)	1	1(100.0)
PValue			0.341		0.923
Chi-Square v Test, P Value Not Significant					

Statistically there was no significant difference in cure and treatment completion among different weight bands.

Discussion

In the present study total 830 patients of tuberculosis (both PTB and EPTB) were studied, majority were in the age group between 21-30 years (range 13-78 years).According to India TB report 2019, Majority of TB burden is among the working age group. The 89% of TB cases come from the age group of 15-69 years. Thus, commonly affected age group was similar to present study. In present study out of 830 patients, 458 (55.2) were PTB (55.2%) and 372(44.8) were EPTB. In the present study treatment success rate among PTB & EPTB cases was 78.2% & 85.2% respectively. Similar findings was observed by Sama, J N et al[8] revealed treatment success rate among PTB & EPTB was 89.0% and 82.5%respectively.

In the present study out of 652 (78.6%) patients registered under Category I, 287 (82.2) of PTB patients got cured and 266 (87.8) of EPTB patients completed treatment. Out of 82(9.9%) patients registered for Cat II, 25 (62.5) patients got cured & 29(69) of EPTB patients completed treatment. Out of 96 patients registered for Cat I Retreatment, 46 (74.2) of PTB patients got cured

and 22(81.5) of EPTB patients completed treatment. Cure and Completion rates were lesser in retreatment cases than new cases. However, this data cannot be compared as Cat II was abolished from 01st January 2019. So, number of patients on Cat II and IR were farless. As per study done "Treatment Outcomes of Tuberculosis and Associated Factors in an Ethiopian University Hospital"[9] showed that treatment category was associated with unsuccessful treatment outcome especially for patients who were treated previously. The high proportion of unsuccessful treatment outcome in retreatment cases in the present study could be related to prior suboptimal therapy and drug resistance. As per study named "Profile of drug-resistant-conferring mutations among new and previously treated pulmonary tuberculosis cases from Aligarh region of Northern India."[10] Previously treated cases have high rate (20.03%) of MDR-TB than new TB cases (11.02%). In the present study, no significant difference was observed in treatment completion and weight bands of the patients.

Conclusion

Majority of tuberculosis patients were in the age group between 21-30 years and more common in males. Percentage of people suffering from PTB was higher as compared to EPTB. Pulmonary tuberculosis was more common than extrapulmonary tuberculosis (most common site was Lymph nodes among extrapulmonary tuberculosis). Among treatment categories, most patients (78.6%) were registered under Category I (new patients) as compared to retreatment cases (Category II and Category I Retreatment). Mean compliance of patients was 84.46% in IP and 84.82 during CP. Among PTB patients cure rate was 78.2%, while among EPTB patients treatment completion rate was 85.2%.

'Conflict of Interest Declaration': No conflict of interest

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Ethical Clearance: Approved by institutional ethical committee. Name-Institutional Ethical Committee Human Research, Lokmanya Tilak Municipal Medical College & General Hospital. Date-12/01/2018Reference number-IEC/135/18

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