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Review Article

Revised National TB Control Program in India Benefit of Transition from Intermittent to Daily Therapy

Ravindran Chetambath*

Professor of Pulmonary Medicine, DM Wayanad Institute of Medical Sciences, Wayanad, Kerala, India

***Corresponding Author**: Ravindran Chetambath, Professor of Pulmonary Medicine, DM Wayanad Institute of Medical Sciences, Wayanad, Kerala, India.

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Abstract

Revised National TB Control Program (RNTCP) was implemented in India in 1997 using a thrice weekly regimen administered by directly observed therapy. At the same time many countries followed daily regimen. Cure rates in India have been comparable with countries using daily dosing. However, during the maintenance phase many states reported multidrug resistance and extensive drug resistance. This prompted reconsideration of the existing program and introduction of daily regimen in place of intermittent regimen. When a new program is being implemented it is important that one should take stock of the deficiencies of the previous program leading to its failure. This will help the administrators to plan a foolproof program.

Keywords: *Revised National Tuberculosis Control Program; Directly Observed Short Course; Multidrug Resistance; Daily Regimen*

Introduction

The World Health Organization (WHO) declared tuberculosis (TB) a global public health emergency in 1993 and since then intensified its efforts to control the disease worldwide [1]. India accounts for 25% of global TB burden. More than 40% of the population is infected in the country. There are 2.5 million prevalent cases of all forms of TB. About 2.2 lakhs of people die of TB annually. 3% among new TB cases and 12 - 17% among previously treated TB cases have MDR-TB. An estimated 1.1 lakh HIV associated TB occurred in 2014 and 31000 patients died among them.

RNTCP was launched as a national program with a plan to scale up in a phased manner. It adopted the internationally recommended directly observed short course strategy. It enjoyed the backup of the well-knit network of health care system of the country, a new hierarchal human resource chain and huge external funding. The concept of daily, directly observed therapy, incorporating a full six months of Rifampicin has been adopted by the majority of countries worldwide as a major part of Stop TB Strategy [2]. Lower rates of cure in the earlier National TB Control program (NTP) highlight the operational challenges of delivering a daily regimen over an extended period of time [2,3]. Effective and patient friendly treatment with short course chemotherapy was given under direct observation. Accountability through proper recording and reporting and effective supervision were emphasized. The objective of RNTCP was to achieve 85% cure rate among new smear positive cases and a case detection rate of at least 70% from the community. The entire country was covered by RNTCP in 2006. RNTCP adopted thrice weekly regimen for drug sensitive TB. For new TB cases category - I treatment was given in the form of 2R3H3Z3E3 + 4R3H3E3. Retreatment cases, treatment after default and failure cases are given Category II regimen which include 2S3R3H3Z3E3 + 1R3H3Z3E3 + 6R3H3E3.

The program has consistently been achieving global benchmarks of case detection and treatment success rate since 2007. Cure rates in India have been comparable with countries using daily dosing. TB mortality has dropped significantly, and the prevalence of TB has declined slightly over the last two decades [4]. The therapeutic regimens given under direct observation as recommended by WHO have been shown to be highly effective for both preventing and treating TB [5]. However, during the maintenance phase many states reported multidrug resistance and extensive drug resistance. It took 30 years for the previous national tuberculosis control program to be declared a failure, but it took only 10 years or less to say that RNTCP is not achieving the desired result.

RNTCP program is now introducing daily regimen for drug sensitive tuberculosis. This will be introduced in 104 districts of the country in the first phase and then scaled up to cover the entire country. Treatment in intensive phase will consist of 8 weeks of INH, Rifampicin, Pyrazinamide and Ethambutol in daily dosage as per four weight band categories. Pyrazinamide will be stopped in the continuation phase while other 3 drugs will be continued for another 16 weeks as daily doses. In the previously treated cases, intensive phase (IP) will be of 12 weeks, where injection streptomycin will be stopped after 8 weeks and the remaining 4 in daily dosage as per weight band will be continued for another 4 weeks. At the start of continuation phase (CP), pyrazinamide will be discontinued, while the other 3 drugs will be continued for 20 weeks. In this context it will be better to take stock of the deficiency of intermittent regimen and, to know whether it is the failure of the regimen or failure of the program implementation. Unless we take measures to correct this, within no time the new program will go for another revision.

Directly observed therapy short course

Due to the fact that India has the maximum number of cases and highest burden of TB in the world, an effective TB control program in India is essential. It also will have global implications in the international TB control effort. Directly observed therapy short course (DOTS) is the internationally recommended strategy to ensure cure of tuberculosis. It has become the standard for the diagnosis, treatment and monitoring of tuberculosis worldwide and has been implemented in 182 of 211 countries, covering more than 77% of world's population [6,7].

Incidence of TB in India is 2.8 million in 2017 out of a global burden of 10.4 million. The reported smear positive cases among this are 902702. Treatment outcome for the notified cases under RNTCP in 2015 is as follows. New smear positive patient cured is 83% and an additional 4% completed treatment. Death among new smear positive cases is 4%. Treatment failure was reported in 2% and default reported in 5%. 89% among sputum smear cases completed treatment with a death rate of 4%, and default of 6%. Percentage of smear-positive re-treatment cases out of all smear-positive cases is 24% [8]. The causes of re-treatment include relapse, failure, and default in treatment. Retreatment success after treatment relapse is 74%, retreatment success after treatment default is 66% and retreatment success after treatment failure is 58%. Death among retreatment smear positive cases is 8%. RNTCP does not follow up the patients for any period of time after successful completion of treatment to determine whether they relapse. There is no statistically significant difference between the two treatment groups in terms of cure or treatment completion. Hill categorically admits that superiority of DOTS over unsupervised therapy for routine TB, care has not yet been shown in an evidence-based fashion [9]. His contention is that it is not better in suboptimal settings and indicates that the program quality must be strong enough to yield its optimal benefits. Of the new smear-positive patients registered under Category 1, the default and failure rates were 16% and 4%, respectively, reported by Thomas., *et al*. in 2005 [10] and 12% and 5%, respectively, reported by Chandrasekaran., *et al*. in 2007 [11]. Mehra and colleagues (2008) recorded a failure rate of 3.4% [12]. The distribution of default and failure cases in Category 2 patients was 22% and 14% respectively, in the study by Mukherjee [13]. Hill in his review of studies from around the world calculated an average failure rate to be 2.4 ± 2.2% for 21 culture-based studies and 2.5 ± 1.7% for 9 smear-based studies [9]. Nevertheless, high relapse rate of 11- 13% has been reported in patients treated by DOT under RNTCP from several locations in India over the last many years [10,14,15].

Most authorities are convinced that DOTS improve treatment effectiveness, drug resistance rates, and overall TB control. It is a fact that the intermittent regimen used under the program is equally effective under direct observation as compared to the daily regimen and

choosing a daily regimen does not undermine the successes of the program [16,17]. There are no good quality studies that may cast light over the preferences, adherence, and felt problems of the beneficiaries of RNTCP. Without studying the felt needs of the patients, the decision to modify a strategy so strongly advocated by the WHO, may not be a correct strategy. Role of HIV, Multi Drug Resistant (MDR) TB, re-infection with a different strain of *Mycobacterium tuberculosis* and outcomes in the pediatric age group, also need to be investigated for relapse. However, based on the above evidences and in the interest of having uniformity of care across all healthcare sectors it is decided to introduce daily regimen under RNTCP. It is argued that this will help to achieve universal access to quality TB care and prevent development of drug resistance. When such a decision is taken, and program is being reintroduced, it will be better to take stock of what went wrong in the previous programs. It will help the program managers to take corrective steps so that the new program will not have the same fate after a few years.

Administrative failure

The initial enthusiasm during the launch of the program faded away too quickly. There was lack of commitment on the part of administrators. Most of the program managers and contractual staff were committed and RNTCP gained a lot of ground among common man due to their hard work. Most of the medical college faculty who were suspicious initially cooperated and it was bringing good result. This was mainly due to the concerted effort of program managers, District TB officers, medical college core committee members and contractual staff. But after a few years these staff were shuffled, and their grievances were never attended. Contractual staff on meager wages struggled to get that amount released in time. District program managers of National Health Mission were responsible for dealing finances. Since they have many other programs to look after, due importance to TB program was never given. Once commitment is lost and enthusiastic workers left for greener pastures, the program lost its direction.

Treatment adherence is a critical determinant of treatment outcomes. Poor outcome and emergence of drug resistance are mainly due to irregular and incomplete treatment. The DOTS strategy has been the backbone of TB programs for the last decade. In certain places, strict adherence to the program by healthcare worker has resulted in cost-effective and sustainable control of TB epidemics. However, accumulating evidence has pointed to the effectiveness of a wide variety of approaches including community and family-centered DOTS, which is more achievable for most developing healthcare systems and produce comparable outcomes to healthcare worker supervised DOTS.

Treatment support system developed with mutual trust and respect between the patient, family, providers, treatment supporters and the health system will promptly identify and address all possible factors that could lead to treatment interruptions. This includes not only medical factors such as co-morbidities, adverse drug reactions and emergencies, but also various social, vocational, nutritional, economic and psychological stress experienced by the patient throughout the course of treatment. Regular and effective supervision by the health supervisors at various levels and close monitoring of the progress made by the patient on treatment are critical components to ensure high standards of care. Capacity building among health care workers and engaging local community-based organizations, self-help groups and patient support groups could prove to be effective interventions to promote treatment adherence [18,19]. Supervision and support should be individualized and should include a range of recommended interventions including patient counseling and education. An important element of the patient centered strategy is to assess and promote adherence to the treatment regimen, and, to address poor adherence when it occurs. These measures should be tailored based on the patient's clinical and social history. It also should be mutually acceptable to the patient and the provider.

Role of private practitioners

India continues to have high TB incidence, and, the mortality due to TB is still unacceptably high. The challenges of TB control in India are magnified by the existence of parallel systems for TB diagnosis and treatment – the public and the private. Each system takes care of approximately half of the TB cases [20]. The methods and standards vary greatly depending on whether public or private care is accessed

and furthermore what type of private care is sought, from super-specialty tertiary institutions to non-qualified providers [21]. RNTCP was implemented through the existing health care system, the pivotal role being played by district TB centers. There were additional staff supplement with adequate materials and funds. Every peripheral health center is empowered to take up the challenge of diagnosing, treating and monitoring TB patients. Since medical colleges are opinion leaders in health care and trains new generation of doctors and paramedics, there was an attempt to bring all medical colleges in the loop and hence task force is being organized in public and private medical education institutions. At the same time, we are all aware that 50-60% of health care delivery in the country is through private practitioners. They work in institutions as well as individually. RNTCP, to a large extent, failed to bring these practitioners into its fold. There were many concerns for them which were not addressed properly. Hence treatment of tuberculosis through private practitioners remained largely out of the program. Many institutions do not want to join a Govt. run program for fear of auditing. But most important of all is the fear of exposing their know how in treating tuberculosis. It is known that many practitioners use non-rifampicin containing regimen, non-pyrazinamide containing regimen and levofloxacin containing regimen for treatment of new smear positive cases. - Many have more concern on liver dysfunction, peripheral neuropathy etc. and hence loads the patient with two or more vitamins. This will all lead to non-compliance. Once treatment response is not adequate, these patients are referred to the program. The previous treatment history is also poorly documented and may be a source of bias. It has been recorded that patients turn up at RNTCP after seeking medical care from many providers in the private sector.

Availability of drugs in the open market

When the Government is committed to provide good quality anti TB drugs to patients in the country, why the drugs were made available in the open market? When these potent drugs are freely available, there is a chance to misuse these drugs to the extent of treating with inadequate regimen, inadequate dosing etc. This will lead on failure and development of resistance. If it was banned when RNTCP was expanded to cover the whole nation, all the patients (suspected or diagnosed) will be brought to the single window of DOTS. This will ensure uniform treatment, treatment completion and follow up.

Overemphasis on sputum microscopy and neglecting clinical and radiological evidence

In NTP the main disadvantage being pointed out is overemphasis on radiology. X ray being highly sensitive but poorly specific leads to more of false positives. When we turned to RNTCP the emphasis shifted to sputum microscopy. This is a highly specific test even though sensitivity is poor. So, we have a proportion of false negatives in the society. Actually, the planners should have developed a more realistic diagnostic test combining both. In the recent guidelines a new entity is included as clinically diagnosed TB which is diagnosed through clinical and radiological methods. Overdependence of sputum microscopy led to a peculiar situation in which clinicians failed to use their clinical judgment but blindly followed sputum microscopy result. Even after improvement in staining and detection, the sputum pick up remained as low as 60%. So, 40% of TB cases roam around without being detected. When these patients are reported as negative after repeated sputum examination, there is hesitancy in starting anti-TB drugs. This leads to delay in starting treatment and progression of disease.

Conclusion

Urgent efforts are necessary for the control of tuberculosis in the country. Both intermittent and daily regimens are proved to be effective in treating tuberculosis. What is most essential is to ensure adherence to the program both from patients' side and provider side. It is important to take stock of the factors leading to failure of previous programs and to take appropriate measures so that what is implemented now remains the standard of care for TB in years to come.

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