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DOTS at a tertiary care center in northern India: successes, challenges & the next steps in tuberculosis control

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***Background & objectives*: The past decade has seen a rapid expansion of directly observed treatment, short-course (DOTS) centers throughout India, under the guidance of the Revised National Tuberculosis Control Programme (RNTCP). While expansion has been rapid and extensive, few reports exist detailing individual DOTS centers' experiences, their challenges, and their successes. We present a brief report on the status of a DOTS center being run at a large tertiary care center in northern India for almost four years (2001-2005).**

***Methods*: The DOTS center followed RNTCP guidelines for the evaluation and treatment of suspected TB cases. A register carrying detailed information of all patients seen at the DOTS center was kept by the senior clinician. Data from this register were extracted and analyzed for descriptive measures.**

***Results*: A total of 1490 patients were evaluated. Of the 768 patients with cough, 27 per cent (211) were found to be sputum positive for acid-fast bacilli (AFB). Among patients who were initiated on anti-tuberculosis medications, cure was achieved in 92 per cent (71 of 77) of new sputum smear positive patients; treatment completion was achieved in 91 per cent (91 of 100) of extrapulmonary TB (EPTB) and 75 per cent (46 of 61) of sputum-negative pulmonary TB patients. Overall treatment success was achieved in 86 per cent (229 of 266).**

***Interpretation & conclusion*: Treatment results were in keeping with the RNTCP guidelines. Tertiary care centers appear to be excellent place for education of medical students and operational research. The latter is much needed, as HIV-TB co-infection, multi-drug resistant TB, and EPTB continue to be major public health threats even in the era of DOTS.**

Key words Directly observed treatment short-course (DOTS) - India - Revised National Tuberculosis Control Programme (RNTCP) - tuberculosis

Tuberculosis (TB) remains one of the top killers in the developing world. This is especially true in India, where each year approximately two million new cases and 500,000 TB related deaths occur[1]. To combat this overwhelming problem, the Government of India piloted and then expanded a strategy of directly observed treatment short-course (DOTS) under the Revised National Tuberculosis Control Programme (RNTCP)[2]. Piloted in 1993 and expanded nationally in 1997, DOTS now covers over 1 billion people, almost entire country[3]. Similar to the WHO-endorsed DOTS strategy throughout the world, the RNTCP aims at achieving 70 per cent case detection rate through sputum microscopy and 85 per cent treatment success rate amongst those who have been detected. While many claims have been made about the success of DOTS expansion in terms of numbers covered[3-10], there are only a few reports providing details about actual treatment success rates[11-13], the problems associated with them[14-17], and failures of DOTS strategy[18].

Here we report our experience of running a DOTS center at All India Institute of Medical Sciences (AIIMS), New Delhi, a large tertiary care teaching hospital and research institution in northern India, from December 2002 to August 2005. Initially, the DOTS programme started as a pilot project that was implemented under Employees Health Scheme (EHS) for AIIMS employees and their dependents, a population of 80,000. Following the publication of the results[11], some concerns were raised about the less than optimal treatment success rate (80%), the low rates of sputum microscopy (39%), and the low yield of culture among smear-positive cases (55%). These poor results at one of India's top medical centers were a cause of alarm for other DOTS centers in the country, the bulk of which were in areas with far fewer resources[19].

Subsequent to the pilot project among AIIMS employees and their dependents, the DOTS center was expanded to cover all the patients in the catchment area surrounding AIIMS. To address some of the challenges and outcomes of the pilot study, we carried out a retrospective analysis of the data from this expanded project.

Material & Methods

Study population: Patients presented to the DOTS center from a population of 100,000 living within a 4 km radius of AIIMS were included in the study. This included a large number of AIIMS employees and their dependents, as also people from the general population.

Classification of cases: Patients were referred to the DOTS center from various out-patient departments of AIIMS, and from other public and private health care providers in the area. RNTCP guidelines were followed, and detailed methodology has been presented in the previous report[11]. Briefly, all patients with cough of three weeks or more (chest symptomatics) submitted three separate sputum samples (spot-morning-spot) for microscopy examination. Patients with at least two positive specimens for acid-fast bacilli (AFB) or one positive AFB specimen with additional radiological features suggestive of lung involvement were diagnosed to have sputum smear-positive pulmonary tuberculosis (PTB). Patients whose specimens were all negative for AFB were given a trial of antibiotics for 1-2 wk and if symptoms persisted were subjected to chest radiographs. If chest radiograph findings were suggestive of tuberculosis, the diagnosis of sputum smear-negative PTB was made.

The diagnosis of extrapulmonary tuberculosis (EPTB) was based on the following criteria: (*i*) suggestive clinical features; (*ii*) positive microbiological or histopathological evidence of *Mycobacterium tuberculosis* from an extrapulmonary site; (*iii*) radiographic changes suggestive of tuberculosis; and (*iv*) a satisfactory response to anti-tuberculosis therapy (ATT)[11].

All diagnosed TB patients were divided in three categories for therapeutic purposes[1]. During the initial, intensive phase of treatment, patients were given directly observed therapy three times a week. The subsequent continuation phase consisted of a first dose under direct supervision followed by a blister pack of medicines for the rest of the week. Patients returned with the empty blister pack every subsequent

week. Medicines were dispensed by the DOTS provider at the DOTS center and home visits for tracing of defaulters were made by DOTS team as per RNTCP guidelines.

Data analysis: Patient data were extracted from the registers maintained and kept at the DOTS center. Data analyses for descriptive statistics were made using SPSS version 10.0.

Results

A total of 1490 patients presented to DOTS center during the study period. Of these, 768 (52%) patients were chest symptomatic and they were subjected to sputum microscopy for AFB. Of these, 211 (27%) were found to be smear-positive. Another 557 (72%) were found to be smear-negative TB. Another 722 of 1490 (48%) were found to have EPTB. Of the 100 patients with EPTB included in the study, 69 had lymph node TB, 12 had osseous TB, 11 had TB pleural effusion, three had disseminated TB, three had abdominal TB and two had genital TB.

Being a tertiary care center many patients belonged to different regions of the country; as per RNTCP guidelines, such patients were referred to DOTS center located in the area of patient's residence. As such, only 269 patients with TB had treatment outcome documented at the AIIMS DOTS center; another 3 patients were transferred during the study period. As a result, only 266 patients were available for analyses of treatment results (Table I). Treatment success rate was highest for new (category I) sputum positive PTB patients, with 71 of 77 (92%) being documented cures. Treatment completion was achieved in 91 per cent (91 of 100) of EPTB patients and 88 per cent (92 of 105) of all sputum positive PTB patients. Overall treatment success was noted in 86 per cent (229 of 266) of patients (Table II).

Overall treatment success rate achieved was higher for EHS cohort (88%) as compared to non-EHS cohort (85%). For new sputum smear positive PTB patients it was 100 per cent (25/25) for EHS cohort. The EHS cohort also showed a lower default rate (1.33%) as compared to non-EHS cohort (8.9%).

Some adverse drug reactions were also noticed during the course of treatment. These included nausea and vomiting in 30 (11%) and transient gastritis in 25 (9%) patients, which subsided following dietary advice and measures aimed at reducing gastric acid secretion. At the end of intensive phase of

Table I. Demographic characteristic of 266 patients at DOTS center

Characteristic	Number (%)
Median age (range) yr	25 (8-70)
Female	115 (43.2)
Male	151 (56.8)
AIIMS employee or dependent	75 (28.2)
Definite contact with TB+	15 (5.6)
Other family members treated with DOTS	25 (9.4)

Table II. Treatment outcome in 266 patients at DOTS center*

TB classification	Number of patients							
	Cat-I†	Cat-II†	Cat-III†	Failure	Defaulter	Died	Total	Treatment Success (%)
Smear-positive pulmonary TB	77 (71)	28 (21)	____	3	7	3	105	92 (88)
Smear-negative pulmonary TB	38 (30)	10 (8)	13(8)	5	6	4	61	46 (75)
Extrapulmonary TB	55 (52)	14 (13)	31(26)	3	5	1	100	91 (91)
Total	170 (153)	52 (42)	44 (34)	11	18	8	266	229 (86)

*Only those patients who were not transferred due to location of residence; †Category and figures in parentheses denote no. of patients who achieved treatment success for each group

treatment, some abnormalities in laboratory tests were also observed. These were as follows: elevated serum aspartate aminotransferase or alanine aminotransferase (>50 IU/l) in 9 (3%), elevated serum alkaline phosphatase (>280 IU/l for adults and >840 IU/l for children) in 2 (1%), elevated serum uric acid (>7.4 mg/dl) in 8 (3%) and low platelet counts (<1.5 lac/µl) were observed in 6 (2%) patients. These patients did not have any clinical symptoms or signs pertaining to the laboratory abnormalities and were closely followed up during the continuation phase of treatment without stopping ATT. These patients did not develop any symptoms and signs suggestive of overt adverse drug reaction and laboratory abnormalities returned to normal at follow up tests done after 1 month of continuation phase. None of the patients developed any treatment limiting adverse reactions.

Discussion

In this cohort of patients presenting to the AIIMS DOTS center, excellent results were achieved at follow up. This reinforces results of the previous study, which suggested that tertiary care centers should be the places where innovative TB control programmes can be developed and monitored[11]. This is especially true as much needed chemotherapeutic and diagnostic technologies become available and require evaluation before being made a part of the national policy. For example, we are having surveillance for multi drug resistant-TB (MDR-TB) in category-II patients by subjecting them to sputum culture and drug sensitivity testing so as to detect MDR-TB cases early in these patients where chances of MDR-TB is quite high as compared to fresh TB cases[20]. Additionally, the DOTS center has provided training for medical and nursing students and residents in the care, prevention, and policy aspects of TB control.

Treatment of EPTB was surprisingly effective. This provides support to the argument that EPTB can and should be more effectively addressed in the national TB control programme. Currently, the focus is on the more infectious smear-positive pulmonary TB; however, as DOTS continues to expand, it has become clear that the ultimate control of TB cannot be achieved simply through treating pulmonary cases. Our center did an excellent job managing the more complicated regimens associated with EPTB; as there were sufficient physical and human resources to support this endeavor than are commonly found in other Indian healthcare settings. During this era of growing HIV epidemic, EPTB becomes more important as chances of developing EPTB in immunocompromised patients are higher than their immunocompetent counterparts[21]. It seems high time that resources for EPTB are allocated to overcome the diagnostic dilemma of varied clinical presentation.

In conclusion, a powerful TB control programme such as RNTCP is required to combat resurgence of TB due to HIV infection. Involvement of medical schools is vital for expansion of DOTS programme as these are involved in the training of medical students. Their importance also lies in the conducting operational research, required to develop new tools against fight of scourge of TB. The latter is especially required for EPTB, MDR-TB and TB-HIV co-infection.

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