Original Article

DEFAULT DURING THE INTENSIVE PHASE OF TREATMENT UNDER DOTS PROGRAMME

V.Chandrasekaran[1], P.G.Gopi[2], R.Subramani[2], A.Thomas[3], K.Jaggarajamma[4] and P.R.Narayanan[5]

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Summary

Objective: To study default and its associated risk factors during the intensive phase of treatment among new sputum smear positive patients registered under a Directly Observed Treatment- Short Course (DOTS) programme in Tiruvallur district, Tamil Nadu.

Design: Analysis of data collected from the Tuberculosis Register, treatment cards and interview schedules during May 1999 to December 2002.

Results: Of the 1463 patients registered, drug regularity results were available for 1406 patients. The cure rate was 76% with an overall default rate of 15%, of which nearly three-fourth occurred during the intensive phase. The potential risk factors were identified by multivariate analysis. A higher likelihood of default was associated with age $\geq$ 45 years (AOR=1.9; 95% CI=1.2-3.0), illiteracy (1.6; 1.0-2.4), alcoholism (2.7; 1.8-4.2), DOTS inconvenience (1.9; 1.1-3.4) and cases identified and referred by the community survey (1.8; 1.1-3.0). Of the 75 defaulters from two cohort periods visited separately, 53 defaulted during the intensive phase. Among these, only 31 patients were interviewed since 17 (32%) migrated, three died, one was untraceable at the address provided while another had treatment elsewhere. Drug related (84%) and work related (32%) problems were the other reasons for default reported by the patients interviewed.

Conclusion: The majority of defaults occurred during intensive phase of treatment. All efforts should be made to retrieve these patients and return them to treatment to achieve the expected goal of the RNTCP.

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Key words: Tuberculosis, cure, default, DOTS.

INTRODUCTION

The crusade to control tuberculosis gathered momentum after the discovery of various anti-tuberculosis drugs since 1944 and evolution of effective regimens for the management of tuberculosis. Yet, the disease is highly prevalent and continues to be a leading cause of death[1]. In India, the National Tuberculosis Control Programme (NTP) was started in 1962. A comprehensive review of this programme highlighted the failure of NTP due to various reasons like reliance on X-ray diagnosis, non-standard regimens, default and incomplete treatment[2]. The Government of India launched the Revised National Tuberculosis Control Programme (RNTCP) in 1993[3-4] in a phased manner using the globally recommended DOTS strategy and with the goals of curing 85% new smear positive patients and detecting a minimum of 70% of these cases. To achieve 85% cure, it is essential that all patients started on treatment should complete the full course of treatment. The main reason for a programme not performing optimally is because patients fail to adhere to treatment rather than due to inadequacy of regimen[5]. Irregular treatment leads to more failures thus enlarging the pool of infectors and increasing the risk of developing drug resistant TB. Patients who complete treatment have a better understanding of the duration of TB treatment than patients who interrupt treatment. Therefore, it is necessary to understand the reasons for default after initiation of treatment and plan strategies to reduce default and thereby increase the successful treatment outcome.

In collaboration with the Tamil Nadu Government, Tuberculosis Research Centre (TRC), Chennai implemented the DOTS Centre strategy in 1999 in a population of 580,000 in Tiruvallur district.

Tuberculosis Research Centre, Chennai

1. Research Officer 2. Assistant Director 3. Deputy Director (Sr. Grade) 4. Medical Social Worker 5. Director

Correspondence: Dr. P.R. Narayanan, Director, Tuberculosis Research Centre, Mayor V.R. Ramanathan Road, Chetput, Chennai-600 031; Phone: 91-(044)-28369600; Fax: 91(044) 28362528; E-mail: nrparanj@md2.vsnl.net.in

Nearly 3500 patients were diagnosed and put on treatment by the end of 2002. In an earlier study[6] from the same area, we analysed the treatment outcomes of a cohort of all patients registered from May, 1999 through April, 2000 and reported an overall default rate of 19% during treatment and identified various risk factors for default among 676 patients. Seventy six percent of the defaults occurred in the intensive phase. Other studies[7-10] conducted elsewhere have documented the default rate of new smear positive patients identified the risk factors associated with default and the remedial actions to reduce the default. However, these studies have not looked into the details of patients defaulting by the end of intensive phase of treatment. The present report summarizes the causes of default among a cohort of new sputum smear positive patients during the intensive phase of treatment under the RNTCP programme and the risk factors associated with default. The need to work together to address these challenges in order to retrieve these patients and return to treatment to achieve more treatment success rate in RNTCP is also emphasized.

MATERIAL AND METHODS

Patients with tuberculosis diagnosed in 209 villages and 9 urban units in the study area (consisting of 17 primary health centres) were treated according to the RNTCP guidelines[3-4]. The treatment was decentralized taking patient's convenience in taking treatment into consideration. Patients reporting at any one of these health facilities with symptoms suggestive of tuberculosis were diagnosed based on three sputum examinations by smear microscopy for acid-fast bacilli (AFB). Cases of tuberculosis were also diagnosed from a community survey that was simultaneously being carried out in the same area to assess the epidemiological impact of DOTS. Information on the date of start of treatment, name, sex, age, category, address, sputum smear results initially and during the treatment and the treatment outcome at the end of treatment were available from Tuberculosis Register (TB Register) maintained in the Tuberculosis Unit (TU) of the area. The RNTCP definitions of terms such as 'cure', 'treatment completed', 'default' and 'failure' were used for assessing treatment outcomes of the patients.

All new sputum positive patients registered from May 1999 to December, 2002 formed the study population. Patients were interviewed at their residence by trained health workers using a semi-structured questionnaire during the intensive phase of the treatment. Information on their socio-economic and demography profile, literacy status, smoking and drinking habits, their perception of tuberculosis and problems in taking drugs regularly was elicited. The treatment cards maintained for each patient registered under this programme provided details about regularity and the consumption of the drugs. A medical social worker separately visited all defaulters of the two cohort periods 1st to 2nd Qr; 1999 and 3rd to 4th Qr; 2001 at their residences to elicit reasons for default. In the case of patients who had migrated or died, the family members were interviewed. Others were contacted and the reasons were elicited and recorded.

Data entry and statistical analysis

The data, after scrutiny, were entered and verified by keying in the entries twice. Subsequently the data was edited and corrected for discrepancy and missing information. The distribution of patients according to treatment outcome was used to assess the potential risk factors for intensive phase defaulters with other patients (excluding expired and failure) as reference group using univariate and multivariate analysis. The analysis was performed using Epi-Info version 6.04d (Centres for Disease Control, Atlanta, GA) and SPSS/PC+, version 4.0 (SPSS Inc. Chicago, IL, 1990). A P value of ≤ 0.05 was considered as statistically significant for interpretation of the findings.

RESULTS

During the period from May 1999 to December 2002, a total of 3485 patients were registered for treatment in all categories (Cat I: 1657, Cat II: 521 and Cat III: 1307) under the programme. Of the 1657 Cat I patients, 1463 were new sputum positive cases. The number of doses consumed was not available for 57 (4%) of 1463 Cat I patients at the time of analysis. Hence, the remaining 1406

(96%) patients only were included in the subsequent analysis. Of these, 1067 (76%) were cured, 208 (15%) defaulted, 58 (4%) died and 73 (5%) failed. Of the 208 defaulters, 117 (56%) defaulted during the first two months and another 33 (16%) during the extension period of treatment in the intensive phase (Table1). In all, 150 (72%) defaulted by the end of the intensive phase. Among the 208 patients defaulters, 31 (15%) defaulted by the end of first month (12 doses) and 68 (33%) patients in the last two weeks of the (19-24 doses) the intensive phase. Another 33(16%) defaulted in the extension phase of treatment. Sputum examination was done for 83 of 150 defaulters and 40% (39 of 83) were negative on smear. Of the 58 patients who died during the course of the treatment, 42 (72%) died by the end of the intensive phase.

(1) Risk factors for default in the intensive phase of treatment: Univariate analysis of the cases of default during the intensive phase of the treatment showed that patients who were aged ≥ 45 years (OR=2.0; 95% CI=1.4-2.8), male (OR=3.0; 95 CI=1.7-5.5), illiterate (OR=1.7; 95% CI=1.1-2.5), alcoholics (OR=3.3; 95% CI=2.2-4.9), smokers (OR=2.7; 95% CI=1.8-4.2), and those who reported DOTS as being inconvenient (OR=1.8; 95% CI=1.0-3.3) and finally those cases referred in the community survey (OR=1.6; 95% CI=1.1-2.6) were likely to default from treatment (Table 2). Variables like occupation of the patient, income, initial weight, interval between onset of symptoms and action taken were not found to be associated with default (not shown in the table). Multivariate analysis (logistic regression) demonstrated that higher likelihood of default was associated with patient's age (≥ 45years) (AOR=1.9; 95% CI=1.2-3.0), illiteracy (AOR=1.6; 95% CI=1.0-2.4), alcoholism (AOR=2.7; 95% CI=1.8-4.2), DOTS inconvenience (AOR=1.9; 95% CI=1.1-3.4) and cases referred by the community survey (AOR=1.8; 95% CI=1.1-3.0).

(2) Reasons for default from a sample of patients: Of the 75 defaulters from two cohort periods, visited by the medical social worker, 53 (71%) patients defaulted by the end of the intensive phase, 17 (32%) had migrated; three died; one had given inadequate address and another reported to have completed the treatment from elsewhere. Among the remaining 31 patients who were interviewed, 84% attributed their default to drug related problems, 32% to work related problems and 23% each to alcoholism and being

Table 1: Drug regularity and unfavaurable outcome of new sputum positive cases registered in a DOTS programme during May 1999- December, 2002

No. of doses		No. of patients		
		Defaulted	Died	Failed
1-6	IP	19	10	-
7-12	IP	12	4	-
13-18	IP	18	4	-
19-24	IP	68	19	-
25-30	Ext. IP	4	-	-
31-36	Ext. IP	29	5	-
25-28 or 37-40	CP	22	4	6
29-32 or 41-44	CP	12	4	14
33-36 or 45-48	CP	11	4	9
37-41 or 49-53	CP	13	4	44
Total		208	58	73

IP = Intensive Phase (2 months – 12 doses per month)
Ext. IP = Extension of Intensive Phase (1 month – 12 doses per month)
CP = Continuation Phase (4 months –4 doses per month)

symptom free followed by domestic problems and taking treatment from outside (all multiple reasons and data not tabulated).

DISCUSSION

The present study highlights the problem of default during the intensive phase and the potential risk factors associated with default. The overall default rate of 15% observed in our study was much higher than the national average[3]. Nearly three-fourth of patients defaulted during the intensive phase of the treatment. Among 208 patients, more than half had defaulted at the end of second month, and one-third of the patients defaulted at the time when sputum smear examination became due. Patients identified in the community survey were less symptomatic and less infectious[7]. Smear positive patients diagnosed in the community survey were less compared to patients diagnosed at health facility (45% vs. 65%). Smear positive community survey patients also had lower grade smears than smear-positive health facility patients. Only 3% of community survey patients had a grade 3 smear compared to 42% of the health facility patients. A significantly higher proportion of community survey smear-positive patients did not have chest symptoms (cough >3 weeks) compared with health facility smear positive patients (28% *vs*. 13%). These symptoms usually subside during the intensive phase and patients are likely to default subsequently because they become symptom free. They do not realize the need to take the entire course of treatment. These findings were similar to those obtained in an earlier study[6]. Illiteracy and inconvenience (due to loss of wages and the lack of a companion for the patient when required) of DOTS (a newly added variable) were the additional risk factors found in the present study. The community survey being conducted in this area to measure the epidemiological impact of DOTS strategy is a special intervention and hence need not be generalized to other settings where only case detection by passive case finding exists.

Similar findings have been reported from other studies conducted elsewhere. A retrospective

Table 2: Risk factors for default during the intensive phase of treatment among new smear positive patients registered under DOTS programme

Factors		No. of pts.	Def.(%)	OR (95% CI)	AOR (95% CI)
Sex	Female	298	15 (5.0)		
	Male	977	135 (13.8)$^{@}$	3.0 (1.7-5.5)	
Age	< 45 years	678	58 (8.6)		
	≥ 45 years	597	92 (15.4)$^{@}$	2.0 (1.4-2.8)	1.9 (1.2-3.0)
Education	Literate	668	53 (7.9)		
	Illiterate	525	66 (12.7)$^{+}$	1.7 (1.1-2.5)	1.6 (1.0-2.4)
Drinking	No	756	45 (6.0)		
	Yes	439	75 (17.1)$^{@}$	3.3 (2.2-4.9)	2.7 (1.8-4.2)
Smoking	No	627	37 (5.9)		
	Yes	567	83 (14.6)$^{@}$	2.7 (1.8-4.2)	
DOTS _ convenient	No	120	18 (15.0) *	1.8 (1.0-3.3)	1.9 (1.1-3.4)
	Yes	928	81 (8.7)		
Diagnosis	Active	198	33 (16.7)*	1.6 (1.1-2.6)	1.8 (1.1-3.0)
	Passive	1077	117 (10.9)		

* $P<0.05$, $^{+}$ $P<0.01$, $^{@}$ $P<0.001$; OR = Odds Ratio; AOR = Adjusted Odds Ratio;CI = Confidence Interval

Note: For 'education, drinking and smoking', the number of patients is less than 1275 due to the non-availability of all patients at the time of interview within a week after treatment started. For 'DOTS_convenient', the number is still lower when interviwed at the end of 2nd month after treatment started.

analysis[8] of 9822 new pulmonary TB cases registered between 1998 and 2000 in twenty four public tuberculosis dispensaries in Istanbul showed that the treatment success and the default rates were 82% and 9% respectively. Another retrospective cohort analysis[9] of new smear positive TB patients diagnosed during 1999-2000 and treated under DOTS in Orel, Russia showed 79% cure and low default (3%) but with an elevated death rate. Factors associated with treatment default and fatality were studied[10] among tuberculosis patients registered during 1999-2000 in Spain where the default rate was as high as 14% and factors like sex, age, homelessness, incarceration, DOT or hospitalization were not associated with default. A retrospective descriptive study[11] in Nicaragua, from 1988-1996 showed that the default rate decreased from 16% in 1988-1991 to 10% in 1992-1996 with an improvement in the treatment success rate among patients.

Extra efforts such as counselling, supervision, home visits and motivation to retrieve those patients likely to default during the intensive phase and return them to treatment would have ensured a favourable treatment outcome (cured or treatment completed) in at least 114 patients (150 x 76%) This would have increased the cure rate from 76% (114/150) to 84% (1181/1406), a figure close to the expected target.

The reasons for default from a cohort of patients interviewed were migration, drug and work related, alcoholism and abatement of symptoms. These are some of the important issues that need to be addressed to reduce default. DOTS providers as well as patients need to be educated properly to overcome these problems during the treatment. Frequent meetings of the DOT providers with the Medical Officers of the health facilities are the need of the hour to address these challenges in addition to improved supervision and monitoring and health education at the grassroots level.

In conclusion, the findings of our study have shown that majority of the default occurs during the intensive phase. The goals of the RNTCP can be achieved by targeting these patients who are likely to default during the intensive phase, thus paving the way for the better control of tuberculosis.

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