

Comparing tuberculosis treatment outcome of daily dose regimen versus intermittent- three times a week dose regimen of dots chemotherapy under RNTCP: A retrospective study

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Abstract

Background: Tuberculosis (TB) is contagious and air-borne disease. Revised National Tuberculosis Control Program (RNTCP) adopted DOTS strategy since 1997. In 2017 the RNTCP had introduced daily regimen for treatment of TB across the country in place of the intermittent – three times a week dose regimen. Primary objective of this study was to compare the treatment outcome of the recently introduced daily dose regimen and the previous Intermittent- three times a week dose regimens of the directly DOTS. Study tools used were RNTCP tuberculosis (TB) registers at Tuberculosis Unit and quarterly reports on the ‘result of treatment of tuberculosis patients registered 13-15 month earlier’. It was a retrospective, record based analysis of treatment outcome of all tuberculosis patients registered at 9 tuberculosis units in district during 2nd quarter of 2016 for intermittent- three times a week dose regimen and all patient registered at same tuberculosis units during 2nd quarter of 2017 for daily dose regimen of directly observed treatment short course was studied. **Results:** Total 477 tuberculosis patients were registered at 9 tuberculosis units in district during 2nd quarter of 2016 for intermittent- three times a week dose regimen and there were 432 patients registered at same tuberculosis units during 2nd quarter of 2017 for daily dose regimen of directly observed treatment short course under RNTCP. Treatment success (favorable outcome) of daily dose regimen and intermittent- three times a week dose regimen of DOTS was 356 (82.6%) and 363 (77.2%) respectively. This difference was statistically significant at 95% confidence interval (p=0.04). Un-favorable treatment outcome of daily dose regimen– patient died-31(7.1%), treatment failure-1(0.2%), defaulted-40(9.3%), switched to category-IV-3(0.7%) and Un-favorable treatment outcome intermittent- three times a week dose regimen of DOTS- patient died-34(7.2%), treatment failure-16(3.4%), defaulted-55(11.7%), switched to category-IV-2(0.4%). One patient on daily and 7 patients on intermittent regimen were transferred out (outcome not evaluated) were excluded from comparison There was statistically significant (p=0.004) decline in failure rate in daily dose regimen as compared to intermittent- three times a week dose regimen of DOTS. Conclusions: ‘Treatment success’ rate is significantly higher with recently introduced daily fixed dose DOTS regimen than previous intermittent-three times a week regimen for treatment of tuberculosis under RNTCP.

Key Word: Treatment outcome, comparison, daily dose regimen, intermittent regimen, DOTS.

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INTRODUCTION

Tuberculosis (TB) is contagious and air-borne disease. TB is one of the top 10 causes of death worldwide^{1,2}. As per the Global TB report 2017 the estimated incidence of TB in India was approximately 2800000 accounting for about a quarter of the world's TB cases³. Revised National TB Control Program (RNTCP) adopted Directly Observed Treatment Short-course (DOTS) strategy with intermittent three times a week regimen since 1997^{4,7}. Many researchers across the world concluded in their study that, daily dose regimen had certain advantages

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over intermittent two or three times a week regimen for treatment of tuberculosis^{8,14}. In 2016, WHO had recommended that, the patients with drug susceptible pulmonary TB, the use of intermittent dosing is not recommended in both the intensive and continuation phases of therapy, and daily dosing is the recommended dosing frequency¹⁵. RNTCP adopted these recommendations immediately³, but there is still confusion whether the daily regimen or the intermittent regimen is superior. In our study, we have tried to fill up this lacuna.

OBJECTIVES

Primary objectives of the study were to compare treatment success rate & to compare unfavorable treatment outcomes of the recently introduced daily regimen and the previous intermittent regimens of the DOTS under RNTCP.

METHODOLOGY

Study tools: RNTCP TB registers at Tuberculosis Unit and quarterly reports on the result of treatment of tuberculosis patients registered 13-15 month earlier.

Study design: A Retrospective, record based analysis of treatment outcome of Tuberculosis patients registered at 9 Tuberculosis Units.

Study population and methods:

Treatment outcome of all Tuberculosis patients registered at 9 tuberculosis units in district during 2nd quarter of 2016 (i.e. from 01.04.2016 to 30.06 2016) for Intermittent- three times a week dose regimen and all patient registered at same tuberculosis units during 2nd quarter of 2017 (i.e. from 01.04.2017 to 30.06 2017) for Daily dose regimen of Directly Observed Treatment Short Course was studied.

Data was collected by visiting all TUs after obtaining clearance from institutional ethical committee, from RNTCP tuberculosis (TB) registers and quarterly reports on 'Result of treatment of tuberculosis patients registered 13-15 month earlier' available at Tuberculosis Units.

Exclusion criteria: All patients registered for Category-IV and Category-V DOTS regimen for MDR and X-DR patient respectively and those patients registered for Non DOTS regimen for tuberculosis treatment were excluded from study.

The following standard case and outcome definitions^{1,3,16,17} were adopted and used for the study.

Successful treatment outcome: A treatment that ends up in cure or treatment completion

- **Unsuccessful treatment outcome:** A treatment that end up in treatment default, treatment failure, treatment regimen changed, treatment

outcome not evaluated (patient transferred) or treatment outcome 'patient died'.

- **New TB case:** A TB patient who has never had treatment for tuberculosis or has taken anti-tuberculosis drugs for less than one month.
- **Retreatment TB case:** A TB patient who received anti-tuberculosis treatment for one month or more from any source and returns to treatment.

Treatment outcomes:

- **Cured:** Initially sputum- smear/ culture- positive patient who has completed treatment and had negative sputum smears/culture at the end of treatment
- **Treatment completed:** - Sputum smear-positive patient who has completed treatment, with negative smears at the end of the intensive phase but none at the end of treatment. Or: Sputum smear-negative TB patient who has received a full course of treatment and has not become smear-positive during or at the end of treatment. Or: Extra-pulmonary TB patient who has received a full course of treatment and has not become smear-positive during or at the end of treatment.
- **Died:-** Patient who died during the course of treatment regardless of cause
- **Failure:-** Any TB patient who is smear positive at 5 months or more after starting treatment.
- **Defaulted/Lost to follow-up:-** A patient who has not taken anti-TB drugs for 1 months or more consecutively after starting treatment.
- **Transferred out/Not evaluated:-** A patient who has been transferred to another Tuberculosis Unit/District and his/her treatment result (outcome) is not known.

Data analysis- The analysis was carried out using the SPSS/PC Windows version 21.0 software package (IBM, Inc.). The results were compared by using the chi square test and Z- test.

RESULTS AND DISCUSSIONS

Total 477 tuberculosis patients were registered at 9 tuberculosis units in district during 2nd quarter of 2016 (i.e. from 01.04.2016 to 30.06 2016) for intermittent-three times a week dose regimen and there were 432 patients registered at same tuberculosis units during 2nd quarter of 2017 (i.e. from 01.04.2017 to 30.06 2017) for Daily dose regimen of directly observed treatment short course under RNTCP (Fig-1). Maximum number of cases was registered at TU No. 9, which covers population of Municipal Corporation area.

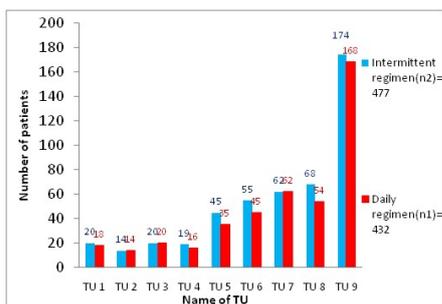


Figure 1: TU wise No. of cases registered under DOTS

In our study, we found that, the proportion of retreatment cases was increased to 20.4% in 2nd quarter of 2017, which was 18.7% in 2nd quarter of 2016(Fig-2). As per India TB report 2018³, proportion of retreatment cases in India were 21.4%. Similar observation were noted in Report of first national anti tubercular drug resistance survey India 2014-16.¹⁸

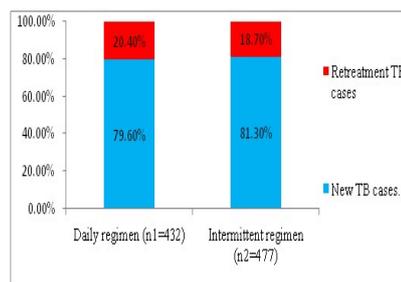


Figure 2: Percentage of New and Retreatment TB cases

In this study we observed that, the proportion of TB patients tested for HIV was 99.4% and 99.5% in 2016 and 2017 respectively. The proportion of TB patients positive for HIV was increased to 10.6% in 2017, from 8.8% in 2016 (Fig-3). As per India TB report 2018³, percentages of TB patient tested for HIV were 88% in 2016. Percentage of TB patients positive for HIV was 4% at National level and 7% in Maharashtra.^{3,18}

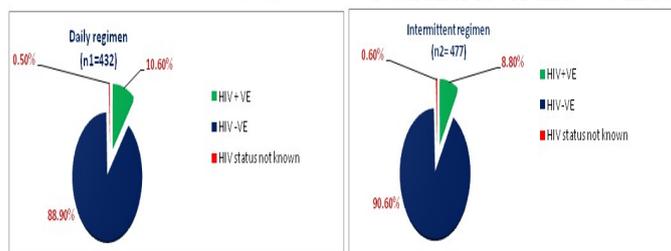


Figure 3: HIV status of patients registered under DOTS

Treatment success (favorable outcome) of daily dose regimen and intermittent- three times a week dose regimen of DOTS was 356 (82.41%) and 363 (76.1%) respectively. (Table-1), this difference was statistically significant at 95% confidence interval (p-0.04).

Table 1: Favorable and Unfavorable treatment outcome of TB cases

| Type of treatment regimen | Favorable | | Un-favorable | | χ ² | P-value |
|---|-----------|-------|--------------|-------|----------------|---------|
| | No. | % | No. | % | | |
| Daily regimen (n =431#) ₁ | 356 | 82.41 | 75 | 17.4% | 4.01 | 0.04 |
| Intermittent regimen (n =470#) ₂ | 363 | 76.1 | 107 | 22.8% | | |

One patient on daily and 7 patients on intermittent regimen were transferred out (outcome not evaluated) were excluded from comparison

Un-favorable treatment outcome (Table-2) of daily dose regimen – patient died-31(7.1%), treatment failure-1(0.2%), defaulted-40(9.3%), switched to category-IV-3(0.7%) and that of intermittent- three times a week dose regimen of DOTS- patient died-34(7.2%), treatment failure-16(3.4%), defaulted-55(11.7%),switched to cat IV 2(0.4%). Outcome ‘Transferred out’ (outcome not evaluated) were excluded for comparison

Table 2: DOTS Treatment outcome of TB cases

| Treatment outcome | Daily regimen (n ₁ =431#) | | Intermittent regimen (n ₂ =470#) | | Z Value |
|---------------------|--------------------------------------|-------|---|-------|---------|
| | No | % | No | % | |
| Cured | 137 | 31.8% | 173 | 36.8% | -1.58 |
| Treatment completed | 219 | 50.7% | 190 | 40.4% | 3.12 |
| Failure | 1 | 0.2% | 16 | 3.4% | -3.49 |
| Died | 31 | 7.1% | 34 | 7.2% | -0.02 |
| Defaulted | 40 | 9.3% | 55 | 11.7% | -1.18 |
| Switched to Cat.-4 | 3 | 0.7% | 2 | 0.4% | 0.55 |

One patient on daily and 7 patients on intermittent regimen were transferred out (outcome not evaluated) were excluded from comparison

No statistically significant difference in ‘treatment success’ of daily regimen and intermittent regimen of DOTS in HIV + Ve TB cases, this may be due to HIV status of patient (Table-3).

Table 3: DOTS Treatment outcome of HIV positive TB cases

| Type of treatment regimen | Favorable outcome | | Un-favorable outcome | | Total | χ ² | P-value |
|---|-------------------|------|----------------------|-------|-------|----------------|---------|
| | No. | % | No. | % | | | |
| Daily Fixed dose regimen (n ₁ =46) | 30 | 65.2 | 16 | 34.8% | 46 | 0.3 | 0.58 |
| Three times a week regimen (n ₂ =42) | 25 | 59.5 | 17 | 40.5% | 42 | | |

Table 4: DOTS Treatment outcome of HIV negative TB cases

| Type of treatment regimen | Favorable outcome | | Un-favorable outcome | | Total | χ ² | P-value |
|--|-------------------|------|----------------------|------|-------|----------------|---------|
| | No. | % | No. | % | | | |
| Daily Fixed dose regimen (n ₁ =385) | 326 | 84.7 | 59 | 15.3 | 385 | 4.4 | 0.03 |
| Three times a week regimen (n ₂ =428) | 338 | 79.0 | 90 | 21.0 | 428 | | |

In case of HIV –Ve cases the favorable treatment outcome of daily dose regimen was (84.7%), significantly higher as compared to intermittent three times a week regimen (79.0%). X² 4.4 and p value 0.03, statistically significant at 95% CI.

CONCLUSIONS

We compared data of one quarter and came to a conclusion that, ‘Treatment success’ rate was significantly higher and ‘Treatment failure rate’ was significantly lower with recently introduced daily dose DOTS regimen than previous intermittent regimen. Treatment outcome cure with daily regimen was 31.8%, which was 36.8% with intermittent regimen; although this difference was not significant, data of one year of bacteriological positive cases need to be compared to get more details.

No statistically significant difference in ‘treatment success’ of daily regimen and intermittent regimen of DOTS in HIV + Ve TB cases.

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