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Original Research Article

A comparative assessment of daily dosage regimen versus intermittent treatment regimen of tuberculosis at the RNTCP centres in Chitradurga district

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ABSTRACT

Background : The treatment of pulmonary tuberculosis is quite challenging. The national tuberculosis programs are shifting the trend to adopt daily regimen than the intermittent regimen. Hence, this study was undertaken to study the effectiveness and adverse drug reactions of the daily and intermittent regimens.
Material and Methods : A retrospective study was conducted in the department of Chest and TB in Basaveshwara Medical College and Hospital, Chitradurga and District Tuberculosis Centre, Chitradurga, India. About 55 patients on daily regimen and 50 patients on intermittent regimen constituted the study sample. The details regarding the age, sex, initiation and termination of the treatment, outcome and adverse drug reactions were collected using a predesigned proforma.
Results : Majority of the patients in daily regimen were 56 – 65 years and intermittent regimen was aged between 26 – 35 years. More number of the cases in both the regimen were males. Vomiting was the main adverse drug reaction in patients on daily regimen and Abdominal pain in intermittent regimen. About 54.5% of the patients on daily regimen and 62% on intermittent regimen were cured. The death and defaulter rate was higher in patients on intermittent regimen.
Conclusions : Even though the cure rate is good in intermittent regimen, the adverse reactions are quite high in this study.

1. Introduction

Pulmonary tuberculosis is an important public health problem even with the availability of effective TB pharmacotherapy since 50 years. This disease has made a perfect bond with HIV to worsen the situation[1,2]. High number of cases, poor adherence to the TB treatment secondary to high pill burden, toxicity, adverse reactions and treatment inconvenience are the factors responsible for the unfavourable treatment[3].

The tuberculosis treatment consists of two phases, intensive and continuation phase and involves four man drugs including ethambutol, isoniazid, rifampicin and Pyrazinamide[4]. The research available shows that, intermittent pulmonary tuberculosis (TB) chemotherapy is effective, but intensity (daily versus intermittent) and duration of rifampicin use (intensive phase only versus both phases) have not been distinguished[5]. The studies shows that, the evidence of implementation of the daily versus intermittent regimens leading to decrease in treatment failure or relapse but are inconvenient and lead to noncompliance and drug resistance[2,6,7].

A number of studies are available to compare the efficacy of daily and intermittent regimen against tuberculosis in HIV patients. But, the studies are lacking to compare the efficacy, adverse reactions and outcome of the daily and intermittent regimen against pulmonary tuberculosis. Hence, this study was undertaken to compare the outcome and adverse drug reactions.

2. Material and Methods

A retrospective study was conducted in the department of Chest and TB in Basaveshwara Medical College and

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Hospital, Chitradurga and District Tuberculosis Centre, Chitradurga between January, 2017 to December, 2019. About 55 patients on daily regimen and 50 patients on intermittent regimen during the study period constituted the study sample. Clearance from institution ethics committee was obtained before the study was started. The permission from appropriate authorities was obtained to access the data. All the new pulmonary TB cases and those who were aged more than 12 years were included in to the study. The patients with Drug resistant tuberculosis, retreatment of previously treated cases, confection with HIV, patients with comorbidities including COPD, asthma, bronchitis etc were excluded from the study. All the patients were subjected for four sputum smear examinations, before starting the treatment, two and four months after starting the treatment and at the end of the treatment. The sputum smears were examined as per RNTCP protocol. All the patients were followed up for every 15 days by telephone or personal visit every 15 days with regards any adverse reactions in the form of GI intolerance, Peripheral neuropathy, hypersensitivity reactions, hepatic dysfunction and vertigo/ deafness. A patient is considered as cured if he/she presents with negative sputum smear after completion of the regimen. A patient is considered as defaulter if the patient has missed the dose for more than two months. Relapse was patients presenting the positive sputum smear after declaring the patient as cured. Multi drug resistance was considered if the patient had resistance to primary line drugs Rifampcin and Isoniazid. A predesigned proforma was used to collect the data. The data thus collected was complied and analyzed using Statistical Package for Social Services (SPSS vs 20). The data was presented as frequencies and percentages and chi square test was used as test of significance.

3. Results

This study had shown that, about 25.4% of the patients on daily regimen were aged between 56 – 65 years and 30% on intermittent regimen were aged between 26 – 35 years.

Majority of the patients on daily and intermittent regimen were males in this study.

Almost 65.5% of the patients on daily regimen and 76.0% of the patients on intermittent regimen had no adverse drug reactions. Vomiting was the main adverse drug reaction in patients on daily regimen followed by abdominal pain, allergic reaction on face, blurred vision, itching and nausea. Abdominal pain was the most common adverse drug reaction in patients on intermittent regimen followed by burning of the hand and feet, fatigue, itching, stomach pain, nausea, skin rashes, vomiting and yellowish skin.

About 54.5% of the patients on daily regimen and 62% on intermittent regimen were cured. The death and defaulter rate was higher in patients on intermittent regimen. The patient's status was unknown in 12.7% of the patients on daily regimen and relapse was noted in 12.6% of the cases. This difference was statistically significant between the two types of the regimen.

4. Discussion

This study was mainly undertaken to study the efficacy and adverse effects of daily regimen over intermittent regimen in treatment of pulmonary tuberculosis. Most of the patients in this study on daily regimen were aged between 56 – 65 years and 30% on intermittent regimen were aged between 26 – 35 years. Most of the patients on both the regimen were males. In a study in HIV patients by Gopalan et al, the mean age was 39 years and almost three fourth were males[8].

Vomiting was the main adverse drug reaction in patients on daily regimen followed by abdominal pain, allergic reaction on face, blurred vision, itching and nausea. Abdominal pain in intermittent regimen was the most common adverse drug reaction followed by burning of the hand and feet, fatigue, itching, stomach pain, nausea, skin rashes, vomiting and yellowish skin. In a study by Gopalan et al., the hepatotoxicity was higher in daily intensive phase of ATT with co-administered ART[8]. In a study by Mandal et al., overall toxicity et al was 35% cases in the daily regimen group, whereas it was 27.9% in cases in the intermittent regimen group[2].

About 54.5% of the patients on daily regimen and 62% on intermittent regimen were cured. The death and defaulter rate was higher in patients on intermittent regimen. The patient status was unknown in 12.7% of the patients on daily regimen and relapse was noted in 12.6% of the cases. This difference was statistically significant between the two types of the regimen. In a study by Kasozi et al., the relapse with the intermittent regimen was matched with default in daily regimen.[9] Another study assessing intermittent therapy was administered and recurrence was increased by 4 fold with intermittent therapy (non significant) compared to daily group[9]. In a study in HIV patients., a total of 18 patients died and 18 patients dropped out during the treatment period in the 3 regimens and 6, 4, 6 patients in the daily, part daily and intermittent regimens had TB regimens. Recurrence was similar in daily regimen and intermittent regimen[8]. In a study by Khan et al, the odds of treatment failure increased by two times in daily regimen and 3.7 times when an intermittent rather than a daily intensive phase of ATT was used in HIV patients[10]. An observational cohort study in HIV patients had shown higher mortality in supervised intermittent ATT compared with unsupervised daily regimen with similar default rates and also by many studies[11–14].

5. Conclusions

This study had shown that, even though the cure rate is good in intermittent regimen, the adverse reactions are quite high. Hence, the treating physician should take appropriate

Table 1: Distribution of the study group according to age

Age group	**Daily regimen N (%)**	**Intermittent regimen N (%)**
16 – 25 years	9 (16.3)	5 (10.0)
26 – 35 years	11 (20.0)	15 (30.0)
36 – 45 years	8 (14.5)	10 (20.0)
46 – 55 years	5 (9.2)	13 (26.0)
56 – 65 years	14 (25.4)	3 (6.0)
More than 65 years	8 (14.5)	4 (8.0)
Total	55 (100)	50 (100)

Table 2: Distribution of the study group according to sex

Sex	**Daily regimen N (%)**	**Intermittent regimen N (%)**
Male	39 (70.8)	39 (78.0)
Female	16 (30.2)	11 (22.0)
Total	55 (100)	50 (100)

Table 3: Adverse drug reactions in the study group

Type of ADR	**Daily regimen N (%)**	**Intermittent regimen N (%)**
Abdominal pain	2 (3.6)	4 (8.0)
Allergic reactions on face	2 (3.6)	0
Blurred vision, abdominal pain	2 (3.6)	0
Burning of hands and feet	1 (1.9)	1 (2.0)
Fatigue	0	1 (2.0)
Itching	2 (3.6)	1 (2.0)
Leg stiffness	1 (1.9)	0
Stomach pain	1 (1.9)	1 (2.0)
Nausea	2 (3.6)	1 (2.0)
Skin rashes	0	1 (2.0)
Vomiting	5 (9.1)	1 (2.0)
Weight loss	1 (1.9)	0
Yellowish Skin	0	1 (2.0)
No ADR	36 (65.4)	38 (76.0)
Total	55 (100)	50 (1000
χ^2 **value=12.845**	**df=13**	**p value=0.46, NS**

Table 4: Treatment outcome of the two types of regimens

Outcome status	**Daily regimen N (%)**	**Intermittent regimen N (%)**
Cured	30 (54.5)	31 (62.0)
Died	8 (14.5)	12 (24.0)
Defaulter	1 (1.8)	5 (10.0)
Relapse	7 (12.6)	0
Treatment changed	2 (3.8)	0
Unknown	7 (12.7)	0
Patient refused to take medication	0	2 (4.0)
Total	55 (100)	50 (100)
χ^2 **value=21.293**	**df=6**	**p value=0.002, Sig**

decision during the initiation of treatment to cure the pulmonary tuberculosis.

6. Acknowledgement

None.

7. Conflict of Interest

None.

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