

ORIGINAL ARTICLE

Comparing Daily Versus partially Intermittent Regimen of ATT in non HIV patients with new Pulmonary Tuberculosis (TB) in DOTS program

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ABSTRACT

Introduction: Intermittent regimens can be as effective as daily regimens. It has the advantage of convenience in directly observed treatment which is considered essential for ambulatory programs. While the DOTS strategy was piloted at Ojha Institute of Chest Diseases in April 1995, a three times a week intermittent regimen was introduced in 1997- 98 at two major out door clinics of Ojha Institute of Chest Diseases. When the nation wide DOTS program was implemented daily regimen was adopted as recommended by national tuberculosis program in all units of Ojha Institute of Chest Diseases.

Objective: The primary objective of the study was to compare the efficacy of intermittent regimen given in 1997-8 with daily regimen administered in same clinics ten years later in terms of sputum conversion an the end of intensive phase and treatment success rate.

Material and method: It was a retrospective analysis. Data entered in Tb 03 registers of 3rd and 4th quarter in of 1997 and 1st and 2nd quarter of 1998 was compared with that

entered in 3rd and 4th quarter of 2007 and 1st and 2nd quarter of 2008 and quarterly reports of case finding Tb07, sputum conversion Tb 08 and treatment out come Tb 09

Results: Total number of smear positive case in intermittent therapy group was 702 and in daily therapy group was 1120. Male to female ratio and age distribution was similar. Sputum conversion at end of intensive phase was achieved in 582 out of 702 (83%) in intermittent therapy and 896 out of 1120 (80%) in daily therapy group. Success rate was 78.83 % in intermittent therapy and 78% in daily therapy group. Default rate was 20.51% in intermittent therapy in 1997-8 and 13% in daily therapy group 10 years later.

No serious adverse event was reported with intermittent therapy. Minor side effects like itching (in 2.8%), jaundice (in 4.2%) and vomiting (in 9.9%) were observed in this group. Relapse was observed in 1.2% patients after one year follow up.

Total number of visits for DOTS required by DOTS' supporter were 66 for daily regimen and 36 for intermittent therapy. Total cost of medicine was 33% less in intermittent therapy for category 1 cases.

Conclusion: TB control program has achieved 100% DOTS coverage in the public sector and is not far in achieving the target of treatment success rate in new pulmonary TB case. However it is struggling to reduce the default rate. This can be reduced by strong network of DOTS supporters, while introduction of intermittent regimen can reduce the number of visits so a person can supervise more patients with lesser effort. It will be advantageous to introduce this regimen in areas where population is thin and accessibility is difficult due to less developed roads.

INTRODUCTION

Sixty years after the introduction of effective chemotherapy, the World Health Organization (WHO) estimates, based on surveillance and survey data, that the number of new tuberculosis (TB) cases has reached 8.9 million in 2004, with an annual rate increase of 0.6%¹.

Current standard chemotherapy protocols date back to the 1970s when, with the introduction of rifampin into combination regimens including isoniazid, pyrazinamide and ethambutol, and streptomycin, a short course of 6 months was proven effective².

It was observed in 1964, that intermittent regimens can be as effective as daily regimens, thereby offering the advantage of convenient, directly observed treatment³.

Intermittent regimens are considered essential for ambulatory programs. They have been widely explored over the past 30 years. Isoniazid, rifampicin, pyrazinamide, and streptomycin are all deemed efficacious when given intermittently (two or three times per week), as when given daily, and ethambutol is usually only given intermittently when also given with rifampin⁴.

Intermittent regimens make treatment observation more convenient and feasible for health workers and patients and achieve high levels of treatment success with low relapse rates⁵. Such regimens have now been widely used, with good results. This has been adopted by many countries including India in their tuberculosis control programs

Rationale for intermittent therapy is that certain drugs are also effective when the drug concentration drops temporarily, and even after the drug has disappeared completely from the lesion or the medium after a culture of *Mycobacterium tuberculosis* is exposed

to certain concentration of a certain drugs for some time, it takes several days (the “lag period”) before new growth occurs.

DOTS strategy was piloted at Ojha Institute of Chest Diseases in April 1995. In 1997- 98 a three times a week intermittent regimen was introduced at two major out door clinics of Ojha Institute of Chest Diseases. When the nation wide DOTS program was implemented daily regimen was adopted as recommended by national tuberculosis program in all units of Ojha Institute of Chest Diseases

The study was done to compare the efficacy of intermittent regimen given in 1997-8 with daily regimen as being administered in same clinics ten years later 2007-8

Objectives:

The primary objective of the study was to compare the efficacy of two anti-TB regimens in reducing bacteriological failures in terms of sputum conversion an the end of intensive phase and treatment success rate

The secondary objectives included in the study were:

- a) unfavorable responses (failures, deaths, relapses)
- a) frequency of adverse drug reaction with intermittent regimen

Material and Method:

It was a retrospective analysis.

In 1997 -98 supervised partly intermittent regimen 2R₃H₃Z₃E₃ /2HE was introduced for new smear positive patient at two out patients clinics of Ojha Institute of Chest Disease that is at Nazimabad chest clinic and Malir chest clinic

Those patients who consented to follow the regimen were put on this regimen. The record keeping and data collection was done according to WHO/NTP guidelines.

In 2007-8 out patients departments of Ojha Institute of Chest Disease were managing all tuberculosis patients according to NTP Pakistan guideline administrating the drug on daily basis. The data was collected from same clinics that is Nazimabad chest clinic and Malir chest clinic .The record keeping and data collection was done according to WHO/NTP guidelines.

Document used were:

1. Data entered in Tb 03 registers of 3rd and 4th quarter in of 1997 and 1st and 2nd quarter of 1998 was compared with the data entered in 3rd and 4th quarter of 2007 and 1st and 2nd quarter of 2008.
2. Quarterly reports of case finding Tb07, sputum conversion Tb 08 and treatment out come Tb 09 of the patients registered in respective period were also studied for counter checking

DOTS strategy for the managing patients was followed in both the periods.

Results of both the periods were compared and mentioned in terms of figures and percentages.

Data management:

Data was entered in SPSS -10 and analyses using descriptive statistic and correlations

Results:

The study was conducted in out patients' clinics of Ojha Institute of Chest Disease Karachi in new smear positive cases. Total number of smear positive case in intermittent therapy group was 702 and in daily therapy group was 1120

Male to female ratio showed no significant difference ($p=0.92$). There was no significant change in pattern of age distribution ($p=0.64$)

Fig 1

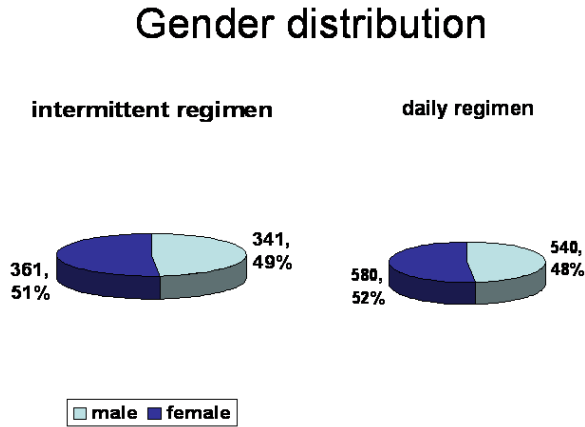
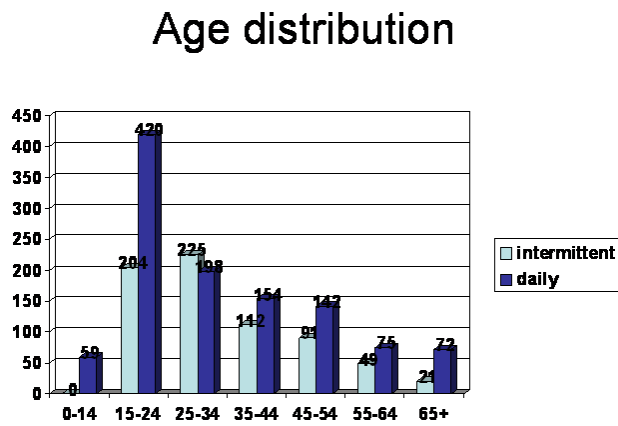


Fig 2



Sputum conversion at end of intensive phase was achieved in 582 out of 702(83%) in intermittent therapy and 896 out of 1120 (80%) in daily therapy group.

Success rate was 78.83 % in intermittent therapy and 78% in daily therapy group. Default rate was 20.51% in intermittent therapy in 1997-8 when system of DOTS supporters was not in place and 13% in daily therapy group even 10 years later. (p=0.48)

No of serious adverse event reported with intermittent therapy were itching in 2 (2.8%), jaundice in 3 (4.2%) and vomiting in 7 (9.9%) patients.

Relapse was observed in 1.2% patients after one year follow up.

Total number of visits for DOTS required by DOTS' supporter are 66 for daily regimen and for intermittent therapy are 36; almost 46% less for category 1 cases.

Total cost of medicine was 33% less in intermittent therapy for category 1 cases.

DISCUSSION

Our study shows that there is no significant advantage of either regimen in terms of treatment outcomes. But it is evident that intermittent regimen is more cost effective.

As higher doses are given the intermittent therapy has slightly more sterilizing effect this is evident by better sputum conversion rate. This feature was common to other studies in other part of the world⁵. The intermittent regimen was highly successful and perhaps slightly more effective than the daily regimen. Intermittent therapy is adopted by several TB control programs in the world including India.

Pakistan TB control has achieved 100% DOTS coverage in the public sector is not far from achieving the target of treatment success rate in new pulmonary TB case. However it is struggling to reduce the default rate. This can be reduced by strong network of DOTs supporters (persons who see that every dose is supervised). Introduction of intermittent

regimen can reduce the number of visits so a person can supervise more patients with lesser effort. It will be advantageous to introduce this regimen in areas where population is thin and accessibility is difficult due to less developed roads.

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