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Observational Study on the Outcome of Supervised and Non-Supervised Therapy in Subject with Pulmonary Tuberculosis

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Abstract
Background: *The success of anti-tuberculosis programme is directly dependent on the adherence to the treatment, patient compliance, and correct combination of anti-tubercular drugs in the optimum doses for right duration. Lack of adherence to drug gives rise to resurgence and resistance which can be prevented if drug are given under direct supervision.*
Aims and Objective: *Supervised short-course therapy can have a good impact over patients on non supervised therapy who discontinue their treatment and become treatment failure case. In view of the above scenario the present study has been conducted at RIMS, a tertiary care hospital and adjoining PHC to study the likely impact of supervised over non supervised treatment.*
Material and Methods: *The present study was carried out in outdoor and indoor patients from the department of medicine, Rajendra institute of medical science, Ranchi and adjoining PHC during the period from October 2016 to April 2017*
Result and Conclusion: *Both supervised and non-supervised therapy are effective but the revised WHO regimen (DOTS regimen) directly observed short course therapy increases the patient's compliance and adherence to the treatment regimens and increased sputum smear conversion rate at the end of two months thereby concluding that supervised therapy is superior to non supervised therapy when outcomes were compared.*
Keywords: *supervised and non supervised, antituberculosis drug, DOTS.*

Introduction

Tuberculosis, one of the oldest diseases known to affect humans, is a major cause of death worldwide. Mycobacterium tuberculosis, which usually affects the lungs, can also involve other organs such as brain, kidney and bones in up to one-third of cases. Based on the surveillance and survey data WHO estimates that about 9.2 million

new cases of tuberculosis occurred in 2006.[1] Of these cases 4.1 million were new smear positive cases.[2] An estimated 1.7 million people died from tuberculosis. It is estimated that about one-third of the current global population is infected asymptomatically with tuberculosis, of which 5-10 per cent will develop clinical disease during their lifetime.[2]

India have the highest TB burden in the world and accounts for nearly one fifth of global burden of tuberculosis[3], accounting for 2/3rd of the cases in South East Asian Region. Every Year approximately 1.8 million persons develop tuberculosis, of which about 0.8 million persons are new smear positive highly infectious cases. [4] Two out of every five Indians are infected with the TB bacillus. Every day about five thousand people develop the disease. [5,6] In India about 0.37 million people die every year due to tuberculosis.[7]

To deal with the growing global TB problem, the WHO declared TB as a global emergency [8] and introduced the Directly Observed Treatment Short-Course (DOTS) strategy in 1994.[9] This has been incorporated in revised national tuberculosis program (RNTCP) in India, It is a comprehensive strategy for tuberculosis control.

DOTS strategy is based on close monitoring of tuberculosis patients to ensure that they fully complete the course of combination of drugs in 6 – 8 months. DOTS are the only strategy which has proven effective in controlling TB on mass basis. The DOTS strategy is in practice in more than 100 countries. India has adopted and tested DOTS in various parts of the country since 1999 with excellent result and RNTCP now covers more than 120 million populations. Worldwide patient's lack of adherence to the treatment regimen is recognized as the most important impediment to cure and thus giving rise to resurgence and resistance. Worldwide, including India multidrug resistant (MDR) tuberculosis is increasing and compounding the problem.

The present study "Observational study on the outcome of supervised and non-supervised therapy in subject with pulmonary tuberculosis" was carried out in patients selected from the outdoor and indoor patients from the department of medicine, Rajendra institute of medical science, Ranchi, which is a pioneer institute of Jharkhand state and PHCs located in Ranchi during the period from October 2016 to April 2017.

Material and Methods

In this study a total of 200 patients of sputum positive pulmonary tuberculosis were randomly selected and divided into two groups supervised and non-supervised, each group consisting of 100 cases respectively and observed after giving drugs for a period of two month referred as Intensive phase. Intensive phase of short course chemotherapy consisted of two months in which five antitubercular drugs –Rifampicin, Isoniazid, Pyrazinamide, Streptomycin and Ethambutol thrice a week according to their body weight.

Each group were further divided according to gender. Groups 1(supervised group) comprising of 100 cases were put on Rifampicin, Isoniazid, Ethambutol, Pyrazinamide and Streptomycin as per DOTS regimen. Group 2 also comprised of 100 cases, they were also put on Rifampicin, Isoniazid, Ethambutol, Pyrazinamide and Streptomycin but were not taking drug infront of DOTS activist as followed in group 1 patients.

Patients in the supervised group were observed swallowing of medicine in the Hospital or DOTS centre, where as the patients in the non supervised group returned home with anti-tubercular drug and asked to report at the interval of two weeks for a follow up period of two months

A.Group-1 (supervised)

It comprised of patients (n=100) attending outdoor and admitted in the indoor, department of medicine, and DOTS centre of PHCs, pulmonary tuberculosis category-2 receiving DOTS regimen of therapy.

B.Group-2(non supervised)

It comprised of patients (n=100) attending regularly the outpatients department of medicine,

of pulmonary tuberculosis category-2 receiving daily regimen of antitubercular drugs.

The selected cases for study were distributed in respect to groups, age, sex and their reporting time as shown in table no.1. After the completion of two months of intensive phase therapy a comparison between two groups was done in view of sputum status, radiological finding, body weight and febrile status.

Exclusion and Inclusion criteria

Patients who did not report were excluded from the study group and to replace them, new sputum positive cases were taken. At the time of selection patient with other major diseases were excluded form study.

Table 1: showing sex wise distribution in Group 1 and 2.

Group	Total no. Of cases	Sex	No.of cases	(%)	Age in years		Reporting to the hospital over 2 months
					range	Mean	
Group-1	100	Male	60	60	14-68	36.18	Thrice a week in the DOTS centre of RIMS and the nearest PHC
		female	40	40	15-65	33.62	
Group -2	100	Male	69	69	18-72	39.11	After two weeks.
		female	31	31	18-60	36.70	

Results

Parameter changing over two months of the intensive phase therapy in group 1 and group 2 were observed and analysed.

The results of range, mean, S.D. and S.E.M. of body weight (in kg) prior to and after two months of intensive phase therapy in group-1 and group 2 were analysed and is found to be statistically non significant as shown in table 2 and fig.1

Table no. 3 shows that there is definite decrease in size of parenchymal lesion in all the cases as evidenced by radiological examination found in both in group 1 and 2 cases indicating that both treatment regimen are equally effective.

The table 4 and Fig 2 shows sputum smear conversion after two months of intensive phase therapy in group 1 cases is 97%(in male 96.67% and female 92.5%).Which shows high degree of sero conversion from positive to negative. sputum smear conversion after two months of intensive phase therapy in group 2 cases is 78 % (in male 81.09% and female 70.97%).overall percentage of smear that remain positive even after supervised and non supervised therapy were 3% and 22% in group 1 and group 2 respectively.

The table 5 and fig 3 shows that 92% of the cases of group1 become afebrile after two month of the intensive phase therapy as compared to group 2 cases in which only 81% become afebrile which is statistically significant. Fever is also a predictor of response to pulmonary tuberculosis therapy as evidenced by this table.

Table no. 5 show 19% cases in group 2 remained febrile after two months of intensive phase therapy. The change from febrile to afebrile state being 81% ;(in male 79.72% and in female 83.83%). The percentage conversion from febrile to afebrile in non-supervised group is less as compared to supervised group.

Table 2: showing changes in body weight before and after intensive phase therapy

		No. Of cases	Body weight(in kg)prior to therapy on day of conclusion in this study				Body weight (in kg)after two months of intensive phase therapy				Results	
			Range	Mean	S.D.	S.E.M.	Range	Mean	S.D.	S.E.M.	t value	p-value
Group1	Male	60	28-51	44.50	6.04	0.780	28.5-53.5	47.10	5.82	0.751		
	Female	40	28-46	37.10	4.70	0.744	31.5-48	39.40	4.34	0.687		
	Total	100	28-51	41.54	6.61	O.661	29.5-53.5	44.02	6.48	0.648	2.701	0.0075 Non-significant
Group-2	Male	69	28.5-67	44.60	10.62	1.27	30-67	46.32	10.57	1.27		
	Female	31	29-55	38.82	6.14	1.10	31-57	40.17	5.85	1.05		
	Total	100	28.5-67	42.81	9.80	0.98	30-67	44.42	9.76	0.976	1.164	0.2458 Non significant

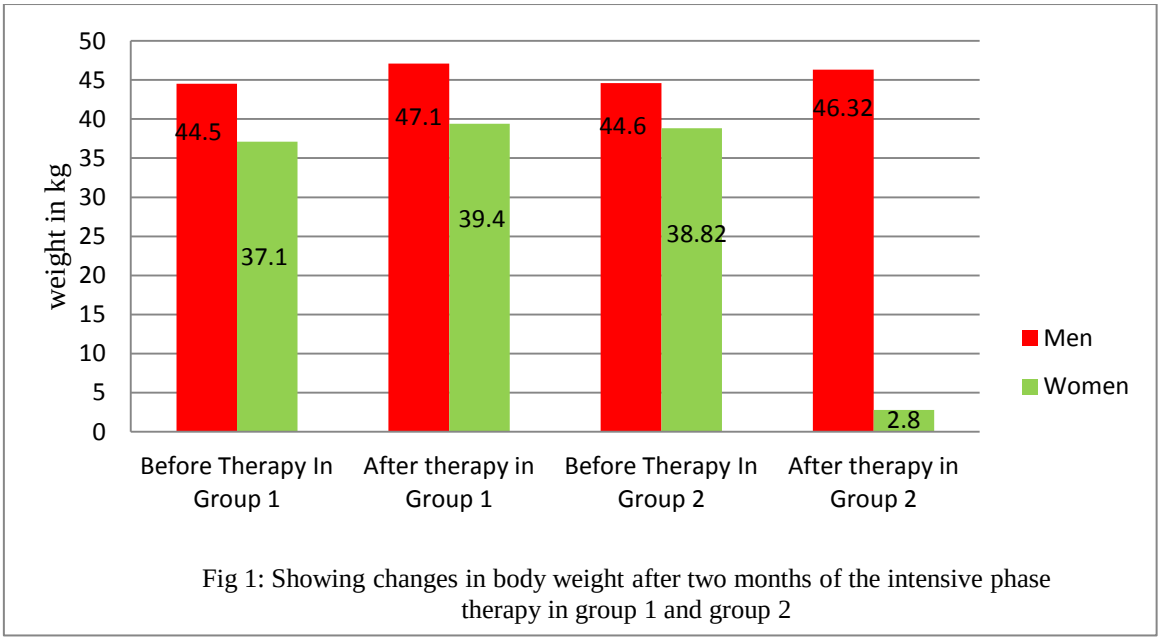

Fig 1: Showing changes in body weight after two months of the intensive phase therapy in group 1 and group 2

Table 3: showing parenchymal changes before and after intensive phase therapy

		No. of cases	Parenchymal lesion radiologically prior to therapy on day of inclusion in this study	Parenchymal lesion radiologically after 2 months of the intensive phase therapy
Group-1	Male	60	Present	Size decreases
	Female	40	Present	Size decreases
	Total	100	Present	Size decreases
Group-2	Male	69	Present	Size decreases
	Female	31	Present	Size decreases
	Total	100	Present	Size decreases

Table 4: showing chages in sputum smear before and after intensive phase therapy

		No. Of cases	No. Of cases sputum smear positive for acid fast bacilli prior to therapy on day of inclusion in this study	Percentage of cases sputum smear positive for acid fast bacilli prior to therapy on day of inclusion in this study	No. of cases sputum smear positive for acid fast bacilli after two months of intensive phase therapy	Percentage of cases sputum smear positive for acid fast bacilli after two months of intensive phase therapy
Group-1	Male	60	60	100	2	3.33%
	Female	40	40	100	1	2.5%
	Total	100	100	100	3	3%
Group-2	Male	69	69	100	13	18.84%
	Female	31	31	100	9	29.03%
	Total	100	100	100	22	22%

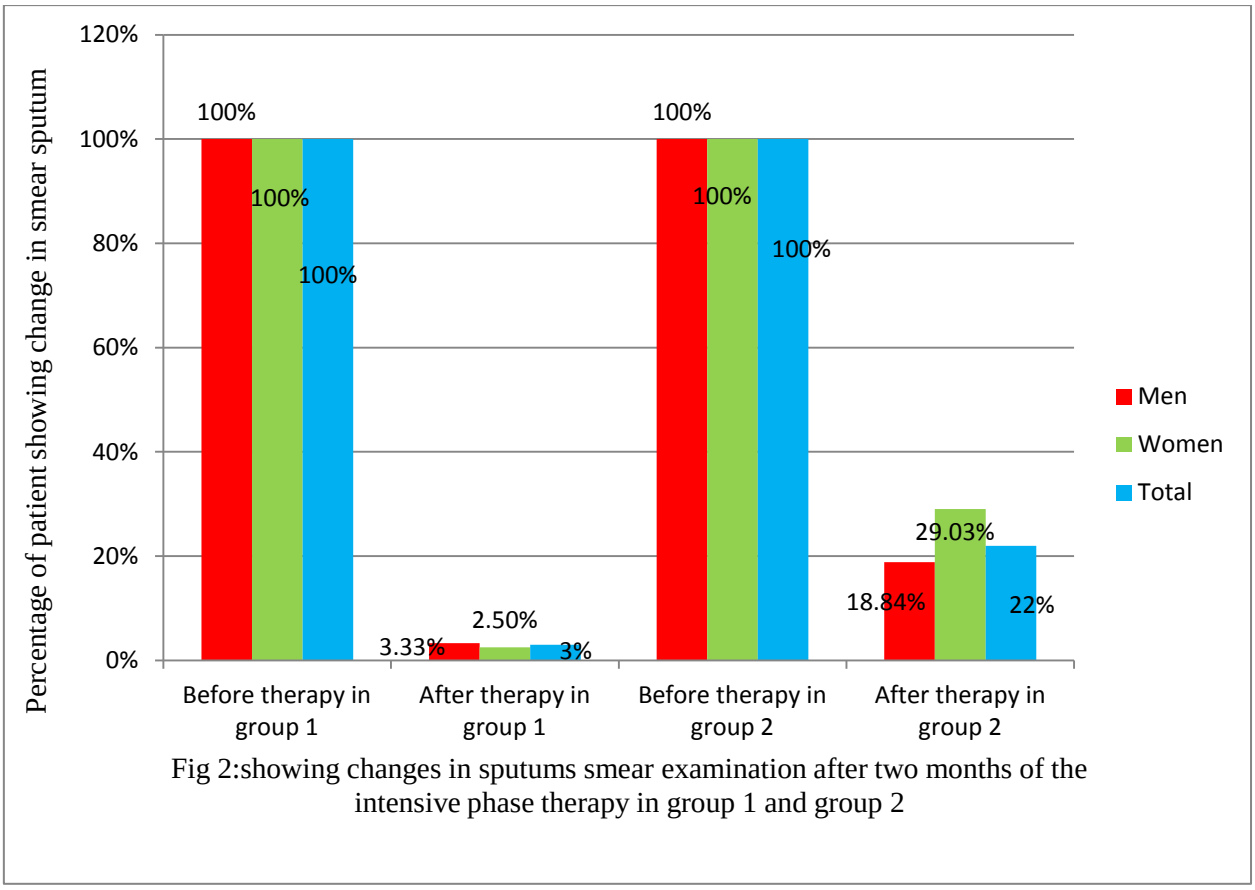

Fig 2:showing changes in sputums smear examination after two months of the intensive phase therapy in group 1 and group 2

Table 5 : Showing changes in the febrile state before and after intensive phase therapy

		No. Of cases	No. Of febrile cases prior to therapy on day of inclusion in this study	Percentage of febrile cases prior to therapy on day of inclusion in this study	No. Of febrile cases after two months of intensive phase therapy	Percentage of febrile cases after two months of intensive phase therapy
Group-1	Male	60	60	100	5	8.33%
	Female	40	40	100	3	7.5%
	Total	100	100	100	8	8%
Group-2	Male	69	69	100	14	20.28%
	Female	31	31	100	5	16.12%
	Total	100	100	100	19	19%

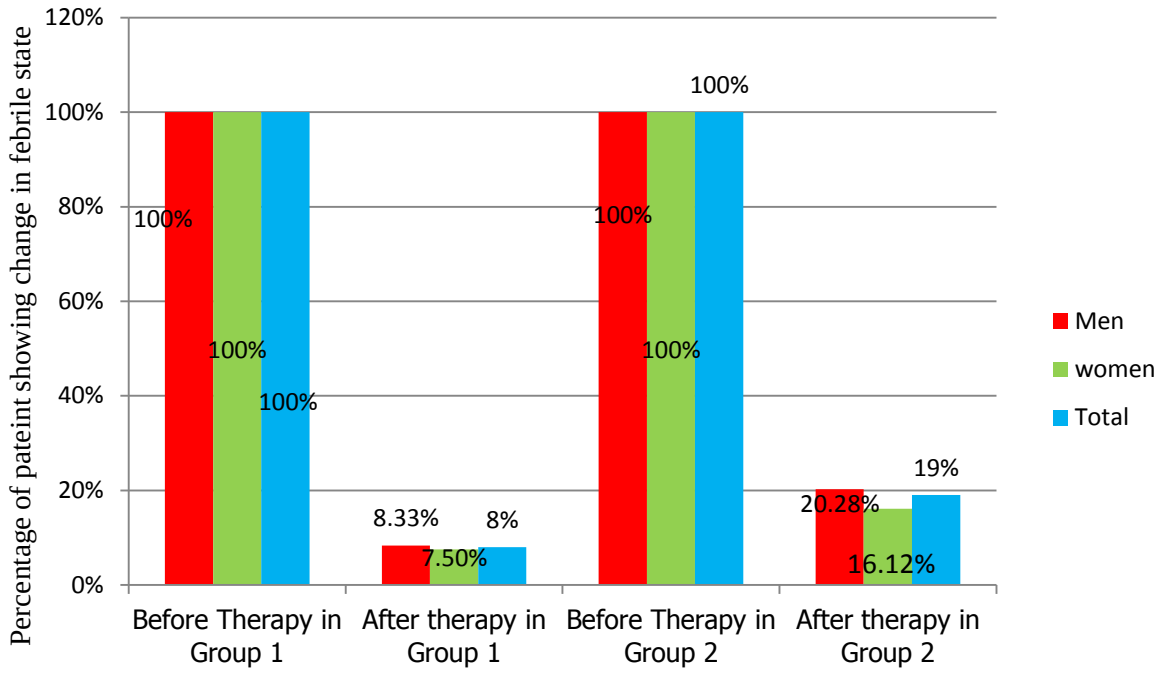

Fig 3:Showing changes in the febrile state of the cases in group -1 and group 2

Discussion

Tuberculosis remains a worldwide public health problem despite the fact that the causative organism was discovered more than 100 years ago. Failure of treatment and development of resistant strains had been attributed mainly to non-compliance of the previous long term (18 months) therapy. Supervised treatment of pulmonary tuberculosis is the preferred treatment over non-supervised as suggested by the various studies done in different places in different time previously. In a study done by Murali et al 91% of the DOTS group and 53% of the non-DOTS group were observed to be cured of tuberculosis, using the sputum smear as the test to monitor cure (statistically significant difference was observed). [10] These results clearly demonstrate that DOTS is a significantly superior health intervention in tuberculosis patients compared to self-administered regimen. Verma et al in his study from Jan- June 2003, in 386 patients found 91.3% of the DOTS group and 34.0% of the non-DOTS group were observed to be smear-negative after 6 months of chemotherapy. In this study defaulter rate, failure rate & death rate were maximum occurred in non-DOTS groups as compared to DOTS groups.[11] The difference in the outcome was observed to be statistically highly significant. Balasubramaniam et al in their study, observed that patients treated without direct observation have a substantially higher risk of adverse outcome than those treated under direct observation.[12] In my study, the mean value for the body weight (in kg) in the supervised group (Group1), prior to therapy on the day of inclusion in this study was found to be 41.54±6.61(in male 44.50 ± 6.04 and in female 37.10±4.70) and after two months of intensive phase therapy was found to be 44.02± 6.48 (in male 47.10 ± 5.82 and in female 39.40 ± 4.34). The difference between the mean values for body weight prior to and after two months of the intensive phase therapy was statistically non significant ($p<0.001$) as shown in table 2. In the non- supervised group (Group2),the mean value for the body weight prior to therapy on the day of inclusion in this study was found to be 42.81±9.80(in male 44.60 ± 10.62 and in female 38.82±6.14) and after two months of

intensive phase therapy was found to be 44.42±9.76 (in male 46.32±10.57 and in female 40.17±5.85).The difference between the mean values for body weight prior to and after two months of the intensive phase therapy was statistically non significant shown in table 2. In the supervised (Group-1) the weight gain in mean body weight after two months of intensive phase therapy was 2.48 kg as compared to non-supervised (Group 2) in which the percentage gain in mean body weight was found to be 1.61 kg after two months of Intensive phase therapy. Thus, the weight gain in body weight in supervised (group1) is more than the non supervised group (group 2). This finding is similar to study done in India where gain of weight was (3.2 kg).[13] Our study also revealed that the sputum smear conversion at the end of two month of intensive phase therapy was found to be 97% (in male 96.67% and in female 97.50%) in supervised group and 78% (in male 81.16% and in female 70.97%) in non supervised group.as shown in table 4. DOTS facilitates higher treatment completion rate and sputum conversion rate was conclusion derived from the one of the study done by chaulk et al. [14] In a study done by Bawri et al conversion of smear positive to smear negative at the end of the 1st month is 71%, at the end of 2nd month is 84% and at the end of 3rd month is 92%.this finding was similar to my study.[15]

In the non supervised group all the 100 cases were febrile prior to therapy on the day of the inclusion in this study. 81% of the cases become afebrile at the end of the two months of the intensive phase therapy (in male 79.72% and in female 83.88 %) as seen in table no 5. similar to study done by Chaulk et al.5 Among febrile cases 92% of cases of the supervised group and 81% cases of non supervised group were found afebrile at the end of the two months of the intensive phase therapy. This observation is similar to study of Rossana et al who found that the fever and hemoptysis disappeared as early as the second month in the majority of patients.[16]

In my study there is decrease in size of parenchymal lesion radiologically after two months of therapy in both supervised and non-supervised group however radiographic evaluation is of lesser importance in evaluation of outcome of pulmonary tuberculosis which is shown by the study of Ann N. Leung, which showed that evaluation of the response of pulmonary TB to antibiotic treatment is best assessed by means of repeated sputum examinations in patients with positive bacteriology.[8] Radiographic evaluation is of lesser importance, although a baseline radiograph at the completion of treatment may be useful for future comparison purposes.

In persons with negative pretreatment sputum, radiographic and clinical evaluation become the major indicators of response to therapy and are the most common methods used in children, in whom bacteriologic confirmation is possible in only about one-third of cases .

Regression of radiographic abnormalities in pulmonary TB is a slow process. In the first 3 months of treatment, worsening of radiographic findings consisting of extension of parenchymal involvement and development or enlargement of nodes may be observed in up to one-third of pediatric patients receiving appropriate therapy; a similar trend with progression of nodal disease has also been observed in adults with tuberculous lymphadenitis. The cause of the disease progression in primary TB is unknown but may be related to the effects of the hypersensitivity reaction that normally occurs 2–10 weeks after initial infection as stated by Leung AN.[17]

In the majority of patients, parenchymal and nodal abnormalities usually regress in parallel. In adults, failures of radiographic findings to improve after 3 months of chemotherapy suggest drug-resistant organisms or a superimposed process. Resolution of parenchymal abnormalities has been observed to require from 6 months to 2 years on radiographs and up to 15 months on CT scans. Lymphadenopathy may persist for several years after treatment.

Chadha et al in their study found radiological lesions showed significant improvement in 76.3% patients.[18]

Based on various study it may be concluded that supervised (DOTS therapy) provides high cure rates upto 95%[10],it also prevents the emergence of MDRTB[19] and is one of the most cost-effective measure of all health Interventions.[20]

Conclusion

In both groups weight of each patient was taken at the time of admission and after 2 months of therapy. In the supervised group the mean weight gain in the body weight was found to be 2.48 kg (in male 2.6 kg and in female 2.3 kg) as compared to non-supervised group in which the mean weight gain was 1.61 kg (in male 1.72 kg and in female 1.35 kg) . There was increase in weight in both the groups but the increase was found to be more in supervised group than the non-supervised group. This indicates that an increase in weight with treatment is not a good predictor of prognosis. The size of the parenchymal lesion (as seen radio logically) was decreased in both supervised and non-supervised cases but presentation can vary from decrease to exacerbation of radiological signs so can't be used specifically as a prognostic factor. Sputum smear conversion rate at the two months of intensive phase therapy was found to be 97% in supervised group and 78% in non – supervised group, which shows high degree of sero-conversion from positive to negative in group I (supervised) cases. 92% cases in supervised group and 81% cases in non – supervised group became afebrile after two months of the intensive phase therapy.

On the basis of above observation made in the present study it can be concluded that both the treatment regimen (supervised and non-supervised) are effective but the revised WHO regimen (DOTS regimen) directly observed short course therapy is the most cost effective and patient compliant therapeutic programme in comparison to non-supervised regimen of anti-tubercular therapy.

Hence each patient of tuberculosis should be given anti-tubercular medicine under the direct supervision as it increases the patient's compliance and adherence to the treatment regimens and increased sputum smear conversion rate at the end of two months.

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