Original Article

Pharmacology

Studies on Effectiveness of DOTs and Weekly three times Treatment of Sputum Positive Tuberculosis Patients

1. Ghullam Rasool Bhurgri 2. Noor Ali Samon 3. Farooq Baig

1. Prof. of Pharmacology and Therapeutics 2. Asstt. Prof. of Community Medicine 3. Asstt. Prof. of Microbiology, Muhammad Medical College Hospital Mirpurkhas

ABSTRACT

Objective: The purpose of this study was to compare the effects of DOTs (Daily Observe Therapy Strategy) and three days in a week, in the treatment of patients of pulmonary tuberculosis.

Place and Duration of Study: This study was conducted at Free TB clinic, Muhammad Medical College Hospital Mirpurkhas from December 31, 2008 to December 30, 2009.

Materials and Methods: 200 Patients were registered at free TB clinic of Muhammad Medical College Hospital Mirpurkhas during the period of study.

Results: In tables and figures showed in DOTs therapy Mean±St.D,S.E.M45.5 ± 26.1,2.7,and 8, 4.50 ± 2.45,.87 patients were dropped from study period, weights of patients were increased after treatment 56.7±10.4, 1.0 and result showed significant >0.05. And in three times therapy in week Mean±St.D,S.E.M30.50±17.46,2.25 and 38, 19.50±11.11, 1.80 patients did not improve from study period, weights of patients were increased after treatment 59.1±10.4, 1.2 and result showed non-significant <0.05. It means that in DOTs group showed significant results as compared three times treatment in a week.

Conclusion: DOTs showed significant results as compared three times in a week in the treatment of pulmonary tuberculosis

Key Words: Pulmonary Tuberculosis, Daily Observe Therapy Strategy, Anti tuberculosis Therapy.

INTRODUCTION

Tuberculosis (TB) is an infection caused by organisms in the family Mycobacteria. These organisms grow slowly and can be identified only with special staining techniques, a trait that led to the name "acid-fast bacteria." Organisms in the Mycobacterium tuberculosis (MTB) group cause human disease, usually a chronic pneumonia. The destruction of MTB may produce holes or cavities in the lung containing huge numbers of organisms. MTB can also cause disease in other individual organs (e.g. lymph nodes, meninges, bone, pericardium, peritoneum, intestines, urogenital tract) and can disseminate to multiple organs, often including the lungs, blood, liver, and spleen. (AIDS 2010)

In a survey held during the year 2000 tuberculosis showed World populations 6,000,000,000, TB infected population is 8 million new cases of disease per year, 2 million deaths per year, 80% of new cases live in 22 high burden countries, Global health emergency declared by WHO in 1993.(Dr Marko2010)

Since 1993, WHO has recommended a strategy through which national governments can meet their responsibility to treat patients and to prevent the spread of tuberculosis (TB). Four of the major elements of the strategy, which came to be known as DOTS, were political commitment by governments, improved laboratory services, a continuous supply of good-quality drugs, and a reporting system to document the progress (and failure) of treatment for individual patients and of the program. (Thomas R Frieden 2006)

The most important component of DOTS is to ensure patient's adherence to treatment by giving every dose under direct observation. Treatment compliance may be a problem due to poor awareness of TB including treatment. Non-adherence to treatment has been recognized as a major problem for cure of TB. (P.G. Gopi 2007)

All first-line anti-tuberculosis drug names have a standard three-letter and a single-letter abbreviation: Ethambutol is EMB or E, isoniazid is INH or H, pyrazinamide is PZA or Z, rifampicin is RMP or R, streptomycin is STM or S. Second line-There are six classes of second-line drugs (SLDs) used for the treatment of TB. A drug may be classed as second-line instead of first-line for one of two possible reasons: it may be less effective than the first-line drugs (e.g., *p*-aminosalicylic acid); or, it may have toxic side-effects (e.g., cycloserine); or it may be unavailable in many developing countries (e.g., fluoroquinolones. Third line-Other drugs that may be useful, but are not on the WHO list of SLDs: rifabutin,macrolides: e.g., clarithromycin (CLR); linezolid (LZD);thioacetazone (T);thioridazine; arginine; vitamin D; (Tuberculosis 2010)

DOTS-stand for "Directly Observed Therapy, Short-course" and is a major plan in the WHO Global Plan to Stop TB. (Elzinga G 2004) The WHO advises that all TB patients should have at least the first two months of

their therapy observed preferably the whole of it observed): this means an independent observer watching patients swallow their anti-TB therapy.(Cohn DL 1999).

Treatment with properly implemented DOTS has a success rate exceeding 95% and prevents the emergence of further multi-drug resistant strains of tuberculosis.(Dye C, 2003) In order for the program to work efficiently and accurately health providers must be fully engage (Elzinga G 2004) must be built between public and private practitioners, health services must be available to all, (Dye C, 2003) and global support is provided to countries trying to reach their TB prevention, and treatment aims. (Grange JM2002) Some researchers suggest that, because the DOTS framework has been so successful in the treatment of tuberculosis in sub-Saharan Africa, DOTS should be expanded to non-communicable diseases such as diabetes mellitus, hypertension, and epilepsy. (Harries AD 2008)

The WHO extended the DOTS program in 1998 to include the treatment of MDR-TB (called "DOTS-Plus").(Iseman1998) Implementation of DOTS-Plus requires the capacity to perform drug-susceptibility testing. (Sterling TR 2003)

Monthly surveillance until cultures convert to negative is recommended for DOTS-Plus, but not for DOTS. If cultures are positive or symptoms do not resolve after three months of treatment, it is necessary to re-evaluate the patient for drug-resistant disease or non adherence to drug regimen. If cultures do not convert to negative despite three months of therapy, some physicians may consider admitting the patient to hospital so as to closely monitor therapy.

MATERIALS AND METHODS

200 Patients were registered from free TB Clinic of Muhammad Medical CollegeHospital Mirpurkhas from Dec 2008 to Dec 2009.

Criteria for enrolling the patients for study:

1. Patients who fulfilled the World Health Organization (WHO) diagnostic criteria who have never received treatment for TB.
2. Patients and their family promised to come regularly and thrice days in a week for eight months.

200 patients were enrolled for study.100 patients of DOTs and 100 patients in three times in a week.Out of 200 patients of DOTs, 2 patients did not follow and 2 were in three times treatment in a week.

Out of the total 196 patients were 120 male and 76 females.Their ages ranged from 20-39 (76) years, and 40-60 (120) enrolled in the study.

Management:

1. Councilling:

A. The patient and his family were informed about TB disease, its spread, progress and treatment. Regular treatment for 8 months will cure the patient. Irregular treatment or interruption of treatment before 8 months will make the disease resistant to treatment and chances of cure will diminish.

B. Diet: Advised to eat everything available. Diet should increase every day some patients are given drugs to stimulate appetite. Few patients needed short course of corticosteroids.

C. Emphasis was on regular visits and not to miss treatment at all.Patients and their family's contact numbers and address were noted.

2. Drug Treatment: All the patients were given daily treatment and 3 days a week under DOTS strategy. The drugs were given as separate drugs and doses were calculated according to weight of the patients as recommended by WHO guidelines for treatment of tuberculosis for 3 days week regimen. During initial phase months Rifamicin, Isoniazid, Pyrazinamide and Ethambutol were given and during continuation phase of six months Rifampcin, Isoniazid, and Ethambutol were given, during initial phase of two months Rifamicin, Isoniazid, Pyrazinamide, Ethambutol and Streptomycin were given. In 3rd months initial phase Streptomycin was stopped and other four drugs were continued. During continuation phase of 5 months Ionized, Rifampin, and Ethambutol were continued.

3. On every visit:

a. Patient was attended straight away on arrival with greetings and enquired about his health, family and job.

b. Temperature and weight recorded. Patients not gaining weight were advised to increase the diet. Some were given drugs to stimulate appetite and few given corticosteroids.

c. A glass of water and medicine given under supervision

d. Any co-existent illness was also treated.

e. On leaving, patient was reminded about the next visit. If he cannot come then medicine were given to his family member to give the patient under his supervision. The patient was made to feel that we care for him and want him to get better.

PROGRESS: X-ray chest, ESR,Hb, and sputum smear for A.F.B were repeated at 2 months, 5 months and end of treatment at 8 months.

RESULTS

Total 200 patients were enrolled in the study. There were four, two patients from each group, not followed the study protocol. In table no 1, DOT group 98 Mean±St.D, S.E.M49.5 ± 28.4 and2.8, , patients from which male 30.5 ± 17.4, 2.24, in 20-39 age group 19.5 ± 11.1,1.8, 40-60 age group 30.5 ± 17.4, 2.24, educated patients were 19.5 ± 11.1,1.8, uneducated 30.5 ± 17.4, 2.24, labour15.5 ± 8.8,1.61, farmers 18.0 ± 10.25,1.73, drivers 15.5 ± 8.8,1.61,extra2 ± 1.00, .58, married 19.5 ± 11.1,1.8, unmarried 30.5 ± 17.4, 2.24.In three times treatment in a week group 98 Mean±St.D, S.E.M49.5 ±

28.4 and2.8, , patients from which male 30.5 ± 17.4, 2.24, in 20-39 age group 19.5 ± 11.1,1.8, 40-60 age group 30.5 ± 17.4, 2.24, educated patients were 19.5 ± 11.1,1.8, uneducated 30.5 ± 17.4, 2.24, labour15.5 ± 8.8,1.61, farmers 18.0 ± 10.25,1.73, drivers 15.5 ± 8.8,1.61,extra2 ± 1.00, .58, married 19.5 ± 11.1,1.8, unmarried 30.5 ± 17.4, 2.24 and weight of patients before DOTs treatment 45.2±8.8,.9,weight of patients before in three times treatment of TB 46.7±8.6,.8.

In table and figure no-2 showed in DOTs therapy Mean±St.D,S.E.M45.5 ± 26.1,2.7,and 8, 4.50 ± 2.45,.87 patients were dropped from study period, weights of patients were increased after treatment 56.7±10.4, 1.0and result showed significant >0.05. And in three times therapy in week Mean±St.D,S.E. M30. 50±17.46,2.25 and 38, 19.50±11.11, 1.80 patients did not improve from study period, weights of patients were increased after treatment 59.1±10.4, 1.2 and result showed nonsignificant<0.05. It means that in DOTs group showed significant results as compared three times treatment in a week.

Table No.1: Frequencies, St.D, Mean And SEM of all variables showed in the table

	Mean±St.D	S.E.M		Mean±St.D	S.E.M
DOTs	49.5 ± 28.4	2.8	Three Times in a week	49.5 ± 28.4	2.8
Male	30.5 ± 17.4	2.24	Male	30.5 ± 17.4	2.24
Female	19.5 ± 11.1	1.8	Female	19.5 ± 11.1	1.8
Age 20-39	29.1 ± 6.87	1.07	Age 20-39	29.1 ± 6.87	1.07
Age 40-60	43.26 ± 12.63	1.28	Age 40-60	43.26±12.63	1.28
Educated	19.5 ± 11.1	1.8	Educated	19.5 ± 11.1	1.8
Uneducated	30.5 ± 17.4	2.24	Uneducated	30.5 ± 17.4	2.24
Labours	15.5 ± 8.8	1.61	Labours	15.5 ± 8.8	1.61
Farmers	18.0 ± 10.25	1.73	Farmers	18.0±10.25	1.73
Drivers	15.5 ± 8.8	1.61	Drivers	15.5 ± 8.8	1.61
Extra	2 ± 1.00	.58	Extra	2 ± 1.00	.58
Married	19.5 ± 11.1	1.8	Married	19.5 ± 11.1	1.8
Unmarried	30.5 ± 17.4	2.24	Unmarried	30.5 ± 17.4	2.24
Weight of Pts before treatment	45.2±8.8	.9	Weight of Pts before treatment	46.7±8.69	.8

Table No.2: Frequencies, St.D, mean, and SEM and p-value shoed in this table.

	Mean±St.D	S.E.M	P-value		Mean±St.D	S.E.M	P-value
No of Pts completed and improved in DOTs Therapy	45.5 ± 26.1	2.7	0.008*	No of Pts completed and improved in Three times Therapy in a week	30.50±17.46	2.25	1.00
No of Pts Dropped in DOTs	4.50 ± 2.45	.87		No of Pts not improved in Three times Therapy	19.50±11.11	1.80	
Weight of Pts after treatment	56.7±10.4	1.0		Weight of Pts after treatment	59.1±10.4	1.12	

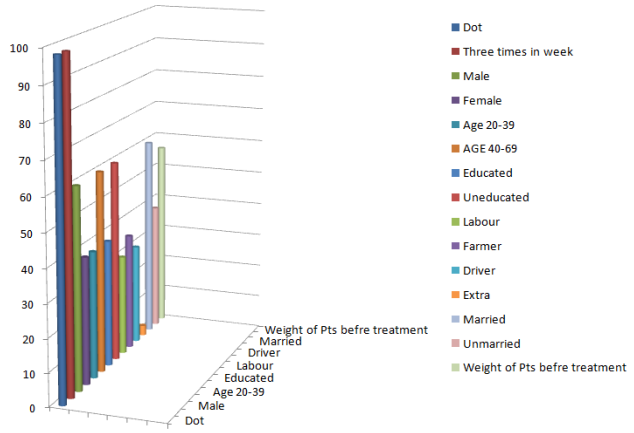

Figure No.1:

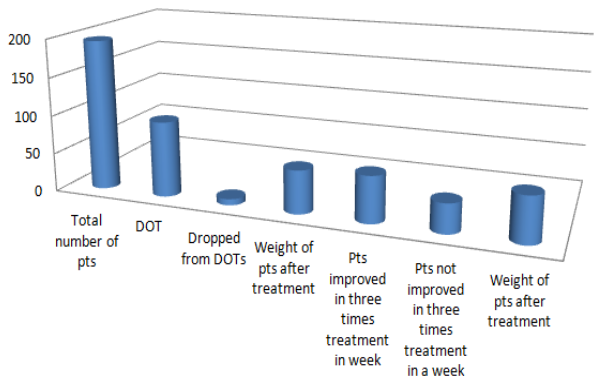

Figure No.2:

DISCUSSION

In DOTs therapy showed Mean±St.D,S.E.M, 45.5 ± 26.1,2.7, and 4.50 ± 2.45,.87 patients were dropped from study period, weights of patients were increased after treatment 56.7±10.4, 1.0 and result showed significant >0.05. And in three times therapy in week Mean±St.D,S.E.M30.50±17.46,2.25 and19.50±11.11, 1.80, patients did not improve from study period, weights of patients were increased after treatment 59.1±10.4, 1.2 and result showed nonsignificant <0.05. It means that in DOTs group showed significant results in the treatment of pulmonary tuberculosis, as compared three times treatment in a week.

This study consistent to the study of health personnel, community member, and family member observers, the proportions who did not practice actual DOT were respectively 11%, 23%, and 35%, and the proportions who changed to no observer or self administration were respectively 11%, 1%, and 2%, during the first 9 months of treatment (Barennes H 2010). In our results DOTs therapy showed Mean±St.D,S.E.M, 45.5 ± 26.1,2.7, and 4.50 ± 2.45,.87 patients were dropped from study period, weights of patients were increased after treatment 56.7±10.4, 1.0 and result showed significant >0.05.

Our study matched with the study of (Cavalcante SC 2010) From November 2000 to December 2004, respectively 339 and 311 pulmonary TB cases were enrolled and 1003 and 960 household were identified in DOTS and DOTS-A communities. Among contacts from DOTS-A communities, 26 (4%) had active TB diagnosed and treated, 429 (61.3%) had LTBI detected and 258 (60.1%) started preventive therapy. TB incidence increased by 5% in DOTS communities and decreased by 10% in DOTS-A communities, for a difference of 15% after 5 years (P = 0.04). DOTS-A was associated with a modest reduction in TB incidence and may be an important strategy for reducing the burden of TB.In DOTs therapy showed Mean±St. D,S.E.M, 45.5 ± 26.1,2.7, and 4.50 ± 2.45,.87 patients were dropped from study period, weights of patients were increased after treatment 56.7±10.4, 1.0 and result showed significant >0.05.in this study.

This study matched with study of (Hoshino H 2006) In Japan, DOTS as a method of directly observed treatment by Short Course Chemotherapy is divided into hospital DOTS and community DOTS. Group 1: A TB patient under PHC where at least daily observation DOTS (daily observation of drug taking at clinic or PHC to TB patients with risk factors of defaulting such as homeless, alcohol abuse, past history of default and so on) is available. Group 2: TB patients under PHC where home-visit DOTS (home-visit for observation of drug taking to the elderly TB patients who have risk to forget to take TB medicines regularly) only is available, Group 3: TB patients under PHC where only confirmation DOTS is available. Group 4: TB patients under PHC where community DOTS is not available. In addition, high death rate of patients under public assistance is analyzed. In group 1 with daily observation DOTS, TB patients under social or national health insurance showed higher treatment success rate and lower defaulter rate. (In three times therapy in week Mean±St.D,S.E.M30.50±17.46,2.25 and 19.50±11.11, 1.80, patients did not improve from study period, weights of patients were increased after treatment 59.1±10.4, 1.2 and result showed nonsignificant<0.05. It means that in DOTs group showed significant results as compared three times treatment in a week. In DOTs therapy showed Mean±St.D,S.E.M, 45.5 ± 26.1,2.7, and 4.50 ± 2.45,.87 patients were dropped from study period, weights of patients were increased after treatment 56.7±10.4, 1.0 and result showed significant >0.05.

The present study showed similarity with the study of (Vasantha M 2009). Among 1557 smear-positive TB patients registered under DOTS programme, the changes in weight ranged from a loss of 4 kgs to a gain of 20 kgs at the end of TB treatment; the average change in weight was 3.22 kgs. The gain in weight at the end of treatment was associated with age (<45 years), DOT at government centers, no problems in taking drugs as reported by patients and cure rate. The findings showed that there is an association between gain in weight with DOT at government centers and cure of patients. In DOTs therapy showed Mean±St.D,S.E.M, weights of patients were increased after treatment 56.7±10.4, 1.0 and result showed significant >0.05.

Our study results matched with (GR et al 2008) in which 3 days a week ATT for category 1 and category 11 pulmonary patients under a caring and strict DOTS strategy is more effective and less costly than half heartily supervised daily regimen. If the total consumption of drugs for 8 months with 3 days a week regimen is compared with that of daily regimen for 8 months there is a saving of 65-70% in cost and time. In DOTs therapy showed Mean±St.D,S.E.M, 45.5 ± 26.1,2.7, and 4.50 ± 2.45,.87 patients were dropped from study period, weights of patients were increased after treatment 56.7±10.4, 1.0 and result showed significant >0.05. And in three times therapy in week Mean±St.D,S.E.M30.50±17.46,2.25 and 38, 19.50± 11.11, 1.80 patients did not improve from study period, weights of patients were increased after treatment 59.1±10.4, 1.2 and result showed nonsignificant<0.05. It means that in DOTs group showed significant results as compared three times treatment in a week.

In the treatment of pulmonary Tuberculosis DOTs showed significant effects because Doctors and his staff be attentative to patients in doses of drugs and given with own supervision and Those patients who taken three times in a week ATT, missed the doses, due this

reason DOTs showed proved more effective in the treatment of tuberculosis.

CONCLUSION

DOTs showed significant results as compared three times in a week in the treatment of pulmonary tuberculosis

REFERENCES

1. Mycobacterium tuberculosis:Treatment in the United States and Other High-Income Nations (AIDS 2006) http://www.aidsetc.org/aidsetc?page=home-00-00
2. DrMarko2010EpidemologyofTuberculosis.http/www.tbalert.org/resources/paper_pub/back_tr
3. Thomas R Frieden 2006 Tuberculosis New York City Department of Health and Mental Hygiene, 125 Worth St., New York, NY, USA. Correspondence to Thomas R Frieden (e-mail: tfrieden@health.nyc.gov). University of Colorado Health Sciences Center School of Medicine, Denver, CO, USA. doi: 10.2471/BLT.06.038927 (Submitted: 17 November 2006 – Final revised version received: 9 February 2007 – Accepted: 9 February 2007)
4. PG Gopi M, Vasantha M, Muniyandi V, Chandrasekaran R, Balasubramanian, Narayanan PR. 2007 risk factors for non-adherence to directly observed treatment (DOT) in a rural tuberculosis unit, south indiahttp://medind.nic.in/ibr/t07/i2/ibrt07i2p66.pdf)
5. Elzinga G, Raviglione MC, Maher D. "Scale up: meeting targets in global tuberculosis control". Lancet 2004;363(9411):814–9.
6. Cohn DL, Catlin BJ, Peterson KL, Judson FN, Sbarbaro JA. "A 62-dose, 6-month therapy for pulmonary and extrapulmonary tuberculosis. A twice-weekly, directly observed, and cost-effective regimen". Annals of Internal Medicine 1990;112 (6): 407–15.
7. Dye C, Watt CJ, Bleed DM, Williams BG. "What is the limit to case detection under the DOTS strategy for tuberculosis control?".Tuberculosis 2003;83 (1-3): 35–43.
8. Grange JM, Zumla A. "The global emergency of tuberculosis: what is the cause?".The Journal of the Royal Society for the Promotion of Health 2002;122 (2): 78–81.
9. Harries AD, Jahn A, Zachariah R, Enarson D. "Adapting the DOTS framework for tuberculosis control to the management of non-communicable diseases in sub-Saharan Africa". PLoS Medicine 2008;5(6): e124.
10. Iseman MD. "MDR-TB and the developing world--a problem no longer to be ignored: the WHO announces 'DOTS Plus' strategy". The International J Tuberculosis and Lung Disease 1998;2 (11): 867.
11. G TR, Lehmann HP, Frieden TR. "Impact of DOTS compared with DOTS-plus on multidrug resistant tuberculosis and tuberculosis deaths: decision analysis". BMJ 2003;326 (7389):574.
12. Tuberculosis2010 http://en.wikipedia.org/wiki/Tuberculosis_treatment#cite_note-Elzinga2004-5
13. Vasantha M, Gopi PG, Subramani R. Weight gain in patients with tuberculosis treated under directly observed treatment short-course (DOTS). Indian J Tuberc 2009;56(1):5-9.
14. Hoshino H, Kobayashi N. Evaluation of effect of community DOTS on treatment outcomes by TB surveillance data, Kekkaku 2006t;81(10):591- 602.
15. Cavalcante SC, Durovni B, Barnes GL, Souza FB, Silva RF, Barroso PF, et al. Community-randomized trial of enhanced DOTS for tuberculosis control in Rio de Janeiro, Brazil, Int J Tuberc Lung Dis 2010;14(2):203-9.
16. Barennes H, Keophithoun T, Nguyen TH, Strobel M, Odermatt P. Survival and health status of DOTS tuberculosis patients in rural Lao PDR. BMC Infect Dis 2010;10:10:265.
17. Rasool G, Rehman S, Murad S, Kumar R. Three-times-weekly-antituberculosis-treatment-of-category-1-and-category-11-patients-of-pulmonary-tuberculosis-under-directly-observed-therapy-dots.http://www.articlesbase.com/medicine-articles/three-times-weekly-antituberculosis-treatment-of-category-1-and-category-11-patients-of-pulmonary-tuberculosis-under-directly-observed-therapy-dots-617665.html#ixzz15Ec00IWw

Address for Corresponding Author:
Dr. Ghullam Rasool Bhurgri,
Prof. of Pharmacology and Therapeutics,
Muhammad Medical College Hospital,
Mirpurkhas