AFRICAN JOURNAL OF MEDICINE
and medical sciences

EDITOR:
B. O. OSOTIMEHIN

ASSISTANT EDITOR:
A. O. UWAIFO

Compliance in pulmonary tuberculosis patients using directly observed treatment short course

E.A. Dosumu.

Department of Medicine, Respiratory Unit,Faculty of Health Sciences, University of Ilorin, Nigeria.

Summary:

Five hundred newly diagnosed cases of pulmonary tuberculosis patients were studied at Iwo Local Government tuberculosis (TB) control clinic Alaye, Iwo, Osun state of Nigeria. The study was to determine (a) the rate of compliance to antituberculous drugs in newly diagnosed pulmonary tuberculosis (PTB) patients over a 2-year period in Iwo, Nigeria treated with directly observed treatment short-course (DOTS). DOTS is a short course treatment lasting 6 - 8 months and (b) the effect of DOTS and the use of home visitors on compliance with a view to formulating a model that can be used all over Nigeria to stem the resurgence of PTB.

All newly diagnosed cases of PTB at Iwo, Osun state of Nigeria were treated with DOTS over a two-year period. TB home visitor provided with a motorcycle was used throughout the treatment period with free drug provision by Damien Foundations of Belgium based in Ibadan, Nigeria. The rate of compliance was noted in all cases. Total (100 percent) compliance and cure rate were recorded with the use of DOTS and TB home visitor in this study. The home visitor carried out 50 visitations during the study period. The use of DOTS with free drug provision and the use of home visitor as used in this study confirmed its effectiveness in enhancing compliance and hence cure of PTB. The study is a model that can be adopted for the whole of Nigeria and other countries globally if tuberculosis must be controlled.

Keywords: *Compliance, pulmonary tuberculosis, Nigeria.*

Résumé

500 nouveaux cas de tuberculose pulmonaire ont été étudie au centre medical public pour le controle de la tuberculose de l'arondussement de Iwo, dans l'état d'Osun an Nigeria. L'étude doit determiner (a) le taux de compliance des patients nouvellement diagnostiques de tuberculose pulmonaire sous traitement effectif de couste devoce (TECD) et d'utilisation des distributions communautaies sur la compliance en vue de formulas en model utilisable dans tout le Nigeria pour elupechez la recrudescence de la tuberculose pulmonaire (TBP).

Tous les nouveaux las de TBP diagnosistiques à Iwo, etat d'Osun au Nigeria etant traiter par le TECD pur une periode de 2ans. Une moto a été attribuce a leh agent de controle tuberculose penidant toute la periode du troutement, et des medicaments avaient fowni gratutement par la fonitation. Damien de Belgique basée à Ibadan au Nigeria. Le

Correspondence: Dr E.A. Dosumu, P.O. Box 29, Ilorin, Kwara State, Nigeria. Tel.: + 234 31-223217, Fax: +234 31-223548, Email ade dos @ unilorin. edu. ng

taux de compliance a été note daus tous les cos.100% de compliance put notée avec l'application du TECD et un agent de controle tuberculosis. Le controleur a effective , 50 visite, a domicile pendant la periode de l'etude.

L'application du TECD avec des medicaments gratuits en utilisant un controlex TB, comme dans cette etudes, a prouve son effience pour accroitie la compliance au traitement de la TBP. L'etude et un model qui peut etre adopté pour tout le Nigeria, ainsi que dans d'autres pays ou la tuberculose doit etre controlée.

Introduction

Compliance with anti-tuberculosis regimen remains globally a major problem militating against effective chemotherapy and therefore control of this grave disease [1-4]. Non-compliance, has also, among others, contributed to the globally reported multidrug-resistance tuberculosis [4]. Directly observed treatment (DOTS) was introduced by the World Health Organisation (WHO) to ensure drug compliance in PTB and to significantly reduce the rates of relapse and drug resistance in the community [5]. DOTS was further introduced by WHO [6] as the only control strategy to consistently produce 85 percent or more cure rate and prevent poor drug compliance. Political and financial commitment and a dependable drug supply are essential parts of the DOTS strategy [6]. This study was carried out using all the five elements of the DOTS strategy [6] to act as a model that can be used in the whole country bringing out the merit and the associated problems with a view of taking a stand on its applicability in the whole country and elsewhere.

Study population and methods

A clinical study was carried out between January 1996 and December 1997 to study compliance in pulmonary tuberculosis patients using DOTS in Iwo, Osun state of Nigeria [7]. Nigeria is the largest single geographical unit in the west coast of Africa. Nigeria is located between Latitude $4^\circ N$ and $14^\circ N$ and between Longitudes $3^\circ E$ and $15^\circ E$. It has an area of 923,800 square kilometers and therefore constitute 14 percent of the land area of West Africa. It has a population of 100-120 million. It is divided into 36 states with Abuja as the Federal capital. The major tribes include the Yorubas, Hausas and Ibos among others. Iwo in osun state where the study was carried out, is located 45 kilometers from Oshogbo and Ibadan both are capitals of Osun and Oyo states respectively. Iwo is a rich agricultural area and the inhabitant are mainly Yorubas by tribe. The subjects used were male and female Nigerians aged 15 year and above residing at Iwo. The age and sex distribution among the 500 patients studied is as shown in Table 3.

Table 1: Plan of PTB by age and sex among 500 newly diagnosed PTB cases in Iwo, Nigeria.

Age groups in Years	No of Male Examined	No of Females Examined	Total No	%
15-20	30	30	60	12
21-25	40	100	140	28
26-30	30	70	100	20
31-35	20	50	70	14
36-40	40	30	70	14
41-45	10	20	30	6
46-50	0	0	0	0
51-55	20	0	20	4
≥ 56	10	0	10	2
Total	200	300	500	100

As the subjects reported at the clinic, those that met the eligibility criteria were recruited accordingly to the study continuously till the study target population was met. Subjects were eligible if, apart from being symptomatic of TB, acid and alcohol fast bacilli (AFB) were demonstrated in their sputum by direct sputum smear using Ziehl-Neelsen stain at least two times in line with WHO recommendations [8]. Chest-x-ray was not made mandatory and was not used as diagnostic criteria since it has been shown by WHO [8] that this should no longer be used as a mandatory tool. However, patients were encouraged to have their chest-x-ray done.

Drugs were provided free by the Damien Foundation of Belgium based in Ibadan, Nigeria for all patients used in this study. All newly diagnosed patients used had ethambutol (E) 25 mg/kg, rifampicin (R)10mg/kg, pyrazinamide (Z) 30mg/ kg, and INH (H) 7.5mg/kg by DOT for the first 2 months, i.e., (2ERZH), and INH (H) 7.5mg/kg and thiacetazone (T)150mg dose for the last six months i.e. (6HT). Patients administered this drug on their own at home daily during the continuation phase of 8 months but were seen monthly at the TB clinic. A TB register was kept and checked daily by the TB supervisor. This was used to assess and monitor compliance to treatment by the patients. The Foundation also provided a motorcycle for the TB supervisor to do three types of visitations. Default preventive visitation (DPV) was done by his usual and random visitation of patients on the list. He usually stayed with each patient for about 10-15 minutes in order to give health talk, stress the significance of regular medication and perform family counselling. The other visitation type is default tracing visit (DTV). This was specifically to trace any patient that was not seen at the clinic. The drugs were then administered at home for the day of default and family counselling done. Thirdly, he does follow-up of cases that have completed the treatments to trace relapse cases (relapse tracing visitation RTV). Apart from this home visitation to assess clinical improvement or relapse, those that completed the 8-month regimen were seen monthly at the clinic for follow-up and for sputum test for AFB to diagnose relapse.

Weight measurement and sputum test for AFB were done for each patient at one, two, three, five and eight months of treatments. Sputum conversion (a change from WHO [8] standard sputum positivity indicating the significant density of AFB in the sputum to no recording of AFB in the sputum of the same patient using the same standard method) was

noted in all the patients and recorded to the months after the commencement of treatment (Table 1).

Table 2: Sputum conversion during treatment in 500 ND PTB cases in Iwo, Nigeria.

Sputum conversion: Months after commencement of treatment	No. of cases and (%)
One	350(70)
Two	498(99.6)
Three	500(100)
Five	500(100)
Eight	500(100)
Total	500(100)

The degree of compliance with the anti-TB drugs was noted for all subjects studied. Other relevant laboratory tests were carried out for all subjects which included packed cell volume, mantoux tests, chest-x-ray, human immuno deficiency virus serological test and liver function tests. Prognosis was assessed at the end of treatment by looking at the record of each patient noting those that died, those that completed treatment, etc., according to the treatment outcome in International Union Against Tuberculosis and Lung Disease (IUATLD)- assisted TB programmes (Table 2). Cured is as defined by WHO [8] and it is a patient who is smear negative at (or one month prior to) the completion of treatment and on at least one previous occasion.

Table 3: Outcome of 500 ND PTB cases after the completion of treatments according to the treatment outcome in International Union Against Tuberculosis and Lung Disease (IUATLD)-assisted TB programmes.

Outcome	No. of cases and (%)
Death (D)	0 (0)
Cured and treatment complete (C)	500 (100)
Defaulted (DF)	0 (0)
Failure (F)	0 (0)
Transfered out (TO)	2 (0.4)
Total	500 (100)

Results
There were no problems encountered in this study about drug compliance. During the intensive phase, DOT was used and this ensured that drugs were taken in the presence of a supervisor. Where any case is not seen, DTV was done and the drugs where administered at home. In 2 years, the supervisor had cause to do DTV on 50 occasions. He therefore, on an average, did 2 such visits per month for the 2 years of the study. A 100 percent cure rate was achieved.

Discussion
It has long been recognised by several workers [1-4] that lack of drug compliance is a major cause of failure of many TB regimens. Reasons given for lack of drug compliance include long treatment periods especially when they feel well [3,9-10] poverty and inability to purchase drugs, preference for native herbal medication, laziness and lack of understanding

and toxic effect of drugs [11]. Others include long distances between the homes of patients and the treatment centres [9,10,12,13], death of some of these patients [2,9] and lack of home visitors or social welfare officers [12,14,16]. A high compliance rate was associated with the presence of complications that were life threatening (haemoptysis) and those associated with breathlessness (lung abscess and pleural effusion) [17] and proximity to the treatment centre [17].

In this study, all these enumerated causes of lack of compliance have been addressed. A short course chemotherapy lasting 8 months was used, thus the issue of long treatment for 18 months was not at play. Directly observed treatment (DOT) was used hence the patients were seen daily during the first 2 months of intensive therapy and monthly during the follow-up period. Where they were not seen the supervisor using the motorcycle provided free and maintained by the Damien Foundation carried out default tracing visitation (DTV) and did family counseling.

The drugs were provided free of charge by the Damien Foundation of Belgium based in Ibadan, Nigeria. The drugs supplied were manufactured by Pharmamed Ltd. Malta and distributed by the International Dispensary Association of the Netherlands. Thus, this ensured that drug used were of high quality. Thus the problem of fake, expired or adulterated drugs being sold all over in Nigeria was taken care off. Due to the strategic location of the treatment centres, no patient lived more than 10 kilometers from the treatment centres in this study. Indeed, majority lived this walking distances from these centres, thus, the consequences of poverty did not arise. Majority 495 (99.5%) were also treated at out-patient clinics thus reducing treatment cost compared to if they were admitted in Hospitals. Several methods to monitor drug compliance have been tried (pill counting, testing urine for isoniazid metabolites, urine colour changes with rifampicin) but they can all be easily countered by the patient intent on non-compliance [4]. Other strategies that have been developed to measure and/or improve adherence to treatment of TB include [18-22] improved contact with medical personnel, DOT, and the use of incentive measures such as compensation or payments, however some of these methods are not easy to apply. Recently the medication event monitoring system (MEMS) [23] was introduced and was found to be more reliable than the pill count or the isoniazid urine test [24]. The MEMS system has been used in several studies to monitor drug compliance and has enabled clear descriptions to be made of the various patterns of non-compliance [25-26]. Unfortunately the MEMS system is not available for use in most low income countries of the world including Nigeria. It should be emphasized that DOTS is now recognised as the most effective strategy for ascertaining compliance in the treatment of TB. This study has aptly demonstrated this.

DOTS was first pioneered by Wallace Fox and the British Medical Research Council tuberculosis research units in 1958 and was later implemented by K. Styblo of IUATLD in 1979 as a way of effecting compliance to medication. It was adopted by WHO in 1995. DOTS has five main elements i.e., government commitment to TB control, sputum smear microscopy test to detect infectious cases, standard short-course anti-TB drugs and monitoring and reporting system for effective program supervision and evaluation with follow-up. As part of DOTS strategy, health workers counsel and observe their patients swallowing each dose of a powerful combination of drugs and the health services monitor the patients progress until each is cured. The five components of

DOTS strategy, i.e., Directly, Observed, Treatment, Short-course and DOTS, i.e., Government support to make TB control a high political priority must be meticulously followed. Unfortunately, DOTS is not used widely in Nigeria and this study is the first report of a large application of DOTS. Multidrug-resistant TB, a global problem has again not been properly documented in Nigeria but the combination of drugs as used in this study has been shown by WHO to be effective even where multidrug-resistant a TB has been reported [8]. However, DOTS as used in this study with the use of TB supervisor, if applied all over Nigeria, will bring a sharp fall in the prevalence of TB. It should be noted however that if this is to be done in the whole of Nigeria, it will involve a large budget to purchase all drugs centrally, and to pay the supervisors and the other staff involved. This is possible for committed and willing Federal, State and Local Governments Councils. In conclusion, DOTS is probably the most effective way to ensure drug compliance and can significantly reduce the rates of relapse of PTB in the community. However, DOTS is not simple, easy or cheap to conduct, but in the long term ensuring completion of treatment is cost-effective.

References
1.   Iseman MD. Short-course chemotherapy of tuberculosis, the harsh realities. Sem Resp Infet 1986; 1:213-219.
2.   American Thoracic Society. Treatment of tuberculosis and tuberculosis infection in adults and children. Am Rev Respir Dis 1986; 134:355-363.
3.   Houston S, Pozinak A and Ray CS. Therapeutic review: Tuberculosis. Cent Afr Jour Med 1991; Vol 37, No.8: 250-259.
4.   Harries A and Maher D. Diagnosis and treatment of pulmonary tuberculosis in adults.   Post Grad Doct Afr 1995; Vol. No. 4: 90-95.
5.   Weis Se, Slocum Pc, Blais F, *et al.* The effect of directly observed therapy on the rates of drug resistance and relapse in tuberculosis. N Engl J Med 1994, 330:1179-1184.
6.   World Health Organisation; Breakthrough in TB control announced by the World Health Organisation. Press Release WHO 23, 19 March 1997.
7.   Dosumu E. A. Clinical patterns and an alternative management of pulmonary tuberculosis using directly observed short course chemotherapy (DOTS) in Iwo, Osun State of Nigeria. An M.D. thesis submitted to the University of Ibadan, Nigeria 1998; 1-100.
8.   Harris AD and Maher D. TB/HIV. A Clinical manual. WHO TB/96. 200 Geneva: World Health Organisation, 1996.
9.   Onadeko BO and Sofowora EO. Comparative trial of thiacetazone with Izoniazid and paraminosalicylic acid (PAS) with isoniazid in the

treatment of pulmonary tuberculosis in Nigeria Jr of Trop Med and Hyg 1975; Vol. 103: 625-639.

10.   Onadeko BO and Sofowora EO. Daily short course (6 months) chemotherapy for treatment of pulmonary tuberculosis in Nigerians: A preliminary report. Afr J Med Sci 1978; 175-181.

11.   Pearson CA. Control of tuberculosis: Voluntary agencies role. proceedings of first Nigeria anti-tuberculosis conference 1973; 65-68.

12.   Adekunle AV, Adeyeri C and Aderele WI. Socio-economic perspective of tuberculosis: Implication for organising services. Nig Med J 1978; vol. 8 No 2: 92-95.

13.   Ogunmekan DA. The socio-economic factors influencing the utilization of Health services in Nigeria. Paper presented at the conference on social research and national development,Unibadan, Ibadan Nigeria 1975.

14.   EKE CUJ. The role of the Nurse in tuberculosis control today. Proceedings of the first Nigerian Anti-tuberculosis conference 1973; 8591.

15.   Ejiade CO. Role of paramedical staff in detection and control of tuberculosis. Proceedings of first Nigerian Anti-tuberculosis conference 1973; 93-97.

16.   Bodede MJ. Role of Home visitor in control of TB. Proceedings of first Nigerian Antituberculosis conference 1973; 99-107.

17.   Erhabor GE, Aghanwa HS, Yusuph H, Adebayo R, Alao J and Eirewele O. Compliance in pulmonary tuberculosis patients. One year evaluation of directly observed therapy in Obafemi Awolowo University Teaching Hospital Complex, Ile-Ife. Nigerian Thoracic Society (NTS) Annual Scientific Conference 1997; (abstract): 06,7.

18.   Fox W. Compliance of patients and physicians: experience and lessons from tuberculosis -II. Brit Med J 1983; 257: 101-105.

19.   Caneo WD and Snider DE. Enhancing patient compliance with tuberculosis therapy. Clin chest Med 1989; 10: 375-380.

20.   Menzies. R, Rocher I and Vissandjee B. Factors associated with compliance in treatment of tuberculosis. Tubercle Lung Dis 1993; 74:32-37.

21.   Pablos-Mendez A, Knirsch CA, Barr G, Larner BH and Frieden TR. Nonadherence in tuberculosis treatment: Predictors and consequences in New York City. Am J Med. 1997; 102:167-170.

22.   Sanmarti LS, Megias JA, Gomez MNA, *et al.* Evaluation of the efficacy of health education on the compliance with antituberculosis chemoprophylaxis in school children. A randomized clinical trial. Tubercle Lung Dis 1993; 74:28-31.

23.   Averbach M, Weintraabn M and Pollack DJ. Compliance assessment in clinical trials: the MEMS device. J Clin Res Pharmacoepidemiol 1990; 4: 199-204.

24.   Fallab-Stobi CL, Zellweger JP, Sauty A, Uldry CH and Ilorillo D, Burnier M. Electronicmonitoring of adherence to treatment in the perventive chemotherapy of tuberculosis. Int J Tuberc Lung Dis July 1998; 2(7) 525530.

25.   Urquhart J. Ascertaining how much compliance is