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Modified short-course chemotherapy of pulmonary tuberculosis in Ibadan, Nigeria - a preliminary report

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Summary

Over a 3 year period 3rd of April 1995 and 6th of April 1998 a controlled clinical trial of the modified short-course chemotherapy (SSC) in newly diagnosed cases of pulmonary tuberculosis in Nigeria was carried out. Between The SCC used was the one adopted from World Health Organisation/ International Union Against Tuberculosis and Lung Diseases for developing countries by the Nigerian National Tuberculosis and Leprosy Control Programme (NTLCP). The regimen used consisted of streptomycin (S), isoniazid (H), Rifampicin (R) and pyrazinamide (Z) in the initial or intensive phase of 2 months. Ethambutol (E) was sometimes substituted for streptomycin. The continuation phase was 6 months of thiacetazone, (T) and isoniazid (H), i.e., 2SHRZ/6TH or 2EHRZ/6TH. Sputum conversion was 90% at the second month of treatment and there was no bacteriological relapse after 18 months of follow-up. Side effects were few and consisted mainly of acne vulgaris which occurred in twenty (20.6%) of 97 patients during the continuation phase. It is concluded that the 8-month chemotherapy regimen adopted by NTLCP is efficacious in treatment of smearpositive pulmonary tuberculosis (PTB)

Keywords:*Pulmonary tuberculosis, modified short-course chemotherapy.*

Résumé

Pendant une periode de plus de 3 ans, de conroil d'essaue ilinique de la modification des lourt trautement dans les nouvedux cas diagnostique de tuberculose pulmonaire au Nigeria a ete faite eritre 3 Avril 1995 et le 6 Avril 1998. Le court traitement (ssc) utilise a ete celui adope par loms et.

L'union internationale contre la tuberculose et les malades pulmonaires darus les psuys developes et par le programme national Nigerian de controil de la tuberculose et la lepre (NTCP). Le traitement utilise etait faite de stiep to mycine (s), isoniazible (H), Rifanipcine (R) ` et - de ha pyriazinanide (Z) dans la phase initiale on intensive de 2 mois. L'ethanibutol (E) etait quelque utdise comme substictuant a la streptomocine. La phase de continuation etait de 6 mois avec la thiacetone (T) et lisoniazide (H) i.e.-2SHRZ/ 6 mois. La convertion des decliets purilant etait de l'ordie de 90% au second uois de traitement et il n'y a pas de re crudescence bacteriologiqueapies 18 unois de seuive. Les acrees qui etaient survenueschez (20.6%) 9+ patvents perdant la phase de continuation. Il a ete conelut que les 8 mois de regine chemotherapeutique adopte par la NTPLCP est eficace daus les traitements de tuberculose pulmonouie (PTB)

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Introduction

Research into shortcourse chemotherapy (SCC) for pulmonary tuberculosis has been conducted since the early 1970s [1-7]. The efficacy of daily SCC for pulmonary tuberculosis (PTB) using regimens containing rifampicin is no longer in doubt [6,7]. Several trials have shown that 6-month regimen consisting of isoniazid(H), rifampicin (R), pyrazinamide(Z) and streptomycin(s) is highly effective [8-11]. The two currently internationally accepted regimens for chemotherapy of tuberculosis for developed countries are: 2SHR/7HR or 2EHR/7HR, and 2SHRZ/4HR or 2EHRZ/ 4HR. These regimens especially the 4-drug intensive phase achieve complete bacteriological sterilization. The continuation phase of 4 months (or 7 months in the 3-drug regimen) ensures that the bacteriological relapse is acceptably low [7,8].

The SCC of tuberculosis adopted from WHO/ IUALTD for developing countries by the NTLCP is 2SHRZ/ 6TH or 2EHRZ/6TH [8-13]. The continuation phase consisting of thiacetazone, a bacteriostatic drug and isoniazid for 6 months is considered adequate in majority of cases [9]. However in Nigeria, there is a dearth of studies on the bacteriological relapse following the use of the 8-month regimen (2SHRZ/6TH or 2EHRZ/6TH). Bacteriological relapse is an essential index of efficacy as a considerably relapse rate leading to retreatment will not be cost effective and will also constitute public health problem.

Recently, in 1995 the Damien Foundation supplied drugs for treatment of tuberculosis to the University College Hospital, Ibadan to enable modified short course regimen to be incorporated into treatment. This study was carried out as a preliminary assessment of the efficacy of the modified SCC in the treatment of PTB in the University College Hospital (UCH), Ibadan.

Methodology

This study was conducted at the Outpatient Clinic of the UCH. Ibadan. Patients were eligible for inclusion into the study if they were newly diagnosed cases of PTB and their sputum contained tubercle bacilli on direct smear and/or culture. No patient weighing under 50 kg was included in the study in order to ensure uniformity in the dosage of the drugs.

Each patient was weighed and detailed general physical examination was done. Blood was taken for full blood count. Ethambutol, 800-1200 mg was given according to the weight. Other drugs given were rifampicin 600 mg; INH 300 mg and pyrazinamide 1.5 g daily for 2 months; these treatments were

directly observed for 2 months. After 2 months of treatment, monthly pre-packed envelopes of TH were given to all the patients for 6 months.

Patients were reviewed at monthly visits. Follow up assessment included documentation of symptoms and measurement of weights at regular intervals for 18 months. Sputum examination by smear and culture was repeated monthly for the first 5 months and at the end of the therapy. Chest radiographs were done on enrollment and thereafter at 3monthly intervals during treatment, and repeated 3 months after treatment and at the end of follow up. The radiographic appearance was assessed according to a precoded format [6]. Thus, minimal lesion when lesion was confined to one zone; moderate if lesion was confined to two zones of the same lungs and severe if lesion was found throughout the lung or three or more zones bilaterally.

Results

Ninety-seven Nigerian patients were assessed. There were 53 males and 44 females (M:F = 1.2:1). aged between 16 and 60 years. About 49.5% (48 out of 97) was between the age 21 of and 30 years.

Table 1 illustrates the sputum status during therapy. At 2 months of treatment 87(90%) of 97 patients had negative sputum for tubercle bacilli on direct smear and culture, while all the 97 patients had negative sputum cultures at 5 months of treatment. At 12 months, 30 patients were available for sputum examination and their sputa remained negative. At 18 months only 15 patients were available for examination but none could produce sputum for examination. The drop out rate was 70% at 12 months and 84.5% at the 18 months of follow-up.

Table 1: Correlation of the months after starting therapy with the number of patients with smear or culture negative sputum

Months after starting treatment	No. of patients (%) with smear/culture negative sputum	
2	87	(90)*
5	97	(100)
8	97	(100)

* *Figure in parentheses are percentages*

Table 2: Radiographic appearance in the 97 patients before treatment

Extent of lesion	No. of patients	(%)
Minimal	50	(51.55)*
Moderate	39	(40.20)
Extensive	8	(8.25)

* *Figure in parentheses are percentages*

The radiographic appearance before treatment was assessed as minimal, moderate and extensive depending on the size of the lesion (Table 2). A total of 89 (91.75%) of the 97 patients had minimal and moderate lesions while 8(8.25%) of the patients had extensive lesions with cavities. Maximal radiological clearance was noticed at the third month of treatment in 89(92%) of the patients.

The side effects observed during therapy are illustrated in Table 3.

Table 3: Frequency of adverse drug reactions in the 97 patients that took the 8-month short course regimen

Reaction	No. of patients	(%)
Nausea	5	(5.2)*
Joint pains	5	(5.2)
Acne vulgaris	20	(20.6)

* *Figure in parentheses are percentages*

Five patients complained of nausea in the first 2 months and were successfully treated with metoclopramide tablets. Joint pains were reported in 5 patients during the intensive phase of treatment and these responded to paracetamol tablets. There was no clinical evidence of gout in any of these patients.

Twenty (20.6%) of the patients had acne vulgaris during the continuation phase which was most likely due to the introduction of thiacetazone to the regimen. The acne disappeared after the end of the treatment in all the patients.

Discussion

This trial has revealed that pyrazinamide, rifampicin, isoniazid and streptomycin or ethambutol are effective in sterilization of the sputum in the intensive phase of treatment without causing serious adverse effects. This is in agreement with the previous trial [3].

Despite using thiacetazone during the continuation phase of therapy there was no bacteriological relapse to warant the use of retreatment therapy during the follow-up. We are of the opinion that if all patients remained sputum negative (30.9% of the patients were available) at 12 months after stopping the regimen 2SHRZ/6TH or 2EHRZ/6TH, it could be concluded that the regimen would be effective in the management of PTB in Nigeria. This 8month SCC adopted by the NTBLCP is less expensive compared with that of 2SHRZ/4HR or 2SHR/7HR and of comparative efficacy. This makes it an acceptable regimen for economically depressed countries of the third world. Serious side effects were not observed in this study and no case of clinical jaundice or blood dyscrasia was noted. Acne vulgaris which was the commonest adverse effect disappeared during the follow up.

In conclusion, in a developing country such as Nigeria where prevalence of pulmonary tuberculosis is still high, an effective 4-drug regimen consisting of SHRZ or EHRZ during the intensive phase would achieve rapid sterilization of the smear positive sputum of PTB patients. The use of thiacethazone and isoniazid (Thiazinah) for the last 6 months reduced the overall cost of treatment without loss of acceptable level of efficacy.

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