

CLINICAL RESEARCH

Ongoing studies

Randomised clinical trial to study the efficacy and tolerability of 3- and 4-month regimens containing moxifloxacin in the treatment of patients with sputum smear and culture positive pulmonary tuberculosis (CTRI/2008/091/000024)

Background

Earlier clinical trials conducted at Tuberculosis Research Centre (TRC) have shown that a 4-month daily regimen which included ofloxacin in the intensive phase was successful in the treatment of sputum positive pulmonary tuberculosis (PTB). But 4-month thrice weekly regimens containing ofloxacin, gatifloxacin or moxifloxacin were less successful with high relapse rates. Following publication of the TRC clinical trial demonstrating the efficacy of an ofloxacin containing regimen in shortening TB treatment to 4 months (Indian Journal of Tuberculosis, 2002), there has been a global interest in the role of quinolones in the primary treatment of TB. Moxifloxacin is now considered as the most effective of the quinolones for the treatment of TB due to its many unique mechanisms involved. TRC is now conducting a randomized clinical trial to study the efficacy and safety of 3- and 4-month moxifloxacin containing regimens for treatment of patients with sputum positive PTB. Newly diagnosed smear positive, PTB patients HIV sero negative for HIV, residing in Chennai and Madurai are randomly allocated to 3-month or 4-month moxifloxacin regimens or a control 6-month regimen. Treatment is given under direct observation and patients are periodically followed up with sputum examinations. The patients are also closely monitored for development of adverse drug reactions. The regimens used in the trial are given in table 1.

Table 1: Trial regimens

Regimens	Intensive phase	Continuation phase	Duration (months)
Test regimen 1	3 RHZEM daily		3
Test regimen 2	2 RHZEM daily	2 RHM daily	4
Test regimen 3	2 RHZEM daily	2 RHM thrice weekly	4
Test regimen 4	2 RHZEM daily	2 RHEM daily	4
Control regimen	2 RHZE thrice weekly	4 RH thrice weekly	6

R – rifampicin; H – isoniazid; Z – pyrazinamide; E – ethambutol; M -moxifloxacin

The sample size for the study is 1650 patients, and 270 patients have been enrolled as of 31st March, 2009.

The baseline characteristics of patients recruited to the trial are given in table 2.

Table 2: Baseline characteristics

Regimen	Test regimen 1 (n=52)	Test regimen 2 (n=56)	Test regimen 3 (n=53)	Test regimen 4 (n=54)	Control regimen (n=55)	Total (n=270)
Sex						
Male	40	42	37	39	40	198
Female	12	14	16	15	15	72
Age						
<40 years	33	31	37	35	36	172
≥40 years	19	25	16	19	19	98
Initial sputum smear grade						
0 or 1+	11	14	10	14	9	58
2+ or 3+	41	42	43	40	46	212
No. of zones involved in chest X-ray						
≤ 2	11	13	11	12	12	59
> 2	41	43	42	42	43	211

Preliminary results indicate that a significantly higher proportion of patients treated with the moxifloxacin regimens became sputum culture negative after first and second month of treatment compared to those treated with the control regimen (table 3).

Table 3: Sputum culture results in patients treated with moxifloxacin and control regimens

Month of treatment	Moxifloxacin regimens (n=186)			Control regimen (n=42)		
	No. of patients	Culture negative		No. of patients	Culture negative	
		No.	%		No.	%
1	184	67	36	41	5	12
2	181	171	95	39	28	72

[Contact person: Dr.M.S.Jawahar (E-Mail ID: jawaharms@trchennai.in)]

Management of patients who fail to Category-II regimen of the TB control programme

Background

The TRC has been conducting drug resistance surveillance of patients treated with Revised National Tuberculosis Control Programme (RNTCP) regimens in a TB Unit in Tiruvallur district in Tamil Nadu, south India (1999 to 2005). It was observed that 52 patients failed to Category-II regimen. The drug susceptibility testing (DST) results showed that 32% had multi drug-resistant TB (MDR-TB), 26% had mono or poly drug-resistant (DR) organisms, but were not MDR-TB (i.e. resistant to isoniazid/streptomycin/streptomycin-isoniazid/ethambutol), 29% harboured fully susceptible organisms, and in 13% there was no growth in the culture.

Directly observed treatment short-course (DOTS) using standardized Category-IV regimen (DOTS plus) is being implemented in India in a phased manner. Limited information is available on the feasibility, effectiveness and profile of adverse reactions of the Category-IV regimen. Also, there are no guidelines on the management of patients who fail to Category-II regimen but are non-MDR.

Aims

- To assess the feasibility, effectiveness and profile of adverse reactions of DOTS plus regimen compared to modified DOTS plus regimen in patients who fail to Category-II regimen and have MDR-TB
- To assess the treatment outcome of a re-treatment regimen in patients who fail to Category-II regimen and not having MDR-TB based on drug sensitivity test

Methods

Management of patients with MDR-TB

Eligibility criteria: Patients harbouring *Mycobacterium tuberculosis* (*M. tuberculosis*) resistant to at least isoniazid (INH) and rifampicin (RMP) with or without resistance to other drugs will be eligible for the study. At least one sputum smear examined within 10 days of starting treatment should be positive for acid-fast bacilli (AFB).

Treatment regimens: Patients are being randomly allocated to one of the following regimens based on the drug resistance pattern (stratified based on resistance to first-line drugs alone or resistance to one or more of any second-line drug along with MDR-TB).

Regimen I: 6(9) (K₇ (Of, Eth, Z, E & Cy)₇ 18 (Of, Eth, E & Cy)₇

Regimen II: 6(9) K₃, (Of, Eth, Z, E & Cy)₇ 18 (Of, Eth, E & Cy)₇

(K – kanamycin; Of - ofloxacin; Z – pyrazinamide; E – ethambutol; Eth – ethionamide;
Cy – cycloserine)

Regimen I: It is a standardized treatment regimen approved by RNTCP (Category-IV regimen - DOTS-Plus) for the treatment of MDR-TB. It consists of an intensive phase of 6 drugs for a period of 6-9 months followed by a continuation phase of 4 drugs for 18 months.

Regimen II: Similar to regimen I but kanamycin given three days a week instead of daily administration.

The study patients from Tiruvallur district are hospitalized for the first 2 - 4 weeks of treatment. Treatment is being arranged from the nearest Primary Health

Centre (PHC) to be administered under direct supervision. The drugs are then supplied from TRC to the DOT provider on a monthly basis. All patients from Chennai Corporation are being given treatment as DOT from TRC or its subcentres by TRC staff.

The sample size for the study has been estimated to be about 75 patients in each arm.

Clinical and laboratory investigations

Before starting treatment, patients undergo detailed history elicitation for previous second-line anti-TB treatment (ATT), chest X-ray, haemogram, liver and renal function tests, pregnancy test for female patients, 3 sputum examinations for smear and culture for including DST first and second line anti-TB drugs and enzyme linked immunosorbent assay (ELISA) for HIV.

After starting treatment patients are being followed up every month and investigations repeated periodically. Patients are being monitored closely for adverse reactions.

Outcome measures: The following outcome measures will be analysed:

- ◆ Sputum smear conversion at 3 and 6 months of treatment
- ◆ Sputum culture conversion at 3 and 6 months of treatment
- ◆ Favourable response (bacteriological) at the end of treatment
- ◆ Adverse reactions to anti-TB drugs

Treatment failures will be managed by individualized regimens based on the DST result.

Management of patients not having MDR-TB

Background

Eligibility of criteria

Patients, who harbour fully susceptible bacilli, or bacilli resistant to isoniazid/streptomycin/streptomycin-isoniazid/ethambutol, come under this group.

Treatment regimens

Patients are allocated to one of the two regimens (stratification based on sensitivity to INH).

Regimen 1 : 6 K(REZ)₃ (REZ)₇

Regimen 2: 6 K(REZH)₃ (REZH)₇

K – kanamycin; H – isoniazid; Z – pyrazinamide; E – ethambutol; R –rifampicin

The sample size for the study has been estimated to be about 75 patients in each arm.

Assessment and follow up procedures are similar to patients having MDR-TB.

Outcome measures: The following outcome measures will be analysed:

- ◆ Sputum smear conversion at 3 and 6 months of starting treatment
- ◆ Sputum culture conversion at 3 and 6 months of starting treatment
- ◆ Favourable response (bacteriological) at the end of treatment

Treatment failures are being managed based on the DST result. Intake to the study was initiated in September, 2007 and upto 31st March 2009, 58 patients have been recruited (42 in MDR and 16 in non-MDR).

The study is in progress.

[Contact person: Dr.Aleyamma Thomas (E-Mail ID: aleyammat@trcchennai.in)]

Utility of two antibiotic algorithms and repeat sputum smear microscopy to improve the efficiency of diagnosis in smear negative TB

Background

The diagnosis of smear negative PTB is vital, since such patients are likely to break down to smear positive cases if left untreated. A break down rate of about 28% in six months and 40% in two years has been reported. Importantly, nearly half of smear negative cases who require treatment develop active disease with in the first three months.

Aims

Primary objectives

- To assess the utility of two antibiotic algorithms to improve the efficiency of diagnosis of smear negative TB

- To study the utility of repeat sputum microscopy in chest symptomatics with persistent symptoms after a course of antibiotics

Secondary objectives

- To study the proportion of TB patients among those confirmed by culture, and their correlation with chest X-ray findings
- To obtain information on the etiological profile of respiratory infections and their sensitivity pattern and studying appropriateness of antibiotic algorithm

Methods

Patients referred with cough of >3 weeks and having 3 smears negative for AFB are eligible to get recruited to the study. At TRC, the patients undergo 3 sputum examinations for AFB by smear and culture, and a chest X-ray is taken. They are randomly allocated to one of the following antibiotic regimens for treatment duration of 10 days:

- ◆ Co-trimoxazole (sulphamethoxazole-800 mg, trimethoprim-160 mg) twice daily for 10 days
- ◆ Doxycycline 100 mg twice a day on first day then once a day for 4 days followed by Amoxicillin 500 mg three times a day for 5 days

At the end of the antibiotics course, chest X-ray and sputum examinations are repeated, and patients are assessed for persistence of symptoms. Patients are started on Category-III regimen, if repeat sputum remains negative by smear and X-ray is still suggestive of TB. In cases of chest X-ray being abnormal but not suggestive of TB, they are followed up for 6 months with monthly sputum examination. If smears or cultures turn positive, the patient will be started on Category-I regimen.

All the patients are being reviewed with culture results. It is proposed to admit 700 patients to each antibiotic arm. Till March 2009, 273 patients have been recruited to the study.

The study is in progress.

[Contact person: Dr.Aleyamma Thomas (E-Mail ID: aleyammat@trcchennai.in)]

**Efficacy and safety of immunomodulator (*Mycobacterium w*) as an adjunct therapy in Category-II pulmonary tuberculosis
(Funded by Department of Biotechnology, India)**

Background

The immunomodulator containing *Mycobacterium w* was developed by the National Institute of Immunology, New Delhi in 1980. It was found to be useful in the prevention of TB in experimental animals. A pilot study conducted to evaluate the role of *Mycobacterium w* in improving sputum conversion rate in PTB, showed that the conversion rate was faster when *Mycobacterium w* was added to the short course chemotherapy (SCC). Immunomodulators work against persistors, which may result in reducing the relapse rates. The addition of immunomodulator to chemotherapy is well tolerated and does not increase adverse reactions to the therapy.

Aim

- To study the cure rate in Category-II PTB patients after the addition of *Mycobacterium w* vaccine to standard anti-TB drugs

Methods

This study was planned as a double blind, randomized, placebo controlled multicentric clinical trial. The patients were randomly chosen to receive either the vaccine or placebo along with the standard Category-II RNTCP regimen.

Results

The study was initiated in March, 2006. In the two year period till March 2008, 268 patients were registered, 115 screened and 59 enrolled into the study. Vaccine acceptability among patients was found to be good. Of the 59 enrolled to the study, 45 have completed treatment and are on follow up, 4 defaulted for treatment - 2 in the intensive phase and 2 in the continuation phase, 4 developed serious adverse events – 2 renal and 2 hepatic. Six patients required change of chemotherapy – 4 for multidrug resistance, one for clinical complication, and one for pregnancy. Two patients who had hepatotoxicity also had change of chemotherapy. Intake to the study has been completed and patients are being followed-up.

[Contact person: Dr.R.Balambal (E-Mail ID: balambal.r@trcchennai.in)]

Preventive therapy for TB among HIV-infected individuals (Funded by United States Agency for International Development)

Background

Available evidence indicates that preventive therapy for TB reduces the frequency of active TB in HIV+ subjects by about 50% to 60%. Protection has been reported to be greatest in adults with a positive tuberculin skin testing (70% reduction in incidence and 25% reduction in mortality). The ideal duration of preventive therapy especially in TB-endemic countries is not known.

Aims

- To study the efficacy of two different preventive therapy regimens in HIV-infected persons in reducing the incidence of TB and overall mortality
- To find out if a long duration regimen with INH daily is superior to a 6-month regimen of INH and ethambutol (EMB)

Outcome Measures

- ◆ Development of pulmonary or extra-pulmonary TB
- ◆ Death due to TB

Study Design

The study was conducted as a two-armed prospective randomized clinical trial among HIV-positive patients without active TB.

The treatment regimens were as follows:

- ◆ EMB (800 mg) and INH (300 mg) daily for six months, self-administered, collected once in fifteen days
- ◆ INH (300 mg) daily for 3 years (in lieu of lifelong prophylaxis) self administered, collected once in fifteen days

Patients in both study groups received 10 mg of pyridoxine daily during treatment.

Patients were followed up for a period of three years from the time of admission to the study. Clinical examination and relevant investigations were done every three months. Patients suspected to have TB at any time were completely evaluated and treated appropriately. Any positive culture was subjected to drug

susceptibility testing. The cause of death was ascertained by a panel of doctors after thorough evaluation of last available records.

Results

Of the 712 patients admitted to the study from March 2001 – September 2005, 683 were eligible for analysis. The mean age, weight, CD4 cell count and Mantoux were comparable in both the groups.

A total of 300 patients from the INH arm and 320 patients from the EMB/INH arm have completed 36 months of follow-up as of 31st March, 2009.

Eighteen patients in the EMB/INH arm developed active TB giving a breakdown rate of 2.11/100 person years and 11 in the INH group (breakdown rate of 1.55/100 person years). Most of the breakdowns in both the arms had occurred within the first 12 months. There were 25 deaths in patients in the EMB/INH arm, and 20 deaths had occurred in patients who were receiving INH (table 4).

The toxicity patterns in both the groups were similar. In only one patient in the INH arm, the treatment had to be terminated because of severe hepatotoxicity culminating in jaundice.

The interim findings suggest that 6 months of EMB/INH is as effective as 3 years of INH in preventing TB among HIV-infected persons. Patients with low CD4 cell counts were at a higher risk of TB breakdown and death.

Table 4: Incidence of TB and death by regimen (Intent to treat analysis)

	EMB/INH arm	INH arm
TB incidence (per 100 person years)	2.11 (1.42 – 3.46)	1.55 (0.73 – 2.36)
Rate ratio	1.55 (0.79 – 3.03)	1.26 (0.69 – 2.27)
Death (all – cause) (per 100 person years)	2.77 (1.68 – 3.86)	2.21 (1.24 – 3.18)

The above values are mean (range)

[Contact person: Dr. Soumya Swaminathan (E-Mail ID: soumyas@trcchennai.in)]

**A clinical trial to study the efficacy of two different once daily anti-retroviral regimens along with anti-TB treatment, in patients with HIV-1 and TB
(Funded by National AIDS Control Organization, India)**

This randomized clinical trial was designed to study the efficacy and safety of two different once-daily anti-retroviral regimens along with ATT in the treatment of HIV-infected TB patients. The specific aim was to compare the efficacy of a once-daily regimen of didanosine (ddl) and lamivudine (3TC) with either efavirenz (EFV) or nevirapine (NVP) when given along with standard ATT in patients with HIV and TB with CD4 < 250 cells/mm³. The primary outcome measure was suppression of viral load to <400 copies/ml at 24 weeks of anti-retroviral treatment (ART). The secondary outcome variable was to compare the utility of directly observed treatment in this setting with self-administered ART.

Recruitment of patients to the trial was initiated in May, 2006 and was stopped in June, 2008 as per recommendation of the Data Safety & Monitoring Board (DSMB). As of April 1, 2008, 564 patients had been screened for the study at 5 centres (3 sites in Chennai, 1 in Vellore and 1 in Madurai). One hundred and sixteen patients were admitted to the study (demographics in table 5). All patients were randomised at the end of intensive phase of ATT (2 months). Fifty nine patients received the EFV-containing regimen and 57 the NVP-containing regimen. Eighty five of these patients had PTB while 31 had extrapulmonary TB (pleural effusion/TB lymph node). Response to ATT was good with 87.5% of patients being culture negative at 2nd month, and 96% of those who completed 6 months of ATT became culture negative. Overall, cure/completion rate was approximately 90%. The favourable response to ATT was 84% in the NVP regimen and 95% in the EFV regimen. Table 6 shows the outcome, by efficacy and intent to treat analysis at 24 weeks of ART. Only one patient had an adverse reaction to ATT drug which required a change of treatment.

The immunological response to ART has been satisfactory with good improvement in CD4 counts (table 7).

The DSMB met on December 15, 2007 (for first interim analysis) and recommended that intake to the NVP arm be withheld till further analysis. This

was in view of the high failure and death of patients admitted to the NVP arm compared to the EFV arm (favourable response 67% in NVP arm vs. 85% in EFV arm, $p=0.038$).

The second interim analysis was done and presented to the DSMB on June 14, 2008. The DSMB recommended that intake to the study can be stopped, as the primary outcome had been determined to be significantly different between the two regimens.

Table 5: Demographic details

Baseline characteristics*	EFV regimen (n = 59)	NVP regimen (n = 57)
Age (years)	34.5 ± 7.5	37.6 ± 7.8
Weight (kgs)	43.0 ± 8.6	42.0 ± 7.3
Body mass index	16.3 ± 2.6	16.4 ± 2.4
Median CD4 cells/mm ³ (IQR)	85 (47 - 85)	83 (33 - 135)
Median VL copies/ml (IQR)	3,62,000 (41,575-7,50,000)	2,82,000 (1,28,500-6,49,500)

*All values are mean ± SD except CD4 and viral load which are median values and range given in parantheses.

Table 6: Outcome at 24 weeks in the study population

Variable	EFV regimen (n = 59)	NVP regimen (n = 57)
<u>Response to ATT</u> (Efficacy analysis) Favorable	56 (95%)	48 (84%)
<u>Response to ART</u> (ITT analysis) Plasma HIV-RNA < 400 (copies/ml)	50 (85%)	38 (67%)*
Adverse events		
Any grade	65	34
Grade 3/4	7	4
Virological failure	6	11
Death	0	5
Lost to follow-up	3	3

* $p = 0.038$

Table 7: Changes in CD4 counts (cells/mm³) during ART

Regimen	Baseline	0 week	1 month	4 month	6 month
Efavirenz	95 ± 58	125 ± 84	255 ± 141	275 ± 125	325 ± 173
Nevirapine	87 ± 60	132 ± 82	238 ± 163	247 ± 166	283 ± 169

The above values are mean ± SD

[Contact person: Dr. Soumya Swaminathan (E-Mail ID: soumyas@trcchennai.in)]

Innate and adaptive immunity in children starting antiretroviral drugs in India

(Collaboration with University of Miami, Florida, USA)

[Funded by Indo-US JWG Maternal and Child Health (NIH and ICMR)]

Background

Currently, CD4 counts are the mainstay of immunologic assessment for HIV-infected adults and children based on which treatment decisions are made. It would be useful to identify other immunologic markers that can be predictive of disease outcome of perinatally HIV-infected children who are treatment naïve but now have access to antiretroviral therapy as per National AIDS Control Organization (NACO) guidelines.

Aims

- To investigate the relationship of naïve CD4 T-cells with total CD4 T-cells at study entry and prospectively over the course of the disease with and without ART
- To determine the relationship between CD8⁺ T-cells expressing CD127 (IL-7R α), the receptor for cytokine IL-7 and disease progression
- To determine the relationship between dendritic cells (DC) (numbers and function) and immunologic status

Methods

Between February 15, 2007 and March 30, 2009, 62 ART naïve HIV-positive children (28 males/34 females) were screened and recruited to the study. The

age of the study participants ranged from 9 months to 13 years with a median BMI of 14.4 (range: 6.4 – 24.1). The total CD4 counts in the study subjects ranged from 131 to 2396 (median = 777) cells/mm³ and CD8 counts from 573 – 6086 (median = 1625) cells/mm³. During each visit, all children were examined clinically, and venous blood samples were collected for immunological and other parameters as per the protocol.

The number of patients enrolled in the study and their follow-up details as of March, 2009 are given in table 8.

Table 8: Details of patient recruitment and follow-up

	Baseline	1 st follow-up (12 weeks)	2 nd follow-up (24 weeks)	3 rd follow-up (36 weeks)	4 th follow-up (48 weeks)
No. of children	62	62	60	54	46

ART was given as per NACO guidelines wherever necessary. Children not requiring ART as per the treatment guidelines were also monitored regularly and provided with prophylaxis/treatment against opportunistic infections. The children are being followed up to 48 weeks, after which they are transferred to the nearest ART centre for further management.

For this analysis, patients were classified into three groups based on their CD4% as immune category-1 (IC-1) [CD4 % > 25], immune category-2 (IC-2) [CD4 % 15 - 25] and immune category-3 (IC-3) [CD4 % < 15]. Eight age matched healthy children (age 3–13 yrs, median = 5 yrs), were also recruited, who served as HIV-negative control subjects. The control subjects underwent a single blood sampling for immunological and other parameters. Statistical analysis was performed using a general linear model with planned contrasts to compare mean values among the three immune categories. SAS version 9.1 was used for all analysis.

Results

HIV-positive children from all the three immune categories (IC-1, IC-2 and IC-3) had a significantly decreased proportion of naïve CD4 and CD8 T-cells compared

to HIV-negative children. In general, as total CD4% decreased, naïve CD4 and CD8 T-cell % also decreased. Proportion of naïve (CD45RA+ CD62L+) cells was greater in CD4 T-cell population as compared to CD8 T-cells, and in both T-cell subsets (CD4 and CD8), the numbers directly correlated with CD4%.

All HIV-positive groups showed a relative increase in expression of CD38 and HLA-DR on CD4 / CD8 T-cells compared to control subjects. CD38 and HLA-DR expression was higher in children belonging to IC-2 and IC-3 compared to those in IC-1. Expression of immune activation markers (CD38+ HLADR+) was greater in CD8 T-cells and its expression remained high during follow-up in both subsets (CD4 and CD8).

Expression of CD127 (IL-7R α), a marker of memory cells was reduced mainly in CD8 T-cells and its expression was correlated directly with CD4%. Expression of CD127 in CD4+ T-cells was also lower, though not significant.

Myeloid dendritic cells (mDC) from HIV-positive children expressed reduced levels of maturation marker (CD83) upon resiquimod stimulation compared to control subjects. Similar results were obtained with plasmacytoid dendritic cells (pDC) upon stimulation with resiquimod.

No significant differences in cytokine secretion were observed in all the immune category groups. Although induction of cytokines, IFN- α in pDC and TNF- α in both pDC and mDC were normal at baseline, cytokine production was reduced at nine months, predominantly in pDC.

A summary of the key findings of other immunologic markers is presented in table 9.

Conclusions

This cohort of largely clinically stable HIV-infected children has demonstrable immunologic defects dominated by deficits in naïve T-cells and ongoing immune activation, with progressive and subtle defects in innate immunity, involving mainly pDC. All abnormalities showed a gradation in progression from IC-1 group to IC-2 and IC-3, which was parallel to deterioration in immune function (CD4%).

The study is in progress.

[Contact person: Dr. Soumya Swaminathan (E-Mail ID: soumyas@trcchennai.in)]

Table 9: Summary of key immunologic findings

	Baseline compared to controls				At 9months, compared to baseline			
	Total	IC groups			Total	IC groups		
		I	II	III		I	II	III
DC	↔	↔	↔	↔	↔	↔	↔	↔
pDC CD80	↔	↑	↔	↔	↔	↓	↔	↔
mDC CD83	↓	↓	↓	↓	↔	↔	↓	↔
pDC CD83	↓	↓	↓	↓	↔	↔	↔	↔
pDC IFNα	↔	↔	↔	↔	↓	↓	↓	↔
mDC TNFα	↔	↔	↔	↔	↓	↔	↔	↔
pDC TNFα	↔	↔	↔	↔	↓	↓	↓	↓
CD4 DR+ CD38+	↑	↔	↑	↑	↔	↑	↔	↔
CD8 DR+ CD38+	↑	↔	↑	↑	↔	↑	↔	↔
CD4127	↔	↔	↔	↔	↑	↑	↔	↔
CD8127	↓	↔	↔	↔	↑	↑	↔	↔
CD8 Naïve	↓	↓	↓	↓	↔	↔	↔	↑
CD4 Naïve	↓	↓	↓	↓	↔	↔	↔	↔
CD4 Central Memory	↔	↔	↔	↔	↓	↔	↔	↔
CD8 Central Memory	↔	↔	↔	↔	↔	↓	↓	↔
CD4 Effector Memory	↔	↔	↔	↑	↔	↑	↔	↔
CD8 Effector Memory	↑	↔	↑	↑	↓	↔	↔	↔
CD4 Effector	↔	↔	↔	↔	↔	↔	↔	↔
CD8 Effector	↔	↔	↔	↔	↔	↔	↔	↓

↔ no difference, ↑ increase, ↓ decrease

Changes in HIV viral load in patients undergoing treatment for filarial infection

(Collaboration with YRG Care, Chennai and NIAID, NIH, USA)

[Funded by National Institute of Allergy and Infectious Diseases (NIAID)]

The goal of this study is to determine the changes in HIV viral load that occur in patients co-infected with HIV and filaria, over 1 year, following treatment with DEC/Albendazole, and to compare those with changes in viral load among HIV-infected patients without filarial co-infection. Two groups of patients are being recruited for the study; the first is a group with HIV and filarial infection (detected by serum antigen test) and the second, or control group have HIV infection, but not filariasis. The second group of patients is matched with the first group based on age, gender, HIV viral load and CD4 cell counts. The total sample size required for this study is 138 (HIV/Filarial – 46, HIV – 92). Patient recruitment is being done at both TRC and YRG Care. Screening of patients for this study started on May 15, 2007 at TRC and up to March 31 2009, 254 patients were screened, of whom 32 (HIV and Filaria – 10, HIV - 22) patients have been recruited to the study. Patient enrolment to the study is ongoing.

[Contact person: Dr. Soumya Swaminathan (E-Mail ID: soumyas@trcchennai.in)]

Evaluation of a diagnostic algorithm for HIV-positive TB suspects who are initially smear negative

(Collaboration with Government Hospital for Thoracic Medicine, Tambaram and National AIDS Research Institute, Pune)

[Funded by United States Agency for International Development (USAID) through the WHO under the Model DOTS Project]

Background

In HIV-infected patients with active TB disease, sputum smears are more likely to be negative for AFB by smear microscopy. In RNTCP, diagnosis of TB is based on sputum smear examination and response to a course of antibiotics.

Aim

- To determine the utility of initial chest X-ray and sputum culture on Lowenstein-Jensen (LJ) solid medium in the diagnostic algorithm for TB among HIV-infected initially smear negative TB suspects

Methods

This has been planned as a multicentric, prospective study which will enroll 540 HIV-infected patients with suspected TB disease. Those suspects who are smear negative on initial sputum examination have a chest X-ray and sputum culture performed, and receive a course of broad spectrum antibiotics, and are reviewed with a repeat chest X-ray after 15 days. Patients considered seriously ill or with chest X-ray suggestive of TB have ATT started by the site physician.

Results

Out of 270 patients recruited in to the study, 249 (males – 167; females – 82) were included in the analysis. The mean age and mean body weight of the patients were 35.8 years and 46.7kg respectively. The median CD4 cell counts were 182 cells/mm³. About 77% of the patients had cough and breathlessness for > 3 weeks, 64% had fever for > 3 weeks, and 89% had weight loss. Forty eight patients (19.3%) had a positive TB culture initially. Of the 144 patients (58.5%) with an abnormal chest X-ray, 45 (36.6%) demonstrated clinical and radiographic improvement after treatment with antibiotics.

Patient recruitment at Chennai has been completed, while it is ongoing at the National AIDS Research Institute, Pune.

[Contact person: C Padmapriyadarsini (E-Mail ID: padmapriyadarsinic@trc chennai.in)]