SHORT COMMUNICATION

Intermittent Short Course Therapy for Pediatric Tuberculosis

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We conducted this study to assess the efficacy of intermittent short course therapy in all forms of pediatric tuberculosis using a coordinated approach with Revised National Tuberculosis Control Programme (RNTCP). Sixty-five children were treated using RNTCP protocols with some modifications, such as dose adjustments or prolongation of treatment in selected children. Overall response rate was 95% (pulmonary 94% and extra pulmonary 97%). There was one case with possible relapse. With dynamic inputs from both the treating pediatrician and personnel from Directly Observed Treatment – Short-course (DOTS) centers, we could successfully implement RNTCP protocols in childhood tuberculosis.

Key words: *Childhood tuberculosis, Intermittent therapy, RNTCP.*

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Revised National Tuberculosis Control Programme (RNTCP) recommends intermittent short course chemotherapy (ISSC) under Directly Observed Treatment-Short course (DOTS) strategy and the Indian Academy of Pediatrics endorses the same for all forms of childhood tuberculosis(1). Though there are reports of efficacy of ISSC in children with pulmonary tuberculosis (PTB) and other non-serious forms(2-7), there are limited published data on its efficacy in serious extra pulmonary tuberculosis (EPTB)(8-10). Regarding the efficacy of ISSC in tubercular meningitis (TBM), the published evidence is almost non-existent in children, and scarce in adults(11). This lack of published evidence limits the utilization of RNTCP in childhood tuberculosis(1). Concerns regarding inadequate dosages with available pediatric patient-wise boxes in some weight bands(12), and lack of trained personnel at DOTS centers to determine treatment endpoints in children, especially in sputum negative PTB and EPTB, contribute to low referral of pediatric tuberculosis patients to DOTS centers(1). This study evaluated the efficacy of ISCC in both pulmonary and serious extra pulmonary tuberculosis in children using a coordinated approach with DOTS centers.

METHODS

This prospective study conducted between January 2005 and July 2008 enrolled children diagnosed at the pediatric department, St. John's Medical College Hospital with tuberculosis of all forms, except those co-infected with HIV. They were diagnosed, classified and treated using RNTCP protocol(1). All children with PTB, intracranial tuberculoma, abdominal, disseminated and lymph node tuberculosis were started on ISCC (thrice weekly) at the outset. Children with TBM received daily treatment for first 2 weeks followed by ISCC. All children were referred to DOTS centers for drugs and also followed up at the study center by a pediatrician once in 2 weeks in intensive phase, once a month in continuation phase and once in 2 months after completion of treatment. The pediatrician also communicated regularly with the DOTS centers ensuring dosage appropriateness. Doses were calculated according to bodyweight at baseline and

adjusted for gain in weight. Dosages were as follows. INH 10-15 mg/kg rifampicin 10 mg/kg pyrazinamide 30-35 mg/kg ethambutol 30 mg/kg and streptomycin 15 mg/kg. Loose drugs available at DOTS centers were used initially followed by pediatric patient-wise boxes once they became available. 'Top-up' doses were prescribed when available pediatric combinations were found to be under dosed. Adherence to top up doses was ensured by using a family member as the DOTS provider. Treatment was extended to 9 months in PTB if there were slow clinical and radiological responses (<2/3rd clearance at 6 months) not amounting to treatment failure. This individualized treatment was again achieved by coordination between pediatrician and DOTS officers. Ethical clearance for the study was obtained by the Departmental ethical committee and parental consent was obtained.

RESULTS

A total of 65 children with tuberculosis (34 pulmonary and 31 extra-pulmonary) were analyzed. Mean age was 7.6 years (range 5 months to 17 years) with a male to female ratio of 0.8:1. Acid fast bacilli (AFB) positivity was documented in 9 (12%) cases (sputum - 6, lymph node - 1, breast tissue-1, lung tissue-1). 68% of cases were treated as RNTCP category 1, 6.7% as category 2, and 25.3% as category 3.

Treatment outcome is tabulated in ***Table* I**. The overall cure rate was 95% (94% in pulmonary and 97% in extra-pulmonary TB). There were 2 failures among PTB. Additionally, two children required extension of treatment to 9 months. All six children with sputum positive for AFB became negative at the end of intensive phase. Radiological response was noted in 90% of children.

Of the 14 cases with neurotuberculosis, seven had meningitis (2 in stage 3 and 5 in stage 2), six had tuberculoma, and one had spinal arachnoiditis. Twelve (86 %) children had complete cure without sequelae, one (7%) had clinical cure with motor deficit and one (7%) had clinical failure due to poor adherence. There was no mortality. All cases of disseminated, abdominal and lymph node TB responded with a 100% cure rate (***Table* I**).

Of 65 children initiated on ISCC, 1 with PTB died; 1 with failed therapy for meningitis was lost to follow up; and, 4 were lost to follow up after successful completion and response to ISCC. The remaining 59 children were followed up post treatment for a mean period of 9.4 months (SD 8.5 mo), of which 40% were followed for 1 year or more. One child with meningitis had suspected relapse after 6 months. Clinical hepatitis was not encountered in any child. Sixty children were found to be adherent to treatment, having received more than 95% of doses.

Eight children were given 'top-up' doses; 2 children in 6-10 Kg weight band, and 3 each in 11-16 Kg and 17-25 Kg weight bands. Two children with

TABLE I TREATMENT OUTCOME IN CHILDHOOD TUBERCULOSIS

Type of tuberculosis	Number	Cured	Failure	Mean (range) duration of follow up (mo)	Relapse
Pulmonary	34	32	2	10.2 (0-37)	0
Extra pulmonary	31	30	1	8.5 (0-27)	1
Neurological	14	13	1	11.9 (0.27)	1
Lymphadenitis	7	7	0	7.7 (0-24)	0
Abdominal	4	4	0	3.7 (0-12)	0
Disseminated	3	3	0	8 (6-12)	0
Pericardial	1	1	0	1	0
Breast	1	1	0	6	0
Pleural effusion	1	1	0	22	0

WHAT THIS STUDY ADDS

- Intermittent short course chemotherapy is effective in childhood tuberculosis including serious forms of extra-pulmonary tuberculosis.

PTB and one with EPTB required prolongation of treatment to 9 months.

DISCUSSION

This study revealed an overall response of 95%, which is comparable to 90-100% response reported with daily therapy(2,4,5). The 94% cure rate of PTB is again comparable to response reported with daily therapy(2,4). Extension of treatment beyond 6 months was required in 3 (4.6%) children compared with 15% in another report(13). Residual radiological lesions were found in 13% of patients on par with another study(4). Cure rates of 86% in neurotuberculosis is encouraging, though this could not be compared with other studies with daily therapy(14,15), in view of very small numbers. Further studies with a larger number of patients with neurotuberculosis are needed to validate these conclusions. No child developed hepatitis compared to 2.2-5% reported with daily therapy(3,13). More than 95% adherence achieved has an important implication in preventing MDRTB. The main limitation of our study was the absence of a control group.

Though RNTCP guidelines for diagnosis and categorization could be implemented in the existing form, we had to modify the dosage schedules in few children. Under-dosage was a problem in children at the upper end of weight bands across the ranges of 6-10 Kg, 11-16 Kg and 17-25 Kg. We feel that this is an important limitation in RNTCP that needs to be addressed. We recommend to include a revision of the weight bands to narrower ranges and provision for increasing dosage with weight gain during therapy, in addition to having trained personnel at DOTS centers to determine treatment endpoints for children.

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