INTERMITTENT OR DAILY SHORT COURSE CHEMOTHERAPY FOR TUBERCULOSIS IN CHILDREN: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS.

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Abstract
Objective- To compare effectiveness of intermittent dosing of antitubercular chemotherapy with daily dosing of chemotherapy (both containing rifampicin) in childhood tuberculosis (age ≤16yrs) in achieving cure, reducing relapse, decreasing drug related adverse effects and improving compliance by systematic review.

Search strategy- MEDLINE and the Cochrane Library, which consists of the Cochrane Database of Systematic Reviews and the Cochrane Controlled Trials Register, were searched for randomized trials of any multiple drug regimens, containing rifampicin, in children 16 yrs or less with tuberculosis. Articles of potential relevance were retrieved and critically appraised. Two reviewers independently assessed trial eligibility and quality. Data from full articles of selected studies were independently extracted by two authors and analyzed. The odds ratio was obtained for the pooled data in two groups (intermittent therapy and daily therapy) for cure. The other outcome measures compared between the two groups were adherence to therapy, drug related adverse events, relapse and deaths.

Main results- On screening of the electronic databases (CENTRAL and MEDLINE), 17 potentially relevant studies were identified and screened. Three randomized controlled trials including 435 children (pulmonary 419; extrapulmonary 16) met the inclusion criteria for the review. Baseline characteristics (age and sex distribution) were similar in both groups except that exposure to an infective case of tuberculosis (p=0.03) and tuberculin test positivity (p=0.004) were significantly more in the group that received intermittent therapy. Meta-analysis revealed that children receiving intermittent regimen were less likely to be cured than those receiving daily therapy as per protocol [cure: 149/196 in intermittent therapy, 186/217 in daily therapy group; OR (95% CI) = 0.5 (0.28, 0.88); p=0.02]. There were no significant differences between the two regimens in terms of relapse, side effects and adherence to therapy.

Conclusion- Intermittent short course anti-tuberculosis therapy (twice weekly) is less likely to lead to cure in children with tuberculosis as compared to daily therapy. There is a need to for more evidence to evaluate the efficacy of intermittent therapy for childhood tuberculosis.