Is intermittent short-course anti-TB regimen as efficient and safe as daily anti-TB regimen for treating childhood TB?

Soumyadeep Bhaumik[1]

[1]*Executive Editor, Journal of Family Medicine and Primary Care, New Delhi, India*

Clinical Scenario

Childhood tuberculosis (TB) is a common clinical condition in low- and middle-income nations like India where TB is endemic. Different guidelines vary in the recommendations on treatment regimes for childhood TB. Apart from clinical outcomes the decision to use one regimen over another also has an implication in the form of health system burden. The evidence summary presents the comparison between the intermittent regimens with the daily anti-TB regimen for childhood TB.

Keywords: Adolescent, child, antitubercular agents, drug administration schedule, humans, randomized controlled trials as topic, tuberculosis, drug therapy

Background

The World Health Organisation, British Thoracic Society and the Revised National Tuberculosis Control Programme (RNTCP), India, guidelines recommend daily or thrice weekly intermittent therapy for childhood tuberculosis. On the other hand the American Thoracic Society and the Centers for Disease Control and Prevention (CDC), recommends a daily or twice-weekly regimen.

Such differences in guidelines have meant clinicians prescribing a myriad of regimens with varying efficacy and safety. The control of childhood TB is an important part of the global "Stop TB" strategy. Even small incremental efforts to control childhood TB are important since prevalence of childhood TB in a community is a potent indicator of ongoing TB transmission.

How was the study done?

Researchers in The Cochrane Collaboration conducted a systematic review and meta-analyses[1] comparing the safety and efficacy of the of intermittent, short-course anti-TB regimens (twice- or thrice weekly) with daily short-course anti-TB regimens in the treatment of childhood TB (5 months–15 years).

What did the study find?

After searching for relevant studies, researchers identified four randomized controlled trials enrolling 563 children for the comparison between intermittent twice weekly versus daily anti-TB treatment. No randomized controlled trials which compared between the thrice weekly anti-TB short-course regimen and the daily treatment regimen for childhood TB were found. A summary of what the researchers found is depicted in Table 1. Researchers found no difference between twice weekly and daily intermittent childhood TB regimens for achieving cure, adherence to treatment, and death from any cause or treatment limiting adverse events. The research evidence is generally of very low quality. This means we are very uncertain about the differences in estimates for the outcomes in the form of cure; all cause death, relapse, adherence to treatment and treatment-limiting adverse events between intermittent twice weekly and the daily schedule for treating childhood TB.

Implications for clinical practice

There is insufficient evidence to support or refute the usage of either regimens in actual practice.

Implications for research

The review points to the need for conducting properly designed randomised controlled trials in high TB-transmission settings, in

Address for correspondence: Dr. Soumyadeep Bhaumik, F-140, Rail Vihar, 480, Madurdaha, Kolkata - 700 107, India. E-mail: drsoumyadeepbhaumik@gmail.com

Table 1: Summary of available evidence from systematic review					
Outcome	Daily anti-TB regimens	Intermittent short-course anti-TB regimens	No. of participants (trials)	What Happens	Quality of evidence
How many people got cured (follow up: 12-30 months)	836 per 1000	844 per 1000	465 (four trials)	No Significant Difference	Very low
How many deaths occurred ? (any cause)	8 per 1000	13 per 1000	213 (two trials)	No Significant Difference	Very low
How many relapses occurred ?	0 per 1000	0 per 1000	214 (one trial)	No Difference	Very low
How was the adherence to treatment	840 per 1000	847 per 1000	458 (four trials)	No Significant Difference	Very low
Treatment –limiting adverse events	15 per 1000	6 per 1000	441 (four trials)	No Significant Difference	Very low

low- and middle-income countries in order to resolve the issue of different regimens in various national and international guidelines for treating childhood TB.

Conclusion

Trials conducted till now are insufficient to either support or refute the use of either schedule of anti-TB drugs for childhood TB. More research is needed to answer which is better than the other in terms of outcomes.

This evidence summary is based on the following systematic review

Bose A, Kalita S, Rose W, Tharyan P. Intermittent versus daily therapy for treating tuberculosis in children. Cochrane Database of Systematic Reviews 2014, Issue 1. Art. No.: CD007953. DOI: 10.1002/14651858.CD007953.pub2

The Indian Council of Medical Research has brought a nation-wide license such that full text of all systematic reviews in Cochrane Library is freely accessible from anywhere in India.

What is a systematic review?

A systematic review seeks to answer a well-formulated and specific question by identifying, critically appraising, and summarizing the results of all relevant studies, published and unpublished, according to explicit and transparent methods. Systematic reviews of randomized controlled trials, like the current one, occupy the highest position in the hierarchy of evidence.

How was quality of evidence assessed?

The quality of evidence has been assessed using methods developed by the GRADE working group (www.gradeworkinggroup.org). The WHO Guidelines Review Committee also uses the GRADE system.

Reference

1. Bose A, Kalita S, Rose W, Tharyan P. Intermittent versus daily therapy for treating tuberculosis in children. Cochrane Database Syst Rev 2014;1:CD007953.