Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/cegh

Commentary on Evidence Summaries

Intermittent versus daily treatment for childhood tuberculosis: Current evidence

Meenu Singh^{a,*}, Nishant P. Jaiswal^b

^a Professor, Department of Pediatrics, Advanced Pediatrics Centre, Postgraduate Institute of Medical Education and Research, Chandigarh, India

^b Scientist C, ICMR Advanced Centre for Evidence Based Child Health, Department of Pediatrics, Advanced Pediatrics Centre, Postgraduate Institute of Medical Education and Research, Chandigarh, India

ARTICLE INFO

Article history:

Received 5 May 2014

Accepted 18 May 2014

Available online 10 June 2014

Keywords:

Childhood tuberculosis

Treatment guidelines

Systematic review

ABSTRACT

Lack of uniform guidelines for treatment of childhood tuberculosis in high burden countries from Asia and Africa is a major concern. The present Cochrane review has tried to bridge the gap and has found that treatment in terms of radiological evidence and symptoms with twice-weekly regime and daily regime is comparable but the evidence is scares and low-grade and has thus rightly called for adequately powered, multi-centric, multi-country, randomized, non-inferiority, pragmatic trials conducted in high TB-transmission settings, in low- and middle-income countries that compare thrice-weekly, and daily short-course (6 months) dosing, and using the currently recommended four drugs, in HIV-negative children to help inform policy. There is further need for comparing the thrice-weekly regime with the daily and twice-weekly regimes and also a dose wise analysis of the drugs is required. Until this we must follow the WHO guidelines.

Copyright © 2014, INDIACLEN. Publishing Services by Reed Elsevier India Pvt Ltd. All rights reserved.

1. Commentary

The Cochrane review by Bose et al¹ of four randomized controlled trials comparing intermittent versus daily treatment of tuberculosis in children is a well managed, high quality review following standard Cochrane methodology. The review focused on childhood tuberculosis that is a serious problem for low- and middle-income countries in Asia and Africa. The burden of childhood tuberculosis is significantly high in these countries and the treatment guidelines are not

uniform. The review is thus an important attempt to bridge the gap.

The Cochrane review found that cure in terms of symptoms and radiological evidence was comparable in the four trials that compared the twice-weekly and the daily regimens. The review also found that adherence to the twice-weekly intermittent therapy was similar to daily therapy, though the evidence was of low quality for all these outcomes.

The WHO recommends against intermittent regimens in children, with confirmed or suspected pulmonary TB or

DOI of original article: <http://dx.doi.org/10.1016/j.cegh.2014.03.002>.

* Corresponding author. Tel.: +91 9814117152.

E-mail address: meenusingh4@gmail.com (M. Singh).

<http://dx.doi.org/10.1016/j.cegh.2014.05.002>

2213-3984/Copyright © 2014, INDIACLEN. Publishing Services by Reed Elsevier India Pvt Ltd. All rights reserved.

tubercular lymphadenitis living in high HIV burden areas,² but the trials included in the review did not permit any analysis based on the HIV burden of the areas of recruitment or the HIV status of the children recruited, which does not allow extrapolation of the results to such areas. Intermittent short-course regimes may have high adherence but the WHO does not recommend intermittent therapy (thrice-weekly) except for the continuation phase in HIV-negative children in low HIV prevalence areas with well established DOTS programmes. The Cochrane review did not find any trials comparing the recommended (thrice-weekly) intermittent regime and the daily regime. The Indian National Guidelines and those of the Indian Academy of Pediatrics^{3,4} do not recommend the twice-weekly regime; and instead promotes the thrice-weekly regimen for both the initiation and continuation phases for new cases. These guidelines are based on both observational and randomized controlled trials whereas observational studies were beyond the scope of the Cochrane review.

The review did not include an analysis based on the dose of drug administered. This would be very helpful in determining the correct dose to be administered, as there are different doses prescribed. Another analysis using different drug combinations (first line) if done would have helped in determining better combination therapy to be used. The included studies are also very low or low in quality as depicted by the GRADE approach used and there is need for more such studies to show the equivalence of twice-weekly intermittent therapy and the daily regime.

The Cochrane review is an attempt to address important issues regarding pediatric tuberculosis but the available evidence is scanty. The authors have rightly asked for adequately powered, multi-centric, multi-country, randomized, non-inferiority, pragmatic trials conducted in high TB-transmission settings, in low- and middle-income countries that compare thrice-weekly, and daily short-

course (6 months) dosing, and using the currently recommended four drugs, in HIV-negative children to help inform policy. A comparison of twice-weekly regimens and thrice-weekly regimens is also required to establish the equivalence of these two regimens. However, until we get some high quality evidence we must follow the WHO recommended guidelines.

Declaration of interest

Dr Meenu Singh is an editor with the Cochrane Acute Respiratory Infections Review Group.

Conflicts of interest

All authors have none to declare.

REFERENCES

1. Bose A, Kalita S, Rose W, Tharyan P. Intermittent versus daily therapy for treating tuberculosis in children. *Cochrane Database Syst Rev*. 2014. <http://dx.doi.org/10.1002/14651858.CD007953.pub2>. Issue 1. Art. No.: CD007953.
2. Rapid advise treatment of tuberculosis. Available from: http://whqlibdoc.who.int/publications/2010/9789241500449_eng.pdf?ua=1.
3. *National Guidelines on Diagnosis and Treatment of Pediatric Tuberculosis*; 2012. Available from: http://www.tbcindia.nic.in/Paediatric_guidelines_New.pdf.
4. Kumar A, Gupta D, Nagaraja SB, Singh V, Sethi GR, Prasad J. Updated national guidelines for pediatric tuberculosis in India, 2012. *Indian Pediatr*. 2013;50:301–306.