

Recommendations Concerning the Therapeutic Approach to Immunocompromised Children With Tuberculosis

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ABSTRACT

Purpose: This article describes the recommendations of a group of scientific societies concerning the therapeutic approach to immunocompromised children with tuberculosis (TB).

Methods: Using the Consensus Conference method, relevant publications in English were identified by a systematic review of MEDLINE and the Cochrane Database of Systematic Reviews from their inception until December 31, 2014.

Findings: On the basis of their clinical experience and the published evidence, the group of experts concluded that, although immunosuppressed subjects are at greater risk of developing TB, none of the signs or symptoms is sensitive or specific enough to enable a diagnosis. Immunocompromised patients are at greater risk of developing extrapulmonary forms of TB, especially if they are adolescents, whereas pulmonary forms are more prevalent among younger patients. When TB is suspected, a combination of skin and immunologic tests and other clinical, radiologic, and microbiologic examinations can be used to assess the risk of infection or disease. If the TB diagnosis is confirmed,

immunocompromised children should be treated by using a standard regimen with a minimum of 4 drugs for at least 9 to 12 months, during which the tolerability of the drugs and their interactions should be carefully evaluated.

Implications: It is difficult to diagnose and treat TB in immunocompromised children. Thus, all pediatric patients undergoing immunosuppressive therapy who develop TB should be diagnosed and treated at a TB reference center, which should also be responsible for the recommended follow-up. (*Clin Ther.* 2015;■:■■■-■■■) © 2015 Elsevier HS Journals, Inc. All rights reserved.

Key words: children, HIV, immunodeficiency, immunosuppressants, TB, tuberculosis.

INTRODUCTION

Tuberculosis (TB) is the second most frequent cause of death due to infectious disease. An estimated 9 million incident cases of TB occurred worldwide in 2013, of

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Accepted for publication October 9, 2015.

<http://dx.doi.org/10.1016/j.clinthera.2015.10.012>
0149-2918/\$ - see front matter

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which ~550,000 (~6% of the total) involved children aged <15 years.¹ Immune status is one of the fundamental factors conditioning the progression of TB infection, and one of the major risks for progression to active disease is impaired immunity (particularly cell-mediated immunity) in patients infected by HIV, those with congenital immunodeficiency involving T lymphocytes, and those treated with immunosuppressant drugs or antituberculous agents.²

The present article describes the recommendations of a group of scientific societies concerning the therapeutic approach to immunocompromised children with TB.

MATERIALS AND METHODS

Using the Consensus Conference method based on the National Institutes of Health and the Italian National Programme Guidelines^{3,4} (Table I), relevant publications in English were identified by a systematic review of MEDLINE and the Cochrane Database of Systematic Reviews from their inception until December 31, 2014. The search strategy was “children[Title/Abstract] OR pediatric[Title/Abstract] AND immunodeficiency[Title/Abstract] OR immunocompromised[Title/Abstract] OR immunosuppressive drugs [Title/Abstract] AND treatment[Title/Abstract] OR therapy[Title/Abstract] or anti-tuberculous drug [Title/Abstract] AND English[lang]).” The Working Group agreed on a list of clinical problems concerning the therapeutic management of TB in immunocompromised patients (articles dealing with drug-resistant TB were not evaluated for this analysis).

The procedures of the evidence review focused on patients aged 0 to 18 years and included section-specific targeted searches as well as formal systematic reviews of selected aspects. The clinical recommendations made in the updated international guidelines were reviewed and critically compared in the case of debated issues. All of the data were entered into tables of evidence for each subject. Trained personnel critically appraised the acquired literature by using the Scottish Intercollegiate Guidelines Network methodologic checklists,⁵ and the bibliographic material and a preliminary draft document were given to the panel members. The published evidence was presented and discussed at various meetings, and the Delphi method was used to reach a consensus when the evidence did not provide consistent and unambiguous recommendations. The final text was revised on the basis of these discussions and submitted by e-mail to participants at the Consensus Conference for final approval.

The multidisciplinary panel of clinicians and experts in evidence-based medicine were identified with the help of the participating scientific societies. The panel included experts in the fields of general pediatrics, pediatric infectious diseases, neonatology, infectious diseases, pneumology, microbiology, radiology, pharmacology, and methodology. It was coordinated by the Italian Society of Pediatric Infectious Diseases. No panel member declared any conflict of interest concerning the contents of the guideline topics. The panel met on 3 occasions, but many of the consultations involved in developing the document took place interactively by e-mail or telephone.

Table I. Quality of evidence and strength of recommendation.

Quality of evidence

- I Evidence from > 1 properly designed, randomized controlled study and/or systematic review of randomized studies
- II Evidence from 1 properly designed, randomized controlled study
- III Evidence from cohort studies or their meta-analysis
- IV Evidence from retrospective case-control studies or their meta-analysis
- V Evidence from case series without a control group
- VI Evidence from opinions of respected authorities, based on clinical experience

Strength of recommendation

- A The panel strongly supports the recommendation
- B The panel moderately supports the recommendation
- C The panel marginally supports the recommendation

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