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ORIGINAL ARTICLE

Tuberculosis in children from diagnosis to decision to treat

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Abstract
Setting: Confirmation of tuberculosis (TB) in children is difficult, so clinicians use different procedures when deciding to treat.
Objective: Identify criteria to initiate and maintain TB treatment in children younger than 5 years-old, without diagnosis confirmation.
Design: A web-based survey was distributed by email to the corresponding authors of journal articles on childhood TB. The observations were clustered into disjoint groups, and analyzed by Ward's method.
Results: We sent out 260 questionnaires and received 64 (24.6%) responses. Forty-six respondents (71.9%) said that microbiological confirmation was not important for initiation of anti-TB treatment, and that the epidemiological context and signs/symptoms suggestive of disease were most important. Sixty-one respondents (95.3%) said that the decision to continue therapy was mainly dependent on clinical improvement. A cluster of older respondents (median age: 52 years-old) who were active at a hospital or primary health care centre placed the most value

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on immunological test results and chest X-rays. A cluster of younger respondents (median age: 38 years-old) who were less experienced in management of TB placed more value on Interferon Gamma Release Assay (IGRA) results and chest computed tomography (CT) scans. A cluster of respondents with more experience in treating TB and working at specialized TB centres placed greater value on the clinical results and specific radiological alterations (''tree-in-bud'' pattern and pleural effusion).

Conclusion: TB management varied according to the age, work location and experience of the clinicians. It is necessary to establish standardized guidelines used for the diagnosis and decision to treat TB in children.

Introduction

Childhood tuberculosis (TB) is a serious public health problem,[1–3] and a consequence of poor control of TB in the adult population.[3] Early diagnosis and initiation of therapy is crucial for effective TB control. Delayed diagnosis increases the risk of death and TB transmission in the community.[4,5]

In 2014, the World Health Organization (WHO) reported there were approximately 340,000 incident cases of TB among all countries in the European Region. Children under 15 years-old accounted for 3.9% of all cases, and children under 5 years-old accounted for 1.6% of all cases.[1]

Confirmation of a TB diagnosis by identification of the infectious agent can be difficult in children.[6] In 2009, the rate of diagnostic confirmation among paediatric cases was only 19.2%.[7] Sampling is particularly difficult in children under 10 years-old, and even if samples are obtained, the paucibacillary nature of the lesions may produce false-negative results.[5,6,8–10] Thus, gastric lavage is frequently used for the diagnosis of TB in children under 6 years-old.[6,10–12] Currently, clinicians consider clinical presentation, history of recent contact with infected individuals, immunological evidence of infection, radiological signs compatible with TB, and lack of clinical improvement following antibacterial treatment as indicators of TB, and for initiation of TB treatment.[5,6,13,14] However, the variability and low specificity of clinical and radiological findings in children indicate that a diagnosis based on these criteria should be viewed with a high degree of suspicion.[5,15]

This study aims to identify the criteria in Europe that most frequently lead to the initiation and maintenance of empiric antibiotic treatment in children younger than 5 years-old with suspected TB, but without diagnostic confirmation. It is also examined the relationship of different characteristics of clinicians with varying attitudes towards the diagnosis and treatment of childhood TB.

Methods

This study was based on the implementation of a web-based survey, through Google Drive, directed at doctors and researchers in Europe who had experience treating children with TB. This survey consisted of 28 multiple-choice and simple-answer questions, divided into 3 sections: (i) identification (age, gender, country, job title, locality of work, specialization, and years in the job); (ii) experience (years in TB and childhood TB, time spent in those areas, and number of patients with TB diagnoses); and (iii) diagnostic criteria. Several questions in this last section related to clinical experience with children under 5 years-old who had TB, but without confirmation of diagnosis, to identify the most important criteria used to start treatment and to differentiate the most important symptoms and results among radiological, immunological, and confirmation tests in these children. The main criteria used to maintain treatment, without TB confirmation, were also identified. All the responses were anonymous.

The names and addresses of the surveyed researchers were collected using software specifically developed for this purpose (described below). This software combines data from several sources, because we were unable to find a single source with data on research papers and their corresponding authors. The data sources were: PubMed, the Digital Object Identifier (DOI) System, and the web sites of journals that published the papers.

The collection process was driven by a web interface, where the user specified the keywords (''paediatric, tuberculosis'') and time interval (1 January 2005 to 20 December 2015). These data were submitted to a server, and processed in three stages. First, the PubMed database was queried using the Entrez Programming Utilities,[16] which returned data on papers with the selected criteria ($n = 1573$), and the title and DOI of each paper. PubMed does not record the corresponding authors, so this information was retrieved from the journal web sites. Second, the DOI name resolution service[17] was used to obtain each paper's URL from its DOI. Third, using this URL, the paper's web page was retrieved from the journal's web site, and the name and email of the corresponding author was extracted ($n = 260$), when this information was available.

Descriptive statistics (absolute and relative frequencies) are given for categorical variables, and medians, with minima and maxima, are given for quantitative variables. The chi-squared test (or Fisher's test, as adequate) evaluated the independence between two categorical variables while the Mann–Whitney (resp. the Kruskall–Wallis) test accessed the existence of significant differences between