Tuberculin test in the diagnosis of childhood tuberculosis: analysis of quantitative and qualitative features

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Abstract

Abstract: tuberculin test is an indirect method for diagnosing tuberculosis. It is important in the diagnosis of suspected childhood tuberculosis because children are often nonbacillary, or cannot produce sputum.

Objective: to assess the accuracy of quantitative and qualitative features of tuberculin test in the diagnosis of childhood tuberculosis.

Methods: evaluation of diagnostic tests; tuberculin tests with purified protein derivative RT-23 at two tuberculin units were carried out in 158 patients distributed in two groups: 101 Tb-negative and BCG-vaccinated children, and 57 tuberculous children diagnosed clinically, radiologically, and epidemiologically. Test results were analyzed quantitatively (Mantoux s test) and qualitatively (Koch- and Listeria-type reactions).

Results: using cutoff for positivity at 10 mm in Mantoux s test, quantitative results indicated 85.9% of sensitivity, and 86.1% of specificity. Qualitative results (Koch-type reaction) indicated 77.2% of sensitivity and 98% of specificity.

Conclusion: qualitative analysis of tuberculin test proved useful in the diagnosis of childhood tuberculosis in combination with Mantoux s test.


Introduction

Even though tuberculin was first discovered in 1890, it only started being used systematically and using different techniques in 1907 and 1908.1,2 As a general rule, it is known that individuals react to tuberculin injection when infected with Mycobacterium tuberculosis, with other mycobacteria, or, still, when previously vaccinated with BCG.

Taking this into consideration, tuberculin test with purified protein derivative (PPD) according to Mantoux’s technique is used in the diagnosis of tuberculosis. In some cases, it is also used in deciding medical procedures such as in the chemoprophylaxis of children exposed to tuberculous patients.

The importance of the tuberculin test for the diagnosis itself lies more in its negative predictive value, which is very high due to the epidemiological situation in Brazil, than in its positive predictive value.1

Studies of the prevalence of reaction to tuberculin tests allow assessing risk for infection in different communities,
thus indicating the epidemiological importance of this test. Mass BCG vaccination campaigns have, to a certain extent, made it difficult to assess prevalence of tuberculosis infection. That is because reaction to tests may be caused both by *M. tuberculosis* infection and by previous BCG vaccination. There are, however, new methods for distinguishing between allergy produced by *M. tuberculosis* and by other mycobacteria, including BCG. In this sense, it was possible to assess risk for tuberculous infection in Rio de Janeiro and in São Paulo respectively.

Moreover, studies have indicated that Listeria-type reactions to tuberculin test are associated with protective immunity of BCG; whereas Koch-type reactions are associated with ineffectiveness of BCG and tissue damaging hypersensitivity. These findings have lead to the hypothesis that tuberculin test with PPD RT-23 at two tuberculin units would allow quantitative assessment considering the size of induration, and qualitative assessment considering the form of induration. Criteria used to classify reactions are presented in Table 1.

The objective of our study is to determine the accuracy of quantitative and qualitative features of tuberculin test in the diagnosis of childhood tuberculosis.

**Table 1 - Criteria for qualitative classification of tuberculin test**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Reaction type</th>
</tr>
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<tbody>
<tr>
<td>Koch</td>
<td>Listeria</td>
</tr>
<tr>
<td>Induration</td>
<td>Well-delineated</td>
</tr>
<tr>
<td>Consistency</td>
<td>Hard</td>
</tr>
<tr>
<td>Painful</td>
<td>Yes</td>
</tr>
</tbody>
</table>

**Patients and Methods**

The study consisted of the evaluation of diagnostic tests carried out prospectively from July 1986 until December 1989 at city, state, and federal public hospitals and healthcare units in the city of Rio de Janeiro, Brazil.

This study included patients from the Unidade Auxiliar de Cuidados Primários de Saúde Vargem Grande, Jacarépaguá, and, in cases of hospital admission, from the following institutions: Hospital Geral de Nova Iguaçu, Hospital Municipal Jesus, Hospital Estadual São Sebastião, Hospital Raphael de Paula Souza, and Instituto de Puercultura e Pediatria Martagão Gesteira (Universidade Federal do Rio de Janeiro).

We studied children from low-income families, of both sexes, aged from 2 months to 12 years. Patients were randomly selected and then divided into two study groups: group 1 - 57 inpatients who fulfilled criteria for diagnosis of tuberculosis; group 2 - 101 children who were healthy, eutrophic, asymptomatic from a respiratory perspective, not presenting clinical or radiological evidence of tuberculosis nor history of tuberculosis infection, BCG-vaccinated, and who were randomly selected at different outpatient clinics. Tuberculin test was carried out only after the obtainment of verbal consent from the parents or person responsible for the child.

Patients were considered as a case of tuberculosis if the following three diagnostic criteria were fulfilled:

- a) suggestive clinical status, with evolution of fever for over 15 days, with or without respiratory or extrapulmonary symptoms, such as the indication of central nervous system infection or peripheral adenomegaly with continuous evolution for over 3 weeks;

- b) chest X-ray presenting hilar or paratracheal adenomegaly, miliary hypopatency, or alveolar hypopatency persisting for over 15 days with no response to antibiotic therapy using drugs with no proven effect over *M. tuberculosis*;

- c) reported contact with tuberculous adult patient.

Our tuberculin tests were carried out by one of the authors (HMVO), who received previous training at the Tuberculosis and Pneumology Institute, Universidade Federal do Rio de Janeiro. The training consisted of the assessment of 32 tuberculin tests by two different examiners whose intra-class correlation coefficient was equal to 99.2%.

Tuberculin tests were administered to volar forearm, using PPD RT-23 tuberculin, tween 80, at 2 tuberculin units per ml, obtained from the Tuberculin Unit at Tuberculosis and Pneumology Institute, Universidade Federal do Rio de Janeiro. Tests were assessed 72 hours after the administration of tuberculin according to Mantoux’s technique. We also carried out qualitative assessment related to the occurrence of Koch- and Listeria-type reactions according to Stanford et al. The smallest induration size considered for assessment was 4 mm.

Data were collected using specific forms and analyzed using the Epi-info 6 statistical software.

**Results**

Group 1 included 57 patients aged 2 months to 12 years (average = 35 months), and group 2 included 101 children aged 3 months to 12 years (average = 35 months). Table 2 presents age distribution for both groups. We observed a predominance of children with less than 2 years of age (less than 24 months) in our population: 29/57 (50.87%) in group 1 and 55/101 (54.45%) in group 2.
BCG had been administered during the 1st month of age to 33 (57.89%) patients in group 1 and to all patients in group 2.

Table 3 presents tuberculin test results for the 158 children assessed according to Mantoux's technique. Results yielded sensitivity of 85.9% (49/57) and specificity of 86.1% (87/101).

Table 4 presents distribution of children according to Koch-type reaction. Results yielded sensitivity of 77.2% (44/57) and specificity of 98.0% (99/101). We believe that these results are coincidental, since the indicated technical procedures were carefully followed during testing.

Table 5 presents distribution of children according to Listeria-type reaction. Results yielded sensitivity of 12.3% (6/57) and specificity of 54.4% (46/101).
Considering that over half of our population included children with less than 2 years of age, that is, 51% of group 1 and 54% of group 2, and that at 2 years of age there still may be influence of BCG over tuberculin tests, it is important to emphasize that BCG did not affect our tests. In analyzing group 2, whose 101 patients were all BCG-vaccinated, it is possible to observe in Table 3 that reactions to tuberculin test of over 10 mm corresponded to just 10% of the total. Reactions in all the other patients were lower than 10 mm. In this sense, however, Mantoux’s reaction of children with tuberculosis (group 1) indicated that 86% were of over 10 mm. This suggests that stimulus caused by Mycobacterium tuberculosis was more intense than that caused by the vaccine.

In considering the qualitative assessment of tuberculin test, that is, the assessment of the form of induration independently from its size, we observed an important increase in specificity. As we mentioned earlier, Koch-type reactions are related to hypersensitivity, observed in tuberculosis illness or infection; whereas Listeria-type reactions are related to protective immunity of intracutaneous BCG vaccination. Thus it is possible to assess protective immunity of BCG by observing the occurrence of Listeria-type reactions.9

Based on the fact that Koch- and Listeria-type reactions were identified in children with induration greater than or equal to 4 mm, it is possible to understand the practical applicability of this type of assessment even in children considered non-responsive to Mantoux’s test.6

We observed that the qualitative assessment of Koch-type reactions in tuberculin tests, due to its high specificity, is important for the diagnosis of childhood tuberculosis. In this sense, findings of Listeria-type reactions would allow ruling out M. tuberculosis infection.

In general, pediatricians may face difficulties in assessing tuberculin tests in children vaccinated with BCG. Even though there is a tendency of tuberculin reactions towards decreasing its size with time, recent BCG revaccination campaigns in children at school entry age have reestablished the difficulty in assessing tuberculin tests because of the renewed antigenic stimulus. In assessing tuberculin tests qualitatively, we hope to contribute to the understanding of the importance of Mantoux reaction despite previous intracutaneous BCG vaccination in children. This study does not, however, assess children and adolescents revaccinated with BCG. Responses to tuberculin tests among revaccinated subjects have not been extensively studied, and it is possible that Koch-type reactions may be found in individuals revaccinated with BCG.

Recommendations

We recommend carrying out tuberculin tests with PPD RT-23 at two tuberculin units, measuring induration and checking for Koch-type reactions. In following these procedures, tuberculin tests could be useful in corroborating the diagnosis of tuberculosis - as long as it is used in combination with clinical, radiological, and epidemiological results.

We would also like to emphasize that it is very important to observe proper training of healthcare professionals for quantitative and qualitative assessment of tests.

References


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