MÆDICA - a Journal of Clinical Medicine

ORIGINAL PAPERS

Comparative study using tuberculin from Cantacuzino Institute *versus* Statens Serum Institute

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ABSTRACT

Setting: *Iasi County, Romania.*

Objective: *To evaluate the efficiency of the tuberculin produced by Cantacuzino Institute (ICB) compared to Statens Serum Institute (SSI) tuberculin in a group of high school students.*

Design: *36 subjects were tested simultaneously with two tuberculin tipes. For each student, the left arm was tested with ICB tuberculin, while the right arm was tested with SSI tuberculin. All tests were single blind, and the subjects did not know which tuberculin type was used for each arm. The tuberculin administration sequence was random.*

Results: *No significant discrepancies were observed in results of both tuberculin reactions. The correlation coefficient was significant (0.95) between both tests ($p<0.0001$, CI 0.9111-0.9765). Positive results for the tuberculin test were found in 11.1% of the subjects when we used SSI tuberculin. The pain was almost absent at ICB tuberculin injection, comparatively at SSI tuberculin.*

Conclusion: *Tuberculin 2u PPD made by Cantacuzino Institute has the same efficiency as tuberculin PPD RT 23 SSI. The findings of present study recommend, in absence of SSI tuberculin, to use Cantacuzino Institute tuberculin for identification of infections with Mycobacterium tuberculosis complex.*

Key words: IDR, TB infetion

INTRODUCTION

Worldwide, around one third of the population is TB infected. From this huge number of infected people, nine million TB new cases are discovered annually. Until a few years ago, TB infection was diagnosed only with tuberculin tests (1). As a result, the tuberculin test (Mantoux or Heaf techniques) was extensively used, beginning in the 1900s. In spite of this, the interpretation of the results is in debate today.

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Tuberculin solution, also known as "Purified Protein Derivative" (PPD) is obtained from precipitation of tricloracetic acid. It is necessary to remove some polisaharid atigens because they can produce false reactions. Research to produce PPD solution was initiated in 1934. The first standardized tuberculin was named PPD RT (2). Tuberculin test revealed tardive hypersensitivity reaction.

Statens Serum Institute (SSI) in Denmark has a long history in the frontline of tuberculin research. For over 70 years, Statens Serum Institute has been a center for tuberculin production and standardization. The SSI tuberculin is widely used in Europe (3).

In Romania, the SSI tuberculin is not available on the market. For the Mantoux test we use tuberculin produced by the Cantacuzino Institute in Bucharest (ICB). There are two types of this solution: 2u and 10u, in 2 mL ampoules. No comparative study based on IBB tuberculin has been published in the last 20 years. In Romania we use the Mantoux technique for intradermic tuberculin test, using PPD-Standard (PPD IC-65). An appropriate technique requires some basic conditions: tuberculin use before expiration date, storage in special conditions (refrigeration, dark), and homogenization before opening. 1 ml syringe and appropriate needles are used for intradermal injection. The administration area is on the anterior left forearm at the conjunction between the inferior two-third and the superior one-third part. The needle goes almost tangent to the skin surface until disappears into it. After the 0.1 ml liquid injection, a small round wheal or papule of 8-10 mm in diameter should be formed (4).

The reading of the results is performed after 72 hours. It requires good lighting and a good tactile determination of induration. ❑

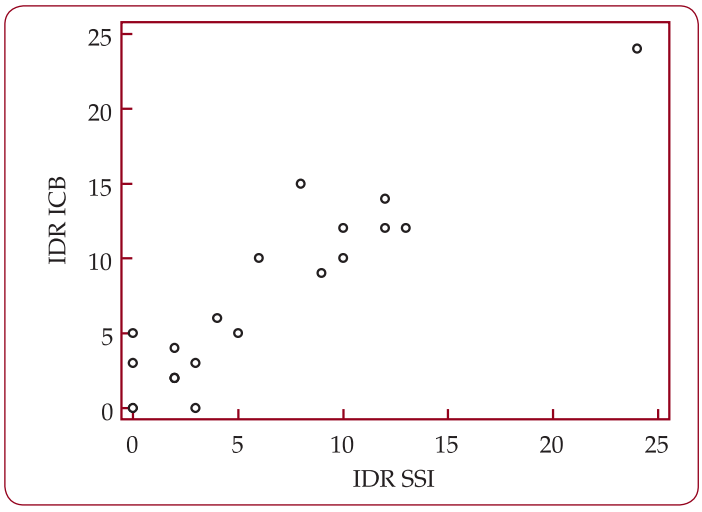

FIGURE 1. Correlation between ICB and SSI tuberculin test results

MATERIAL AND METHOD

The aim of this study is to evaluate the efficiency of the tuberculin produced by ICB compared to SSI tuberculin in a group of high school students. The study was initiated after a TB case was diagnosed in this community. For this study we used 36 high school students. All subjects were BCG vaccinated, with no risk factors for immune suppression (5).

All subjects were simultaneously double tested after obtaining their informed consent. For each student, the left arm was tested with ICB tuberculin, while the right arm was tested with SSI tuberculin. All tests were single blind, and the subjects did not know which tuberculin type was used for each arm. The tuberculin administration sequence was random.

Because the first student claimed pain after the second injection, the researchers asked him to evaluate the pain using a scale from 0 to 10 (0 means no pain and 10 means severely intense pain). The rating was used for each subject and each arm.

The reaction reading was performed 72 hours from the injection time using a flexible scale. We recorded maximal transversal diameter of induration in millimeters for the left and right arm respectively. The cut-off for positive reaction was 10 millimeters. ❑

RESULTS

The age of the subjects was between 14 and 20, with and average of 16.6 years of age. 31 subjects were female (86.1%) and 5 male (13.9%).

No significant discrepancies were observed in results of both tuberculin reactions. The correlation coefficient was significant (0.95) between both tests ($p<0.0001$, CI 0.9111-0.9765) (Figure 1).

Positive results for the tuberculin test were found in 11.1% of the subjects when we used SSI tuberculin. From induration dimensions we figured the bottom results (Figure 2).

T-cell interferon-gamma tests for testing positive reactors were not available. Students

with positive reactions were subsequently tested with xRay and sputum tests.

The subjects responded differently to the pain. The pain was almost absent at ICB tuberculin injection (0.2 points), comparatively 8.8 points for SSI tuberculin (Figure 3). No correlation in results was obtained (p=0.11, IC -0.06-0.55); the correlation coefficient is 0.27. We cannot explain the difference obtained after the injections and we assumed that it could be based on a vitiated perception. ❑

DISCUSSION

It is generally accepted that tuberculin reaction cannot provide very valuable clinical information in BCG vaccinated persons and in high prevalence areas. Even in these conditions the tuberculin test can be used for contact tracing or to investigate people with respiratory simptoms (6). False negative and false positive reactions were produced by the solution injected, technique, and individual immune response.

Regular training is recommended to ensure good clinical practice in tuberculin administration; however, solution quality is only attributable to the producer. For this reason, similar results for concomitant tests with Cantacuzino Institute and Statens Serum Institute tuberculin give a positive perspective on Mantoux tests in Romania, based on a single tuberculin batch from the Romanian market.

The same results on induration diameter show that Romanian tuberculin is good for clinical practice from the perspective of tuberculin quality. Moreover, superior pain tolerability at the intradermal tuberculin injection site for Romanian tuberculin represents a strong argument for the use of this solution.

During our testing, we used the same materials and the same nurse for both injections; however, for more relevant information, double-blinded and further IGRA tests should be performed. Further studies on control groups, based on the criteria above, are necessary. ❑

CONCLUSION

Tuberculin 2u PPD made by Cantacuzino Institute has the same efficiency as tuberculin PPD RT 23 SSI. The findings of present study recommend, in absence of SSI tuberculin, to use Cantacuziono Institute tuberculin for identification of infections with Mycobacterium tuberculosis complex.

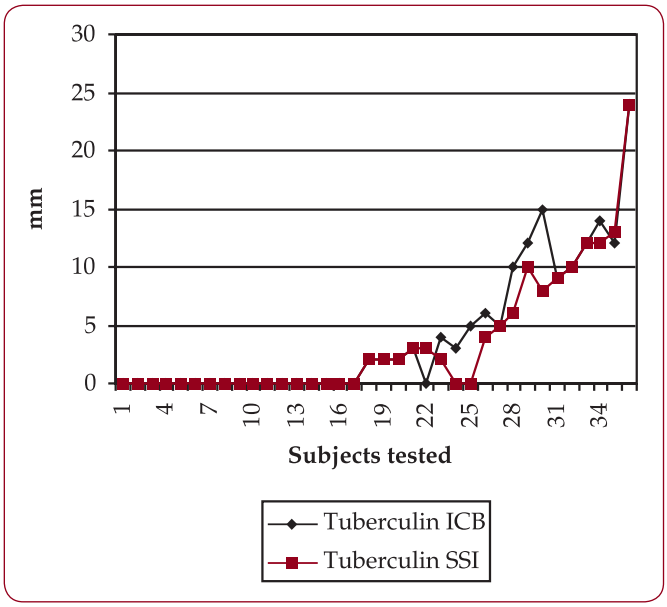

FIGURE 2. Induration measurements

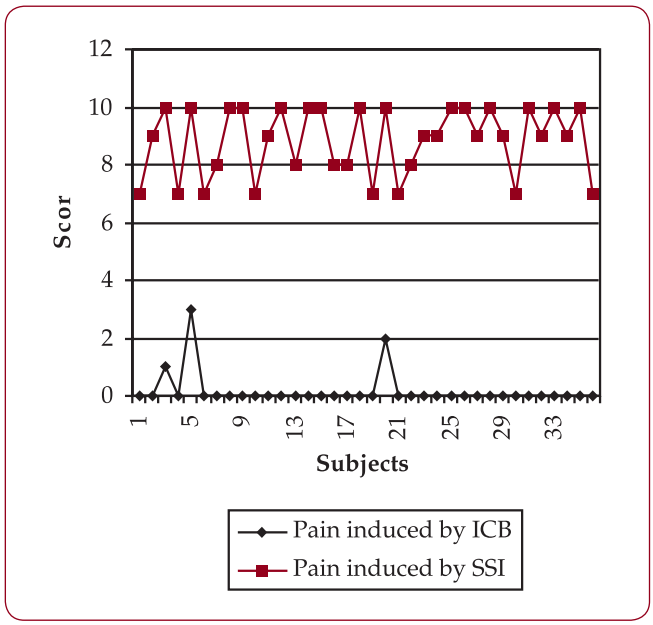

FIGURE 3. Pain induced by the Tuberculin Test

ACKNOWLEDGEMENTS

We would like to thanks to the nurses and all administrative staff who help us.

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