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Comparison of Ultrasonographic Measurement of the Tuberculin Skin Test with the Result of Manual Reading

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This study was conducted in order to determine the ultrasonographic (US) finding of tuberculin skin test and to compare with the result of manual reading. One hundred of hospital staff, in Zahedan a city in Southeast of Iran, were enrolled in this study. A 5-tuberculin unit (TU) PPD Mantoux test was administered to all healthy subjects by two experienced nurses and was applied to the left forearm. At 48 and 72 h, all PPD skin tests were measured by two independent readers and one Radiologist by High-resolution US examinations. Then results was analysed and comparison on results was made. A difference with $p < 0.05$ was considered significant. Fifteen cases had no induration measurable either manually or by US at 48 and 72 h. At 48 and 72 h, 12, 13 cases had induration between 1-4 mm by the first reader and 11, 13 had also induration between 1-4 mm as reported by the second reader. At 48 and 72 h 18, 19 cases had an induration between 5-9 mm by the first reader and at these times, 20, 23 cases had an induration between 5-9 mm by the second reader. At 48 and 72 h, 36, 35 cases had an induration between 10 to 14 by the first reader and at these times, 35, 32 of healthy subjects had induration between 10-15 by the second reader. At 48 and 72 h, 17, 15 cases, had a PPD skin test more than 15 mm, by two manual readers. On US, only 2 cases who had no induration by two readers at 48 and 72 h, showed an induration between 3.5 to 4.5 mm. There was no significant difference between reader 1 and reader 2 with US reader at 48 and 72 h ($p > 0.05$). Also, there was no significant difference between two manual readers at 48 and 72 h, ($p = 0.1$, $p = 0.09$). Result showed that manual finding of TST can be simply and objectively measured in the subjects who should start prophylactic antituberculous especially in children less than 6 year who have a history of contact with tuberculous patients or in patients who should start on tuberculosis treatment immediately.

Key words: Tuberculin skin test, ultrasonographic measurement, manual reading

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INTRODUCTION

Tuberculosis is a significant public health challenge and remain as the deadliest disease in the world. It is estimated that, one-third of the world's population, 2 billion people, are infected with tuberculosis (TB) and that 2.9 million patients die of tuberculosis every year (Matanet, 2004). Almost 95% of tuberculosis cases occur in developing countries (Remington and Hollingworth, 1995; Al-Kassimi *et al.*, 1993). Although most of the infection all over the world was centered in the community, nosocomial outbreaks of TB involving both patients and health care workers have been well documented (Al-Kassimi, 1993; Anonymous, 1994). Documentation of skin test conversion, as evidence by an increase of 10 mm over a previous PPD test over a period of two years, is considered an indication for six months of isoniazid therapy because the risk of developing active TB is greatest during the two years following conversion (Howard and Solomon, 1988; Raad *et al.*, 1989; Pickwell, 1999; Anonymous, 2000). The tuberculin skin test has many potential sources of error and variability. Standardization of the tuberculin reagent and the meaning of the test results have been considered in some detail but the little attention has been paid to the reading itself (Pennie, 1995; Pouchot, 1997; Singh *et al.*, 2002). Measurement of the induration, however, is one of the most important potential sources of error. If the customary technique of palpitation is used, the margins of the induration may be difficult to define (Pouchot, 1997; Singh *et al.*, 2002). Now, the alternative method (ultrasonographic measurement) of the tuberculin skin test although advocated as a new method for measurement of TST but there is a few information about this method and results (Fornage, 1993; Ercument *et al.*, 2005). Here in, we investigated the reliability of this method and compared this technique with the palpitation method.

MATERIALS AND METHODS

This is a cross sectional study, that was conducted between March and June 2005 among health care workers, in a tertiary care hospital in Zahedan a city in Sistan and Baluchestan province, in Southeast of Iran. One hundred of hospital staff were enrolled in this study. The PPD skin test was performed by trained and experienced nursing personnel. Five tuberculin units of purified protein derivative were administered by intradermal injection on the volar surface of the left arm. The results were assessed after 48-72 h and diameter of the induration (not erythema) recorded in millimeters. The readers separately measured

the transverse diameter (relative to the arm) of induration, manually. If there was no palpable induration, the result was entered as zero mm (negative result). Ultrasonographic examination was performed within a half hour of the manual reading at 48, 72 h. All US examinations were performed by an experienced radiologist with a standard US scanner. A water bag was used in all subjects and then a high-frequency linear-array transducer was used for all examinations. For analysis, the measurements were divided into 5 groups: Group 1, had zero induration; Group 2, TST results were between 1-4 mm; Group 3, had an induration between 5-9 mm, Group 4, between 10-14 mm and Group 5 had an induration more than 15 mm. All statistical analysis were performed on SPSS software using paired-samples t-test.

RESULTS AND DISCUSSION

A total of 100 hospital staff participated in the study. Fifteen of one hundred subjects had zero mm induration both manually and ultrasonographically at 48, 72 h. Only two cases who had negative results by two manual reader at 48 and 72 h, showed an induration less than 5 mm by US. The mean induration for reader 1 at 48 and 72 h was 10.2 and 10.4 mm, respectively. The mean induration for reader 2 was 10.2 and 10.3 mm at 48 and 72 h, respectively. Also the mean induration for US reader in two time was 10.8 mm and 10.9 mm, respectively. There were no significant difference between reader 1 and US reader at 48 and 72 h ($p = 0.1$, $p = 0.1$) and also between reader 2 and US reader at these times ($p = 0.09$, $p = 0.1$, respectively). Also, there was no significant difference between reader 1 and reader 2 at two times ($p = 0.1$, $p = 0.09$, respectively). There was a good agreement between the all readers in the results and paired-samples test for comparison of the manual and ultrasonographic measurement did not show significant differences ($p > 0.05$). Out of 36 cases who had tuberculin skin test between 10-14 mm, 34 cases had a history of working more than 11 years in different wards of hospital. Among 19 cases who had PPD test more than 15 mm, 12 cases worked only in infectious ward and 4 cases in internal ward and 3 cases in infectious and pediatric wards. All cases with tuberculin skin test more than 15 mm had a history of working at least 8 years in their wards. As the results show there was no significant difference between two manually readers and US reader, when average manual results and US results were compared for all five groups. Result by reader 2 was slightly more than first manual reader at 72 h when PPD test was between 5-9 mm but this difference was not significant (Table 1).

Table 1: The measurements of the tuberculin skin test in 100 cases by two readers and US at 48 and 72 h according to millimeter

Readers size/mm	0	1-4	5-9	10-14	>15	Mean
Reader 1* 48 h	17 cases	12 cases	18 case	36 cases	17 cases	10.2 mm
Reader 1 72 h	17	13	19	35	15	10.4 mm
Reader 2 48 h	17	11	20	35	17	10.2 mm
Reader 2 72 h	17	13	23	32	15	10.3 mm
US 48 h	15	13	20	34	18	10.8 mm
US 72 h	15	15	21	30	19	10.9 mm

*Reader 1, 48 h: The measurements of the first reader at 48 h

The main reason for the screening for tuberculosis by PPD skin testing is to offer chemoprophylaxis to converters (Pickwell, 1999). Tuberculin is a mixture of antigens obtained from the culture of *M. tuberculosis*. Antigens are foreign particles or proteins that stimulate the immune system to produce antibodies. After 48-72 h, the test site will be examined by a trained person for evidence of swelling (Howard and Solomon, 1988; Pennie, 1995). People who have been exposed to tuberculosis will develop an immune response, causing a slight swelling at the injection site. If there is a lump or swelling, the health care provider will use a ruler to measure the size of the reaction (Howard and Solomon, 1988; Pennie, 1995; Singh *et al.*, 2002). Some public health physicians recommend using a 72 h waiting period as a general practice on the grounds that a 48 h waiting period yields a higher percentage of false negative test results (Howard and Solomon, 1988; Singh *et al.*, 2002). Although the sensitivity and specificity are less than ideal for diagnosis of tuberculosis, no better diagnostic method is widely available (Singh *et al.*, 2002). In addition to manual reading there are a few methods of reading of induration which use ball point pen, ruler and measuring tape. All these methods are subjective and objective method could make the TST a more reliable test (Singh *et al.*, 2002; Fornage, 1993). The US examination of normal skin reveals 2 echogenic lines with a thin hypoechoic layer between them normal skin is less than 2 mm in thickness. When thickened, the dermis often becomes more echogenic. The TST reaction result in homogeneous soft tissue swelling that is slightly hyperechoic when compare with the neighboring muscles and slightly hypoechoic when compare with fatty tissue. The superficial facial is seen as an echogenic structure between the TST reaction and muscles (Fornage, 1993; Ercument *et al.*, 2005). US is a sensitive, widely available, relative inexpensive and noninvasive technique that is useful in assessing the skin and subcutaneous disorders. Recent development in transducer technology and high-resolution imaging has made US of the skin feasible for subcutaneous pathologies such as inflammatory processes (Ercument *et al.*, 2005). There are a few data about US reading of tuberculin skin test (Fornage, 1993; Ercument *et al.*, 2005; Beck *et al.*, 1986). Bech *et al.* (1986)

have used to measure the skin swelling in the tuberculin test by US. In their study, the subcutaneous tissue was not measured and they did not compare it with manual reading. In our study, we tried to standardize the procedure by measuring the transverse diameter of the TST. To our knowledge, there is only one study included a comparison of US and manual reading (Ercument *et al.*, 2005). In this study, There was no difference between results of US measurement and manual reading by two readers but in Ercument study, mean value of US measurement for all data point was higher than of the manual reading and the agreements were weak between the manual reading and US measurements and paired-samples test comparison of the manual and US measurements demonstrated significant differences ($p < 0.05$) (Ercument *et al.*, 2005). Although, manual reading of the TST may frequently result in misclassification when measurements are closed to cutoff point that separates negative from positive results, but with regards to our results, manual finding of TST can be simply and objectively measured in the subjects who should start prophylactic antituberculous, when it is done by experienced people.

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