

MODIFIED LEVINSON'S TEST IN RAPID DIAGNOSIS OF TUBERCULOUS MENINGITIS

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ABSTRACT

Modified Levinson's precipitation test was done in 64 cases of TBM, 54 cases of TBM with inconsistent CSF finding, and 32 cases of pyogenic meningitis. The test was positive in 93.7% cases of TBM (sensitivity, 93.7%), 85.5% cases of TBM with doubtful diagnosis and in 9.4% cases of pyogenic meningitis (specificity 90.6%) compared to 79.7%, 72.2% and 18.8% in original Levinson's test, respectively. With CSF examination only 66% cases of TBM could be diagnosed while with modified Levinson's test and CSF analysis 89% cases could be diagnosed ($p < 0.001$). So modified Levinson's test for diagnosis of TBM is better than Levinson's test ($p < 0.05$) with an added advantage of time saving.

Keywords: Cerebrospinal fluid, Tuberculous meningitis, Pyogenic meningitis, Levinson's test.

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Received for publication: February 15, 1993;

Accepted: September 13, 1993

Tuberculous meningitis (TBM) is one of the main health problems of children in developing countries. The prognosis is related to the stage of disease with a 100% cure rate in Stage I to 50% mortality and 100% permanent handicap in Stage III. Early diagnosis is, therefore, of paramount importance(1-3). CSF examination is the main tool for diagnosis. For confirmation, demonstration of AFB in CSF is needed(4) which is positive only in 3% cases by ordinary centrifuge method done meticulously(5). Culture of AFB requires 6 weeks for the report which is of no help. For confirmation of diagnosis of TBM, various new tests with varying efficacy have been developed(6) which are not available in most laboratories in our country. The need for a simple test which can be made available in all laboratories is, therefore, obvious.

In the past, few qualitative protein tests were developed viz., Pandey test, Non Aplet test, Tryptophan, test and Levinson's test. Of these Levinson's test was most specific for TBM(7,8): These tests are based on principle that globulin albumin ratio is changed in some pathological conditions. The test comprises of comparing the height of precipitate obtained by treatment of CSF with mercuric chloride and sulphosalicylic acid. Recently, some changes have been done in the method of test for making it less time consuming and specific, which is known as Modified Levinson's test(9,10).

The present study was planned with the aim to determine the value of modified Levinson's test in comparison with original Levinson's test in differentiating tuberculous meningitis from pyogenic meningitis.

Material and Methods

The study included 150 patients of meningitis between 6 months to 12 years in age who were admitted to the children

hospital, LLR and Associated Hospital, Kanpur. These were subjected to detailed clinical history, physical examination and routine laboratory investigations, fundus examination, Mantoux test, radiography of chest and CSF examination. CSF examination showing raised protein and increased cell count with lymphocytic predominance was taken as diagnostic criteria for TBM. 55.7% of cases diagnosed having tuberculous meningitis showed X-ray changes. Mantoux test was positive only in 34.4% whereas BCG diagnostic test was positive in 89.6%. CSF examination in case of TBM showed cobweb coagulum in 68.4% cases, raised protein in all the cases, decreased sugar in 61.1% cases, increased cell count with lymphocytic predominance in all cases and positive AFB staining in 3% of cases. In CSF examination of pyogenic meningitis cases, proteins were raised more than 100 mg/dl in 87.5% cases, sugar reduced to less than 20 mg/dl in 65.5% cases and cell count was more than 100 cells/mm³ with predominance of polymorphonuclear cells in 95% cases and Gram staining was positive in 46.5% of cases. Accordingly, cases were divided into 3 major groups. Group A included 64 cases in which clinical features and CSF was in favour of presumptive diagnosis of TBM. In Group B, comprising of 54 cases, patients presented clinically as tuberculous meningitis with inconsistent CSF findings. Group C included 32 cases who were diagnosed clinically and confirmed on CSF examination as pyogenic meningitis. CSF specimen of all cases were subjected to modified Levinson's precipitation test.

Method: 05 ml of CSF sample was taken in each of two same sized, equal bored flat based test tubes. In one test tube an equal amount of 6% mercuric chloride and in other equal amount of 3% sulphosalicylic

was mixed with CSF(7,10). The test tubes were shaken and kept in waterbath at 37°C for half an hour followed by incubation at 4°C (in middle shelf of refrigerator) for 2 hours. The height of precipitate column was measured in both test tubes. A ratio of 3:1 between precipitate with 6% mercuric chloride and that with sulphosalicylic acid was considered as diagnostic criteria for tuberculous meningitis. Traumatic CSF were not included(6). Simultaneously in all cases, original Levinson's test was performed in which after mixing the reagents with CSF, tubes were kept at room temperature for 24 hours. Here concentration of mercuric chloride used was 1%(7,8).

Results

Table I shows results of Modified Levinson's test in CSF in different groups. The test was positive in 60 out of 64 cases of Group A and 46 out of 54 cases of Group B. In Group C, only 3 cases were positive.

Results of original Levinson's test are shown in *Table II*. Comparison between results of modified Levinson's and original Levinson's test (*Table III*) shows that for TBM, modified Levinson's test was positive in 93.7% whereas Levinson's test was positive in 79.7% cases. Chi square test indicated that modified Levinson's test was significantly ($p < 0.05$) better than Levinson's test.

Discussion

Normally CSF contains low quantity of proteins with albumins and globulins in ratio of 6:1. In some diseases, the protein content rises with disturbance in the ratio of albumin and globulin. In TBM local production of immunoglobulin starts changing the ratio drastically, which can be measured by electrophoresis, but this test is not available in every laboratory(5,6). A simpler method to demonstrate this altered ratio is Levinson's

TABLE I—Ratio of Precipitates with Modified Levinson's Test in Different Groups

Ratio of precipitates with mercuric chloride and sulphosalicylic acid	Tuberculous meningitis (n = 64)		Undiagnosed meningitis (n = 54)		Septic meningitis (n = 32)	
	No.	%	No.	%	No.	%
3:1 (Positive)	60	93.7	46	85.5	3	9.4
2:1 (Negative)	3	4.7	6	10.8	2	6.2
1:1 (Negative)	1	1.6	2	3.7	6	18.8
1:2 (Negative)	-	-	-	-	13	40.6
1:3 (Negative)	-	-	-	-	8	25.0

TABLE II—Ratio of Heights of Precipitates with Levinson's Test in Different Groups

Ratio between precipitates with mercuric chloride and sulphosalicylic acid	Tuberculous meningitis (n = 64)		Undiagnosed meningitis (n = 54)		Septic meningitis (n = 32)	
	No.	%	No.	%	No.	%
3:1 (Positive)	38	59.4	28	51.8	3	9.4
2:1 (Negative)	13	20.3	11	20.4	3	9.4
1:1 (Negative)	9	14.1	13	24.1	10	31.2
1:2 (Negative)	4	6.2	2	3.7	6	18.8
1:3 (Negative)	-	-	-	-	10	31.2

TABLE III—Comparison of Sensitivity Results in Levinson's Test and Modified Levinson's Test

Group	Levinson's test		Modified Levinson's test	
	No.	%	No.	%
Tuberculous meningitis	51 (n=64)	79.7	60 (n=64)	93.7
Tuberculous meningitis with doubtful diagnosis	39 (n=54)	72.2	46 (n=54)	85.5
Septic meningitis	6 (n=32)	18.8	3 (n=32)	9.4

test which is specific for TBM. In the present study of 150 cases, among the 64 of Group A taken as positive cases, only 3% showed positive CSF smear for AFB on Zeihl Neelsen's staining. Cobweb formation in CSF was observed in 68.4% cases whereas precipitation test was positive in 93.7% cases.

Fifty four cases of Group B showed most of the clinical features in favor of TBM but inconsistent CSF findings. Cobweb was present in 12 (22.2%) and Zeihl Neelsen staining was positive in 1 (1.8%) case while precipitation test was positive for TBM in 48 (85.5%) cases. These 48 cases recovered after antituberculous treatment. In the remaining, both antibiotics and antituberculous therapy was given and later on the latter was continued. The test was negative in 29 (90.6%) cases out of 32 cases of pyogenic meningitis. Three cases with false positive results were given a trial of both antituberculous treatment and antibiotics. They showed definite response to antibiotic treatment and antitubercular therapy was withdrawn.

So, the test has 93.7% sensitivity and 90.6% specificity and the ability to diagnose 85.5% of doubtful cases. Results of the present study are comparable to those of others(9,10). The original Levinson test could diagnose only 51 out of 64 cases (79.7%) of positive controls and was falsely positive in 18.8% of acute bacterial meningitis cases. It was thus less specific and sensitive.

The present study shows that modified Levinson's test is a highly specific and sensitive bedside test for TBM and is a diagnostic tool for differentiating between cases of TBM and other meningitis where other diagnostic investigations like CSF examination are inconclusive. Modification

of the test has several others advantages: (i) Less time consuming (2.5 hours); and (ii) No difficulty in interpretation of test due to floccular precipitate of mercuric chloride as in the original test.

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