DIAGNOSTIC AND PROGNOSTIC VALUE OF BROMIDE PARTITION TEST IN TUBERCULOUS MENINGITIS

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ABSTRACT

Bromide partition ratio was determined in 32 cases of tuberculous meningitis, 6 pyogenic meningitis, 8 viral meningitis and 9 cases of febrile convulsions. Bromide partition ratio below the critical value of 1.6 was present in 30 out of 32 tuberculous meningitis patients (93.74%) whereas all the control children had a ratio above 1.6. Two children who were on regular chemotherapy showed progressively rising ratio.

It is concluded that in doubtful cases with inconclusive CSF picture, a low bromide partition ratio is a strong reason for starting antituberculous treatment without any delay. A very low ratio also suggests poor prognosis.

Key words: *Bromide partition ratio, Tuberculous meningitis.*

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Meningitides of various types are still common in India. The incidence of tuberculous meningitis (TBM) varies between 1 to 4% of all inpatient admissions(1). The true incidence of TBM in India is not known.

Since most infections of the central nervous system have similar clinical presentations (irrespective of the infecting agent), their differential diagnosis causes a dilemma. In TBM, there may not be any radiological evidence of a primary complex; Mantoux test may be negative and the CSF profile may not always be suggestive of tuberculosis. Moreover, use of antibiotics alter the clinical presentation and the CSF picture and thus precludes early diagnosis. CSF tests such as Lange's colloidal gold qualitative curves are non-specific and not routinely undertaken. In 1929, Walter showed that in a normal individual, there existed a bloodbrain barrier which was decreased in presence of infections. He described the bromide partition ratio (ratio of bromide per unit volume of serum to that per unit volume of CSF)(2). The efficacy of this test has been reported by various workers(3-6).

The study was undertaken to find the diagnostic and prognostic value of bromide partition ratio (BPR) in children with TBM.

Material and Methods

The study was carried out over a 3 year period (1986-1988) on patients of 0-13 year age group who were admitted to Government and private hospitals in Solapur city of Maharashtra State. The study group consisted of 32 children with TBM, 6 children with pyogenic meningitis, 8 with viral meningitis and 9 cases of febrile convulsions formed the control group.

Both groups were subjected to history

taking, thorough clinical examination and routine laboratory investigations such as blood, urine and stool examinations. Other relevant investigations included Mantoux test, fundoscopy, radiography of the chest (PA view) and CSF examination (cytological, biochemical and bacteriological). If the clinical examination revealed any infective foci (*e.g.,* otitis media) culture and antibiotic sensitivity tests were done. Written consent was obtained before the test was performed.

1. *Collection of CSF:* A sterile solution of sodium bromide was administered intramuscularly in the dose of 2 g for children upto 2 years and 4 g for children above 2 years of age. This sterile solution was prepared by dissolving 60 g of sodium bromide in pyrogen free water to make 100 ml solution. After an equilibration time of 24 hours, 2 ml CSF was collected in plain bulb by lumbar puncture using all aseptic precautions. The sample was analyzed within 24 hours. In case of temporary delay in analysing, the sample was stored at 4°C.

2. *Collection of serum:* 5 ml blood was collected in plain bulb by peripheral venepuncture and the serum was allowed to separate out. The serum bromide levels were done within 24 hours.

3. *Bromide level estimation:* This was estimated by the gold chloride method(2). The proteins were precipitated using trichloroacetic acid and bromide levels were estimated by reading the resulting optical density (*Table I*) of gold chloride at 470 nm using a spectrophotometer, and comparing with a standard curve (*Fig. 1*). A standard bromide solution was made so as to correct errors due to absorption of bromide in the precipitated proteins. The BPR was calculated as follows:

$$BPR = \frac{\text{Bromide per unit volume of serum}}{\text{Bromide per unit volume of CSF}}$$

TABLE I–*Standard for Reading Optical Density*

Standard solution of bromide (mmol/litre)	Optical density
0	0
2.5	6
5.0	12
10.0	27
15.0	46
20.0	58

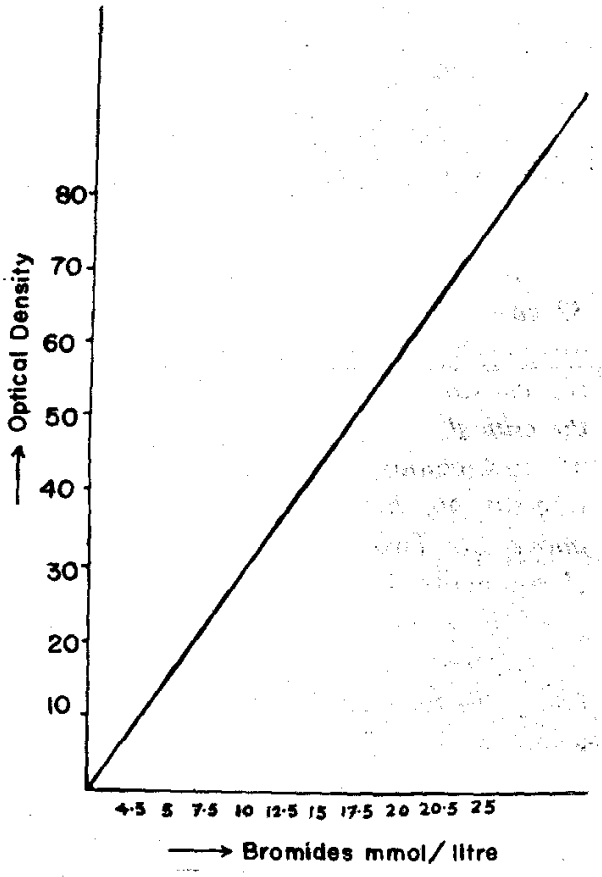

Fig. 1. Standard curve for reading optical density.

Results

Out of 2,256 pediatric inpatients in the hospitals taken up for the study, 32 (1.41%) were suffering from TBM. These formed the study group. The maximum incidence of TBM in this group was between 3-5 years (39.28%). Both groups showed a preponderance of male children.

A total of 15 TBM patients (46.87%) were Mantoux positive while 12 (37.5%) showed radiological evidence of primary complex. Twenty eight children (87.5%) had a CSF picture suggestive of tuberculosis. However, CSF profile was normal in 4 cases of TBM.

In the study group, all except two children (who were on anti-tubercular drugs for 6 months) had a BPR below the critical value of 1.6 (*Table II*). In the control group, all cases had a ratio above 1.6 (*Fig. 2*). Two children in the study group with BPR of 0.7 and 0.8 subsequently expired.

Discussion

The peak incidence (39.28%) of TBM in the age group of 3-5 years compares with observations of 39.28% by Udani *et al.*(7) and 34% by Benkappa *et al.*(8). The preponderance of male children in both study and control group is difficult to explain except for the traditional practice of boys getting preference over girls for medical attention.

In TBM, hypersensitivity in tuberculoproteins increases the permeability of the meninges. This permeability can be measured by estimating the partitioning of bromide between the blood and CSF(2). The ratio of serum bromide level to CSF bromide level is expressed as BPR. The use of radioactive isotopes of bromide to estimate the relative concentration of bromide in blood and CSF has also been described(9). Though this method is accurate and reliable, the cost is prohibitive for most medical centres in the developing

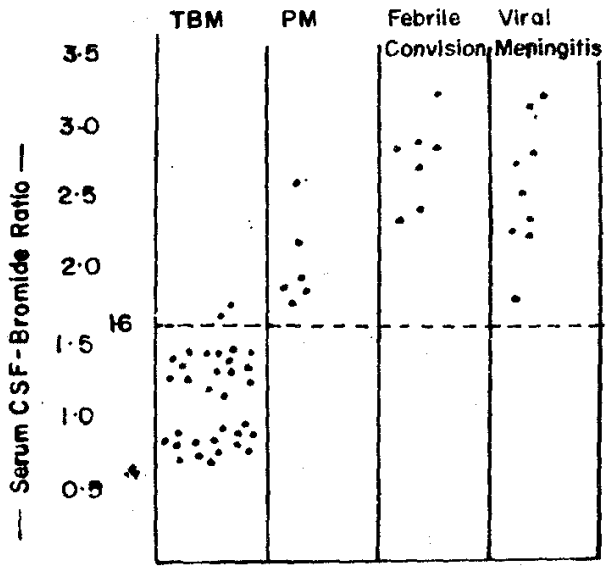

Fig. 2. Scatterogram showing bromide partition ratio in the study and control groups.

TABLE II—*Bromide Partition Ratio (BPR) in Study and Control Group*

BPR	Study group				Control group			
	TBM		PM*		VM¶		FC§	
	No.	%	No.	%	No.	%	No.	%
0.5-0.99	15	46.9	0	0.0	0	0.00	0	0.0
1.0-1.49	15	46.9	0	0.0	0	0.00	0	0.0
1.5-1.99	2	6.3	4	66.7	1	12.5	0	0.0
2.0-2.49	0	0.0	1	16.7	3	3.7	2	22.2
2.5-2.99	0	0.0	1	16.7	2	25.0	4	44.4
3.0-3.49	0	0.0	0	0.0	2	25.0	3	33.3

*PM = Pyogenic meningitis, ¶VM = Viral Meningitis, §FC = Febrile convulsions.

world. Besides, most hospitals may not have the facilities for a nuclear medicine laboratory.

Bromide partition ratio in the normal individual varies between 2 and 3. In TBM, the blood brain barrier is affected and there is an early fall in the ratio, when the disease responds to chemotherapy, the ratio returns to normal. However, in pyogenic meningitis, this fall may or may not occur(10).

The CSF may be atypical in many cases of meningitis(6). Inability to differentiate between various types of meningitides results in unnecessary chemotherapy (with its accompanying hazards) and prolonged hospitalization. There is thus a need for a simple, cheap and reliable test. The BPR test is simple and the reagents are cheap. The bromide solution can be autoclaved and stored upto eight weeks. In our study, intramuscular administration of bromide solution did not cause any untoward effects.

The present study showed that in 93.74% of cases of TBM the BPR was below 1.6. This rate of positivity is confirmed by other workers(3,6,12,13). Nicol *et al.* showed 100% accuracy of this test, with no false negatives. In their study clinical improvement was accompanied by a rising ratio(4). In the present study two children who were on regular chemotherapy showed progressively rising ratio.

In summary, a low bromide partition ratio may not be pathognomonic of TBM(6). Clinical and laboratory parameters have to be considered before attempting a diagnosis. In doubtful cases with inconclusive CSF picture, a low bromide partition ratio is a strong reason for starting antituberculous treatment without any delay. The bromide partition test may be useful in differential diagnosis of meningitides, when CSF profile is inconclusive and prognosis of TBM. A very low ratio would suggest poor prognosis, while a progressively rising ratio would signify improvement of recovery.

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