CEREBROSPINAL FLUID FREE SIALIC ACID AND ASPARTATE TRANSAMINASE LEVELS IN MENINGITIS

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ABSTRACT

Background: Sialic acid (SA) is a nine carbon sugar derived from mannosamine and pyruvate. High levels of sialic acid and aspartate transaminase (AST) levels in cerebrospinal fluid have been described in pyogenic meningitis (PM) compared to tubercular meningitis (TBM).

Objectives: To evaluate the levels of CSF free SA in PM and TBM and to assess the correlation between CSF free SA and CSF glucose or total protein levels.

Patients and Methods: A total of 122 subjects were studied and divided into children and adults. Further, these have been subdivided into controls, PM and TBM. CSF free SA was estimated by thiobarbituric acid assay of Warren and AST by Reitmann and Frankel method.

Results: CSF free SA and AST levels in children and adults were significantly high in PM ($p < 0.001$) as compared to TBM and controls.

Conclusion: A very high CSF free SA and AST were found to be characteristic of PM, making them useful parameters to differentiate PM from TBM.

KEY WORDS

Meningitis, Free Sialic Acid.

INTRODUCTION

Meningitis is one of the most dreadful disease affecting the mankind at all ages. In India, the most common types of meningitis are pyogenic and tubercular. Clinical presentation of these forms of meningitis may not always be typical and hence may overlap.

Standard routine analysis of CSF does not always provide definitive information and culture results are much delayed. Therefore, quest for additional diagnostic methods for meningitis continues. Several studies have reported that the levels of CSF free SA and AST are increased significantly in PM in comparison to TBM.

MATERIALS AND METHODS

A total of 122 subjects were studied ranging from 2

months to 80 years, and divided into children and adults. Further, children were divided into 20 each of PM, TBM and controls. Adults were divided into 21 each of PM, TBM and 20 controls. The diagnosis of meningitis was established by detailed clinical history, neurological examination and laboratory findings. The patients were grouped into PM and TBM after confirming the diagnosis by biochemical and pathological findings. Controls were non-meningitic patients and those undergoing spinal anaesthesia. CSF examination was done in all cases. CSF appearance, sugar, total protein and AST were noted. Gram staining, microscopic examination of the cobweb for acid fast bacilli after Ziel-Neelson's staining and CSF culture were performed. Estimation of CSF free SA was done by thiobarbituric acid assay of Warren (1). CSF AST was measured by Reitmann and Frankel method (2). Mann-Whitney test was used for statistical comparison.

RESULTS

It is seen from the Table 1 and Fig. 1 that the CSF free SA in PM, TBM and matched controls in children were 107.0 ± 31.2 moles/L, 15.2 ± 5.7 moles/L and 11.7 ± 4.0 moles/L respectively. Similarly from Table

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Table 1. Comparative statistical analysis of study in children

Sl. No.	Group	CSF free Sialic acid moles/L	Glucose mg/dl	AST IU/L	Total Protein mg/dl
1	Controls (n=20)				
	Range	7.6 - 22.0	28.0 - 100.0	3.0 - 14.0	18.0 - 58.0
	Mean $\pm$ SD	11.7 $\pm$ 4.0	71.9 $\pm$ 16.4	7.6 $\pm$ 2.6	29.9 $\pm$ 9.9
2	Pyogenic meningitis (n=20)				
	Range	60.0 - 196.8	10.0 - 86.0	15.0 - 40.0	54.2 - 420.0
	Mean $\pm$ SD	107.0 $\pm$ 31.2	32.4 $\pm$ 18.9	26.0 $\pm$ 6.6	172.4 $\pm$ 97.7
	'p' (comparison with controls)	<0.001 (HS)	< 0.001 (HS)	< 0.001 (HS)	< 0.001 (HS)
3	Tubercular meningitis (n=20)				
	Range	6.4 - 22.0	16.0 - 86.0	6.0 - 15.0	45.0 - 192.0
	Mean $\pm$ SD	15.2 $\pm$ 5.7	40.9 $\pm$ 16.7	10.6 $\pm$ 3.0	116.1 $\pm$ 40.6
	'p' (comparison with controls)	> 0.05 (NS)	< 0.001 (HS)	< 0.01 (S)	< 0.001 (HS)

Table 2. Comparative statistical analysis of the present study in adults

Sl.No.	Group	CSF free Sialic acid mmoles/L	Glucose mg/dl	AST IU/L	Total Protein mg/dl
1	Controls (n=20)				
	Range	5.0 - 18.8	57.8 - 156.0	4.0 - 12.0	15.6 - 62.0
	Mean $\pm$ SD	12.10 $\pm$ 3.78	72.99 $\pm$ 21.78	7.4 $\pm$ 2.37	31.79 $\pm$ 12.51
2	Pyogenic meningitis (n=21)				
	Range	17.0 - 177.0	10.0 - 80.0	10.0 - 44.0	40.0 - 418.0
	Mean $\pm$ SD	106.6 $\pm$ 34.7	31.6 $\pm$ 15.4	29.5 $\pm$ 9.0	182.1 $\pm$ 98.9
	'p' (comparison with controls)	<0.001 (HS)	< 0.001 (HS)	< 0.001 (HS)	< 0.001 (HS)
3	Tubercular meningitis (n=21)				
	Range	6.0 - 80.5	13.8 - 87.0	5.0 - 21.0	50.0 - 192.0
	Mean $\pm$ SD	22.0 $\pm$ 18.6	34.1 $\pm$ 16.7	11.1 $\pm$ 3.6	109.6 $\pm$ 43.9
	'p' (comparison with controls)	> 0.05 (NS)	< 0.001 (HS)	< 0.01 (S)	< 0.001 (HS)

HS - Highly Significant; NS - Not Significant; S - Significant

2 and Fig. 2, it is evident that the CSF free SA in PM, TBM and matched controls in adults were 106.6 $\pm$ 34.7 moles/L, 22.0 $\pm$ 18.6 moles/L and 12.10 $\pm$ 3.78 moles/L respectively. The CSF free SA were significantly high in PM (p<0.001) when compared to TBM and controls both in children and adults.

From Table 1 and 2 and Fig. 3 and 4 it is observed

that the CSF AST levels in PM, TBM and matched controls in children were 26.0 $\pm$ 6.6 I.U./L, 10.6 $\pm$ 3.0 I.U/L and 7.6 $\pm$ 2.6 I.U./L respectively. In adults, the CSF AST levels in PM, TBM and matched controls were 29.5 $\pm$ 9.0 I.U/L, 11.1 $\pm$ 3.6 I.U/L and 7.4 $\pm$ 2.37 I.U/L respectively. The CSF AST levels were significantly high in PM (p<0.001) when compared to TBM and matched controls in both children and adults.

Bar diagram 1. Mean CSF concentrations of free sialic acid in controls and in children with tubercular and pyogenic meningitis

Bar diagram 3. Mean CSF concentrations of AST in controls and in children with tubercular and pyogenic meningitis

Bar diagram 2. Mean CSF concentrations of free sialic acid in controls and in adults with tubercular and pyogenic meningitis

Bar diagram 4. Mean CSF concentrations of AST in controls and in adults with tubercular and pyogenic meningitis

Table 3. Table showing the Correlation of CSF free Sialic Acid with Glucose and Total Protein in Controls, Tubercular meningitis and Pyogenic meningitis in both Children and Adults

Correlation between	Children			Adults		
	Controls	Tubercular meningitis	Pyogenic meningitis	Controls	Tubercular meningitis	Pyogenic meningitis
Sialic acid and Glucose	r = - 0.32 p = 0.17 NS	r = - 0.05 p = 0.82 NS	r = 0.27 p = 0.25 NS	r = - 0.34 p = 0.14 NS	r = 0.03 p = 0.91 NS	r = - 0.12 p = 0.61 NS
Sialic acid and Total protein	r = - 0.10 p = 0.71 NS	r = 0.26 p = 0.28 NS	r = - 0.08 p = 0.73 NS	r = - 0.20 p = 0.40 NS	r = - 0.42 p = 0.06 NS	r = 0.30 p = 0.19 NS

Pearson's correlation coefficient (r-value)
p > 0.05: Not significant (NS).

There was no significant correlation between CSF free SA and CSF glucose or total protein levels in both the meningitides in children as well as in adults as shown in Table 3.

DISCUSSION

Sialic acid (N-acetyl neuraminic acid) is an important nine carbon sugar bound to glycoproteins and glycolipids found in the brain tissue. It exists in non-dialysable form, which is released from serum proteins and a dialysable free form derived probably from metabolic activity in CNS. The exact mechanism for increased free SA in PM is not known. However, it could be due to: glycoprotein and glycolipid bearing neurons which are rich in sialic acid and contiguous with infected meninges are acted upon by the enzyme neuraminidase elaborated by pyogenic organisms. This enzyme cleaves terminal N-acetyl neuraminic acid from the adjacent sugar of glycoprotein or glycolipids and releases into CSF. In the present study we observed significantly increased concentrations of CSF free SA in both children and adults with PM in comparison to matched controls. These findings are comparable with those reported by Kumar *et al.* (PM = 177.6 moles/L, control = 17.4 moles/L) and other studies (3, 4, 5, 6, 7, 8).

Similarly we have observed slightly increased but statistically non significant CSF free SA levels in both children and adult subjects with TBM in comparison to controls. These observations are comparable with those reported by Ahmed *et al.* (TBM = 22.1 moles/L, controls = 17.4 moles/L) The non-significant differences of CSF free SA in TBM are explained on the basis of lack of neuraminidase enzyme in tubercle bacilli.

AST is an intracellular aminotransferase which catalyzes the transfer of an amino group from an α -amino acid to α -keto acid. CNS contains more AST than hepatic tissue and almost as much as cardiac tissue. Hence any injury or disease of CNS will increase the AST levels in CSF. The increased CSF AST levels in PM may be due to (a) increased outflow of enzymes from the destroyed cells of CNS and (b) hypoxia, which impairs blood brain and blood CSF barriers leading to decreased elimination of this enzyme from CSF. The decreased CSF AST activity in TBM when compared to PM was attributed to subacute nature of the disease and delay in early diagnosis leading to regression of enzyme levels. These findings are in agreement with the results of other studies (9, 10, 11).

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