Original Article

Evaluation of various parameters in tuberculous meningitis

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Abstract

Introduction: Meningitis still remains a condition of significance mortality and morbidity in pediatric practice. Tubercular and bacterial meningitis form an important group of neurological diseases associated with considerable mortality and morbidity in children. Tuberculous meningitis is the most serious complication of Mycobacterium tuberculosis infection. In children, at the time of primary infection, leptomeninges might get seeded and they may develop this disease subsequently. **Aims and Objectives:** To Evaluate Various Parameters in Tuberculous Meningitis **Methodology:** The present study was carried out in the Department of Biochemistry at Government Medical College and Hospital, Aurangabad during the period June 1999 to June 2001. The study was carried out on 8 patients of tubercular meningitis and 20 controls from pediatric age group. The diagnosis of meningitis was made on clinical findings, microscopic examination of CSF, biochemical examination of CSF, culture studies and radiological studies. Estimation of Blood Glucose done by Trinders methods. Estimation of CSF total proteins by turbidometric method (Meulemans I960):- (Wooten I.D.P., 1964). Colorimetric Method used for Estimation of CSF Lactate Dehydrogenase (LDH): **(Wooten I.D.P., 1964)· Estimation of CSF GOT and CSF GPT**(Reitman and Frankel, 1957; Wooten I.D.P., 1964)were done in Laboratory. Unpaired t –test was used to see statistical significance. **Result:** The decrease in mean CSF Sugar value in group in Controls and Tuberculousmeningitis is statistically significant (P<0.05). Decrease in mean CSF Sugar /blood sugar ratio in Controls and Tuberculousmeningitisis statistically significant (P<0.05). Increase in mean CSF protein value inControls and Tuberculousmeningitis is statistically significant (P<0.05). The increase in mean CSF GOT value inControls and Tuberculous meningitis. The increase is statistically significant (P<0.05). The increase in mean CSF GPT value in Controls and Tuberculousmeningitisis statistically significant (P<0.05). **Conclusion:** Thus we have concluded that CSF GOT, GPT and LDH help the clinician for diagnosing Tuberculous meningitis in addition to the routine investigations.

Keywords: Tuberculous Meningitis, CSF GOT, CSF GPT, CSF LDH.

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INTRODUCTION

Meningitis still remains a condition of significance mortality and morbidity in pediatric practice. Tubercular and bacterial meningitis form an important group of neurological diseases associated with considerable mortality and morbidity in children. Tuberculous meningitis is the most serious complication of Mycobacterium tuberculosis infection. In children, at the time of primary infection, leptomeninges might get seeded and they may develop this disease subsequently. Bacterial meningitis is a fatal disease if untreated. With availability of modern antibacterial agents, mortality has been substantially reduced but is associated with significant morbidity in the form of serious neurological and mental sequelae like psychomotor retardation, deafness, and seizures. A late diagnosis and inadequate chemotherapy increases the incidence of these crippling sequelae. Incidence of mortality is clearly related to the

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late initiation of the treatment. A late or missed diagnosis of tubercular meningitis can have serious consequences and diagnosis is far from easy. It is an inflammation of the leptomeninges and cerebrospinal fluid (CSF) by infectious or non infectious processes. The most common infectious agents are: Bacterial, tubercular, viral, protozoal and fungal. The non- infectious agents are malignancy, subarachnoid hemorrhage and sarcoidosis (Andreoli T.E., 1990)[1]. Acute bacterial meningitis: It is defined as an inflammation in response to bacterial infection of the pia, arachnoid and the fluid residing in the space as it encloses and also the fluid in the ventricles of the brain. Since subarachnoid space is continuous space around the brain, the spinal cord and optic nerves, meningitis is always cerebrospinal (Harter D.H. *et al*, 1991)[2]. Bacterial meningitis is caused by bacterial agents like Streptococcus pneumoniae, *Escherichia coli, Hemophilusinfluenzae*, Neisseria meningitis etc. Estimation of the serum levels of enzymes is a helpful investigation in diagnosis of hepatic, myocardial, muscular and neoplastic diseases. Presently these tests are being utilized in diagnosing neurological disorders like meningitis. The applied tests are estimation of transaminases (GOT and GPT) and lactate dehydrogenase (LDH) in cerebrospinal fluid. Transmlnases (GOT, GPT) and LDH : Transminases (GOT and GPTj are the enzymes which transfer amino group from one a amino acid to a ketoacids and lactate dehydrogenase is an oxidoreductase which reversibly catalyse the conversion of lactate to pyruvate (Wooten I.D.P., 1964)[3].These enzymes are widely distributed in all the tissues of the body but appears to be most concentrated in myocardium, liver, skeletal muscles, brain and kidney. Acute injury to any of the tissue results in raised level of enzymes in serum. Since brain is rich in these enzymes (GOT, GPT and LDH). The various pathological processes could cause a release of CSF is most readily accessible biological fluid and in neurological disorders the enzyme i.e. GOT, GPT and LDH are liberated into CSF whenever there is either destruction of neurons or any serious impairment of physiological function. As these enzymes in CSF are not utilised for any function, hence their presence indicates transit from the neuronal cells [Aronson S.M., 1960)[4]. Lending M. *et al* (1959)[5] had shown that the major source of increased CSF enzyme activity was due to increase in cerebral cell permeability rather than increased permeability of the blood cerebrospinal fluid. Mellick R.S. *et al* (1964)[6] have reported elevated CSF GOT levels in cerebrovascular accident and epilepsy. Belsey M.A. (1969)[8] have reported elevated CSF GOT in acute bacterial meningitis and attributed the elevated CSF GOT activity in acute purulent meningitis to changes in CSF blood brain barrier, to damage of brain tissue or to the presence of white blood cells [WBCJ or bacteria or to a combination of these factors. Chawhan R.N. *et al* (1985)[7] reported the mechanism by which the activity of CSF LDH is increased in meningitides is still a subject of speculation and also reported various authors have attributed the rise to altered blood- brain/CSF barrier, the presence of micro-organisms in the CSF, and pleocytosis and bacteria. Nelson *et al* confirmed granulocytes as the source of CSF LDH and demonstrated that lymphocytes also possess enzyme activity. These lymphocytes could be the origin of CSF LDH in case of TBM. Various authors have studied CSF enzymes GOT, GPT and LDH in neurological disorders of inflammatory as well as noninflammatory origin (Mellick R.S. *et al*, 1964; Belsey M.A., 1969; Srivastava G., 1971; Shirole D.B. *et al*, 1974; Wroblewski F. *et al*, 1958; Nelson P.V. *et al*, 1975) [6,8,9,10,11,12].Most of the studies have shown elevation of CSF GOT (Reddy S.V.R. *et al*, 1972; Shirole D.B. *et al*, 1974)[10,13] GPT (Shirole D.B. *et al*, 1974)[10] and LDH (Beaty H.N. and Oppenheimer S., 1968, Das AK *et al*, 1988; Jain MX *et al*, 1991)[14,15,16] in pyogenic meningitis.

MATERIAL AND METHODS

The present study was carried out in the Department of Biochemistry at Government Medical College and Hospital, Aurangabad during the period June 1999 to June 2001.The study was carried out on 8 patients of tubercular meningitis and 20 controls from pediatric age group. The diagnosis of meningitis was made on clinical findings, microscopic examination of CSF, biochemical examination of CSF, culture studies and radiological studies. Estimation of Blood Glucose done by Trinders Methods. Estimation of CSF total proteins by turbidometric method (Meulemans I960):- (Wooten I.D.P., 1964)[3].Colorimetric Method used for Estimation of CSF Lactate Dehydrogenase (LDH): **(Wooten I.D.P., 1964)[3]. Estimation of CSF GOT and CSF GPT** (Reitman and Frankel, 1957; Wooten I.D.P., 1964)[3] were done in Laboratory. Unpaired t –test was used to see statistical significance.

RESULT

Table 1: Comparison of biochemical parameters in Tuberculous meningitis

Parameters	Controls (n=20)	Tuberculous meningitis (n=8)
BSL (mg%)		
Range	75-118	67-131
Mean ± S.D.	91.7 ± 12.86	89.25±23.64
CSF sugar mg%)		
Range	58-80	19-43
Mean ± S.D.	64.4±5.42	31.62±9.08
CSF/Blood Sugar ratio		
Range	0.56-0.8	0.28-0.43
Mean ± S.D.	0.7±0.06	0.35±0.05

CSF Proteinsmg%)		
Range	18-40	95-274
Mean ± S.D.	27.25±7.23	160±66.26
CSF GOT (IU/L)		
Range	7-11	9-19
Mean ± S.D.	9.1±1.88	13.25±3.41
CSF GPT (IU/L)		
Range	5-11	7-17
Mean ± S.D.	7.3±1.97	12.12±3.22
CSF LDH (IU/L)		
Range	5-44	49-119
Mean ± S.D.	26.85±10.79	69.75±21.76

Table 2: CSF Sugar (mg %) Showing comparison between Controls and Tuberculous meningitis

Study group	Mean	S.D.	't' value	P Value
Group I(Controls)	64.4	5.42	15.77	<0.05
Group IV(Tuberculous meningitis)	31.62	9.08		

Above table shows decrease in mean CSF Sugar value in group in Controls and Tuberculous meningitis The decrease is statistically significant (P<0.05).

Table 3: CSF Sugar / Blood Sugar ratio Showing comparison between Controls and Tuberculous meningitis

Study group	Mean	S.D.	't' value	P Value
Group I(Controls)	0.7	0.06	7.44	<0.05
Group IV(Tuberculous meningitis)	0.35	0.05		

Above table shows decrease in mean CSF Sugar /blood sugar ratio inControls and Tuberculousmeningitis. The decrease is statistically significant (P<0.05).

Table 4: CSF Proteins (mg%) Showing comparison between Controls and Tuberculous meningitis

Study group	Mean	S.D.	't' value	P Value
Group I(Controls)	27.25	7.23	9.08	<0.05
Group IV(Tuberculous meningitis)	160	66.26		

Above table shows increase in mean CSF protein value inControls and Tuberculous meningitis. The increase is statistically significant (P<0.05).

Table 5: CSF GOT (IU/L) Showing comparison between Controls and Tuberculous meningitis

Study group	Mean	S.D.	't' value	P Value
Group I(Controls)	9.1	1.88	4.98	<0.05
Group IV(Tuberculous meningitis)	13.25	3.41		

Above table shows increase in mean CSF GOT value in Controls and Tuberculous meningitis. The increase is statistically significant (P<0.05).

Table 6: CSF GPT (IU/L) Showing comparison between Controls and Tuberculous meningitis

Study group	Mean	S.D.	't' value	P Value
Group I(Controls)	7.3	1.97	4.84	<0.05
Group IV(Tuberculous meningitis)	12.12	3.22		

Above table shows increase in mean CSF GPT value in Controls and Tuberculous meningitis. The increase is statistically significant (P<0.05).

DISCUSSION

There is increased permeability of membrane in meningitis for which we get increased protein content in the CSF but glucose transport is not by simple diffusion method. So the glucose transport mechanism has been postulated to be mainly due to damage to the specific mechanism in the cell membrane that can readily transfer glucose molecules despite their insolubility in lipids (carrier facilitated diffusion). It has been explained by Goldring *et al* that low CSF sugar and low CSF/blood sugar ratio in pyogenic meningitis than in tuberculous meningitis is due to preponderance of polymorphs in pyogenic meningitis which utilize glucose morethan in tuberculous meningitis where the preponderant lymphocytes take up glucose less avidly. In tuberculous meningitis cases the blood brain barrier is altered due to inflammatory process and increases the passage of serum proteins especially so the globulin fraction with which enzyme is associated in CSF. These was also a rise in GOT levels with cell counts especially in the cases of pyogenic meningitis probably this may be due to the liberation of endogenous enzymes in the cells. It has been proposed that low CSF sugar is due to synergistic effect of glycosis by bacteria and leucocytes. It is postulated that increased GOT level in CSF was due to release of the enzyme from destroyed cells of nervous tissue and an altered intracellular metabolism in the disease state. It is also said that anoxia impair blood/brain and blood CSF barriers leading to decreased elimination of the enzyme from CSF and increased outflow of the enzyme from serum through an incompetent blood/CSF barrier. It is likely that the transaminases might have been liberated into the CSF from the cells of the affected brain tissue following the inflammatory process and thus higher levels of transaminases in the CSF may reflect a greater brain damage. In our study we have found that decrease in mean CSF Sugar value in group in Controls and Tuberculous meningitis The decrease is statistically significant (P<0.05).Decrease in mean CSF Sugar /blood sugar ratio in Controls and Tuberculousmeningitis. The

decrease is statistically significant (P<0.05).increase in mean CSF protein value in Controls and Tuberculous meningitis. The increase is statistically significant (P<0.05). The increase in mean CSF GOT value in Controls and Tuberculous meningitis. The increase is statistically significant (P<0.05).The increase in mean CSF GPT value in Controls and Tuberculousmeningitis. The increase is statistically significant (P<0.05). These findings are in confirmation with Belsey M.A. *et al* (1969)[8]Raizada N. *et al* (1995)[17]Shirole D.B. *et al* (1974)[10.]

CONCLUSION

Thus we have concluded that CSF GOT, GPT and LDH help the clinician for diagnosing Tuberculous meningitis in addition to the routine investigations.

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