CEREBROSPINAL FLUID OSMOLAL CHANGES IN BACTERIAL MENINGITIS

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ABSTRACT

Sixty children with acute bacterial meningitis (ABM) were prospectively studied for their serum sodium values and cerebrospinal fluid (CSF), serum and urinary osmolality. The results have been compared with 20 age and nutritionally matched controls. Even though mean serum osmolality (283.2 ± 13.84 mOsm/kg) and serum sodium levels (130.5 ± 8.15 mEq/L) were significantly lower in ABM in comparison to controls ($p < 0.05$ and < 0.001, respectively), the overall mean CSF osmolality in patients with ABM (282.5 ± 12.3 mOsm/kg) was not significantly different as compared to controls (288.2 ± 7.89 mOsm/kg). As expected, cases of ABM with syndrome of inappropriate secretion of antidiuretic hormone (SIADH) had significantly lower CSF osmolality (272 ± 9.42 mOsm/kg) as compared to those without SIADH(288.5 ± 9.34 mOsm/kg) and controls (288.2 ± 7.89 mOsm/kg). However, our observations indicate that whereas the mean CSF osmolality was lower than the serum osmolality in the control group as well as in ABM without SIADH, it was greater than serum osmolality in ABM with SIADH ($p < 0.05$). Our results suggest that in the presence of SIADH, hypo-osmolality of serum may eventually result in hypo-osmolality of CSF, but the fall in CSF osmolality is not of the same degree as that of serum. Low CSF osmolality was observed to be associated with an unfavorable prognosis ($p < 0.05$).

Key words: *Bacterial meningitis, Syndrome of inappropriate secretion of ADH, Osmolality, Cerebrospinal fluid.*

Acute bacterial meningitis (ABM) is a serious medical problem in children with high mortality particularly in developing countries. With the advent of newer antibiotics the outlook has remarkably improved, but certain associated factors such as electrolyte imbalance and syndrome of inappropriate secretion of ADH (SIADH) may significantly alter the course and prognosis of the disease resulting in death or serious neurological deficits(1). Hyponatremia and low serum osmolality with inappropriately high urine osmolality can serve as a useful guide to the presence of SIADH in these cases(2,3). Like serum, cerebrospinal fluid (CSF) is also likely to suffer from osmolal changes as a result of meningitis. However, CSF changes in ABM have received scant attention in children mainly due to lack of normal values of CSF osmolality for comparison. We have undertaken this study to determine the mean CSF osmolality in ABM in comparison with the controls and to find its correlation with serum osmolality and serum sodium levels in cases with and without SIADH.

Material and Methods

Children of either sex below the age of 12 years admitted in one of the general pediatric wards of Kalawati Saran Children's Hospital (Pediatrics Wing of Lady Hardinge Medical College, New Delhi) with the diagnosis of ABM were included in the study and results compared with age and nutritionally matched children (control group)

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in whom lumbar puncture was performed on suspicion of CNS pathology and were eventually found to have no neurological disease. Cases of ABM with dehydration, pulmonary disease and other conditions which could affect ADH release were excluded from the study. CSF samples were subjected to microscopic examination, Gram's staining and biochemical analysis including osmolality at the time of admission. Culture and latex agglutination tests of CSF were undertaken to identify the etiological agents. Osmolality of CSF, serum and urine was determined by freezing point depression(4), using Roebling's osmometer. The criteria of diagnosis of SIADH included serum sodium <135 mEqL, serum osmolality <270 mOsm/kg, urine osmolality greater than 2 times the serum osmolality and absence of clinical findings suggestive of hypovolemia or dehydration(5).

Results

This prospective study was conducted from June 1987 to April 1988 and included 60 children diagnosed to have ABM, from 1 month to 12 years of age (mean age 3.18 years) with 45 males (75%) and 15 females (25%). The results have been compared with 20 age (mean age 4.2 years) and nutritionally matched controls. Twenty five cases (41.7%) presented with convulsions and 32 cases (53.3%) had altered sensorium. Out of these, only 44 cases could be followed till the time of discharge. Twelve cases died by 3rd day and 4 more patients expired thereafter. *H. influenzae* was the commonest etiological organism in 14 cases (23.3%) followed by *N. meningitis* in 5 (8.3%), *S. pneumoniae* in 4 (6.7%), *Klebsiella* in 2(3.3%) and *E. coli* in 2 cases (3.3%). In 33 cases (55%), the etiological agent could not be identified but the clinical and CSF picture was suggestive of ABM.

CSF osmolality in patients with ABM was not significantly different from the control group ($p > 0.05$). However, there was a statistically significant difference in serum osmolality ($p < 0.05$) and serum sodium levels ($p < 0.001$) in the two groups (*Table I*). Comparison of CSF and serum osmolality suggested higher mean values of serum osmolality than the CSF but the difference was not statistically significant. CSF osmo-

TABLE I –*Mean Values of Serum Sodium and CSF, Serum and Urinary Osmolality*

Parameter	Cases (n=60)			Controls (n=20)			p value
	Range	Mean	SD	Range	Mean	SD	
Serum sodium (mEq/L)	107-146	130.5	8.15	135-143	137.4	1.9	<0.001
CSF osmolality (mOsm/kg)	268-310	282.5	12.3	278-306	288.2	7.89	>0.05
Serum osmolality (mOsm/kg)	260-316	283.2	13.84	280-316	293.0	11.4	<0.05
Urinary osmolality (mOsm/kg)	278-714	496.7	216.0	208-627	412.8	202.5	>0.1

lality was reduced in ABM due to *Streptococcus pneumoniae* (mean 269 ± 1.4 mOsm/kg) which was statistically significant ($p<0.05$). CSF osmolality was also lower in cases with convulsions (280 ± 13.7 mOsm/kg) and altered sensorium (287 ± 13.0 mOsm/kg) but the difference was not statistically significant.

SIADH was diagnosed in 22 cases (36.7%) on admission. The duration of illness in these cases varied from 7-10 days. As expected, the mean CSF osmolality in ABM with SIADH was significantly lower (*Table II*) as compared to those cases without SIADH ($p<0.05$) and controls ($p<0.05$). It was also observed that, whereas the mean CSF osmolality was lower as compared to serum osmolality in patients without SIADH and in the control group, it was greater than serum osmolality in cases with SIADH ($p<0.05$).

Twelve out of 16 cases (75%) who expired were diagnosed to have SIADH. CSF osmolality ranged from 261-280 mOsm/kg in these cases with fatal outcome and the mean values (271 ± 8.63 mOsm/kg) were significantly lower ($p<0.05$) than those who recovered fully (287 ± 8.3 mOsm/kg). However, within the group which survived, there was no significant difference between those who had recovered with sequelae(mean 284 ± 17.8 mOsm/kg) and those without sequelae (mean 287 ± 17.8 mOsm/kg).

Discussion

Examination of CSF in ABM has been the focus of many studies in view of its importance as protective envelope to the brain. However, CSF osmolality in ABM has not incited many workers and most of the studies have correlated it to serum osmolality(2). Lack of normal values have led us to believe that CSF osmolality may be similar to serum osmolality(6) or lower by about 9 mOsm/kg(7). Studies in younger age group are lacking even though Forfar(8) has given a range of 273-304 mOsm/kg for normal children. The present study suggests CSF osmolality of 1-5 mOsm/kg lower than the corresponding serum osmolality in the

TABLE II—*Comparison of Serum Sodium and CSF, Serum and Urinary Osmolality in Cases with and without SIADH*

Parameter	Cases without SIADH (n = 38)		Cases with SIADH (n = 22)		Controls (n = 20)	
	Mean	SD	Mean	SD	Mean	SD
Serum sodium (mEq/L)	135.47	3.36	121.9	6.73	137.4	1.9
CSF osmolality (mOsm/kg)	288.5	9.34	272	9.42	288.2	7.89
Serum osmolality (mOsm/kg)	290.84	11.1	264	5.12	293	11.4
Urinary osmolality (mOsm/kg)	427.1	218.0	593.3	131.9	412.8	202.5

control group who did not have any neurological disease. CSF osmolality in the control group ranging from 278-300 mOsm/kg may be taken as normal values for comparison, in the absence of these values in normal healthy children which could not be determined for ethical reasons.

Overall CSF osmolality in total patients of ABM was not significantly different when compared with controls even though serum osmolality and serum sodium levels were observed to be lower in these patients. Thus meningeal inflammation alone does not appear to alter CSF osmolality even if serum osmolality and serum sodium is lower than normal.

SIADH was detected in 36.7% of our cases on admission. Estimates of frequency of SIADH vary from 7-50%(5,9). The clincial significance of this biochemical aberration and its effect on osmolality is questioned(10). However, in its presence osmolality of CSF was significantly lower than those cases without SIADH and in controls. This observation suggests that hypo-osmolality of serum may eventually result in hypo-osmolality of CSF as well. However, the fall in CSF osmolality is not of the same degree as that of serum as shown by our observations that in patients of ABM with SIADH even though CSF osmolality is lower as compared to ABM without SIADH and controls, the mean values tend to be higher than serum osmolality. Similar observations have been made by other workers(11,12). The correlation of lower CSF osmolality with etiology of ABM, as was observed in cases with *S. pneumoniae* is not clearly explained but is postulated to be related to degree of meningeal inflammation(13), stress action and hypoxic insult which may differ with different organisms.

Comparison of CSF osmolality with the clinical outcome showed significantly lower values in cases who had a fatal outcome than those who recovered fully. In the patients who recovered there was no significant difference in CSF osmolality in the cases with or without sequelae. Besides the degree and duration of hyponatremia in ABM which correlates significantly with the complications(9), low CSF osmolality consequent to hypo-osmolality of serum due to SIADH probably reflects underlying cerebral edema and severe inflammatory changes which might contribute to high mortality.

REFERENCES

1. Feigin RD, Dodge PR. Bacterial meningitis–Newer concepts of pathophysiology and neurologic sequelae. Ped Clin N Am 1976, 23: 541-560.
2. Bartter FC, Schwartz WB. The syndrome of inappropriate secretion of antidiuretic hormone. Am J Med 1967, 42: 790-806.
3. Berry PL, Belsha CW. Hyponatremia–euvolemic hyponatremia. Ped Clin N Am 1990, 37: 356-359.
4. Jeul R. Serum osmolality –A CAP survey analysis. Am J Pathol 1977, 86 (Suppl): 165-169.
5. Kanakriyeh M, Carvajal HF, Vallone AM. Initial fluid therapy for children with meningitis with consideration of syndrome of inappropriate antidiuretic hormone. Clin Pediatr 1987, 26: 126-130.
6. Davson H, Welch K, Segal MB. Physiology and Pathophysiology of CSF. 1st edn. Edinburgh, Churchill Livingstone, 1987.
7. Guyton AC. Text Book of Medical Physiology, V edn. Philadelphia, WB Saunders Co, 1974, pp 782-785.
8. Forfar JO, Arneil GC. Text Book of Pediatrics. III edn, Vol II. Edinburgh, Churchill Livingstone, 1984, p 1986.
9. Kaplan SL, Feigin RD. The syndrome of inappropriate secretion of anti-duretic

hormone in children with bacterial meningitis. J Pediatr 1978, 92: 758-761.

10. Prince AS, Neu HC. Fluid management in *Hemophilus influenzae* meningitis. Infection 1980, 8: 5-7.
11. Holliday MA, Kalayci MN, Harrah J. Factors that limit brain volume changes in response to acute hyper and hyponatremia. J Clin Invest 1968, 47: 1916-1928.
12. Di Mattio J, Hochwald GM, Malhan C, Wald A. Effects of changes in serum osmolality on bulk flow of fluid into cerebral ventricles and on brain water content. Pfluegers Arch 1975, 359: 253-264.
13. Reynolds DW, Dweck HS, Cassady G. Inappropriate antidiuretic hormone secretion in a neonate with meningitis. Am J Dis Child 1972, 123: 251-253.

NOTES AND NEWS

THIRD ASIAN CONFERENCE OF SEXOLOGY

The Third Asian Conference of Sexology, with a study tour to the ancient temples of India depicting erotica, has been organized by the Department of Sexual Medicine, Seth G.S. Medical College and KEM Hospital, Bombay under the auspices of the Asian Federation for Sexology from *November 27 to December 01, 1994* at the Taj Palace Intercontinental, New Delhi, India.

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