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Study of Hyponatremia in Children with Acute Central Nervous System Diseases - An Observational Study

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Abstract:
Introduction: *Hyponatremia is a common electrolyte disturbance in acute central nervous system disease and its potential for neurological sequelae make its diagnosis mandatory before any therapeutic intervention.Due to lack of consensus on this subject, fluid management and management of hyponatremia in CNS infections is still not well defined.The present study was hence taken up to outline the probable incidence, etiology and prognostic value of hyponatremia with acute CNS disorders in children.*
Materials And Methods: *This is a cross-sectional hospital based study. The study population included 86 children between 4months to 14 years of age admitted to pediatric emergency services, Institute of child health Niloufer hospital from December2009 to may2010. Detailed history, thorough physical examination, Vital signs including blood pressure, Features of dehydration, presence of oedema and complete neurological examination were done in children with acute CNS disease. Investigations were done as per the unit protocol which included venous blood samples for serum sodium and potassium by an automated machine using the principle of potentiometry (Ion-selective electrode method), If hyponatremia (<130meq/l) was detected in the child then further investigations were done to identify the cause. Details collected were recorded in a pre-typed proforma and then analysed.All quantitative data were expressed as mean ± SD. Chi-square test was used to test the significance of difference in morbidity and mortality in patients with normal and abnormal electrolytes. The analysis was done using SPSS 15.0 Version (Statistical package for Social Sciences).*
Results: *Of the 21 patients with hyponatremia, 13 (61.9%) were clinically euvolemic and 8 (38.1%) were hypovolemic. All the13 euvolemic patients had SIADH. All the 8 hypovolemic cases had CSW which was confirmed both clinically and lab wise including elevated hematocrit.*
Conclusions: *From this study, we conclude that hyponatremia is not uncommon in patients with acute CNS diseases. The diagnosis of SIADH and CSW is very important and essential as hyponatremia occurs in both conditions but management differs. In SIADH we need to restrict the fluids where as in CSW we need to correct the dehydration.*
Key Words*: Acute central nervous system diseases, cerebral salt wasting (CSW), Hyponatremia, Syndrome of inappropriate secretion of ADH (SIADH).*

I. Introduction

Infections are among the commonest cause of acute neurological disorders in children and with effective antimicrobial agents available for many of the CNS infections other factors that significantly influence the mortality and morbidity of this condition have assumed greater importance. One such factor that has been long debated about is hyponatremia, which can result in morbidity and mortality irrespective of the primary problem in children.

Timely recognition, a high index of suspicion and a thorough understanding of common electrolyte abnormalities and their etiology is necessary to ensure their timely correction. Hyponatremia occurs in 20-45% of children with Meningitis, Encephalitis and Guillian Barre syndrome.

CSW has been documented as a cause of hyponatremia in individuals with head trauma, CNS surgery, infection and tumors. But reports of CSW in children have been less common and hence this syndrome has not been well recognized in pediatric age group.

There are many CNS diseases which can present with electrolyte abnormalities. Out of them the commonly encountered conditions are CNS infections like Pyomeningitis, Tuberculous meningitis. Viral meningoencephalitis, Guillain-Barre syndrome, Transverse Myelitis, Brain tumors, Traumatic brain injury, Sub-arachnoid hemorrhage and Hypoxic ischemia.

II. Aims and Objectives

To study the incidence of hyponatremia in children with acute CNS diseases and to identify the cause of hyponatremia in these children.

III. Materials and Methods

This is a cross sectional hospital based study conducted at Institute of Child Health, Niloufer Hospital, Hyderabad. The study population included 86 children age group ranging from 4 months to 14yrs, who were admitted to Paediatric Emergency Services from December 2009 to May 2010. Detailed history, thorough physical examination. Vital signs including blood pressure, signs of dehydration, presence of oedema were noted.

Complete neurological examination of the children included in the study was done.Investigations were done as per the unit protocol which also included venous blood samples for serum sodium and potassium by an automated machine using the principle of potentiometry (Ion-selective electrode method), serum creatinine by Jaffe's method, Plasma osmolality by calculated method, blood glucose by hexokinase method, blood urea by DAM (Diacetyl mono-oxime method). If hyponatremia (<130meq/l) was detected in the child then further investigations were done to identify the cause which included urine sodium and osmolality, urine specific gravity, hematocrit. Other investigations like CSF analysis, CT brain, etc were done where ever feasible.

Estimation of serum sodium by flame emission spectrophotometry gives sodium concentration in mEq/l of plasma, not in mEq/l of plasma water, the stated sodium concentration will be low. Direct reading potentiometry (ion selective electrode), measures sodium activity in plasma water, is not affected by the proportion of serum occupied by lipids and proteins and thus limits the error. Age, sex and provisional diagnosis were recorded in all cases. Causes of hyponatremia include SIADH and CSW.The cause of hyponatremia was identified based on following criteria:

SIADH

- Hypotonic hyponatremia(<130meq/l)
- Euvolemic state
- Urine sodium> 20meq/l
- Urine output decreased or normal
- High urine Osmolality > 100meq/l
- Hematocrit -decreased

CSW

- Hypotonic hyponatremia(<130meq/l)
- Features of hypovolemia (Features of dehydration, and/or blood pressure below 50th percentile for the age and height)
- Urine sodium > 20meq/l
- Urine output increased
- Urine Osmolality – low or normal
- Hematocrit - increased

Inclusion Criteria:

All conditions with acute central nervous system disease excluding conditions in exclusion criteria were included.

Exclusion Criteria:

1. Neonates
2. Children beyond 14 yrs
3. Trauma
4. Gastroenteritis
5. Febrile seizures
6. Pneumonia
7. Children on drugs known to cause hyponatremia
8. Children with cardiac, renal and liver disorders

Details collected were recorded in a pre-typed proforma and then analysed. All quantitative data were expressed as mean ± SD. Chi-square test was used to test the significance of difference in morbidity and mortality in patients with normal and abnormal electrolytes. The analysis was done using SPSS 15.0 Version (Statistical package for Social Sciences).

IV. Results

Total number of patients included in this study was 86. Youngest patient was 4 months and the oldest patient was 14 years. Amongst the children studied 53 were males and 33 were females. But the difference between males and females is not statistically significant.

Table 1: Gender distribution and diagnosis of children included in the study

Diagnosis	Males	Females	Total
Pyomeningitis	11	6	17
TBM	8	11	19
VME	24	8	32
Others	10	8	18
Total	53	33	86

Hyponatremia was detected in 21 of the 86 paediatric patients (24.4%) with acute CNS diseases studied.

Table 2: Final diagnosis and incidence of hyponatremia

Disease	No. Of patients with hyponatremia	Percentage
Pyomeningitis	5	23.8%
TBM	10	47.6%
VME	3	14.3%
Others	3	14.3%

It was found that tuberculous meningitis had higher incidence of hyponatremia which is statistically significant ($p = 0.001$). Even dehydration was strongly correlated with hyponatremia in our study ($p < 0.001$). There was a significant correlation between hyponatremia and the female sex. ($p = 0.042$) However there was no correlation between age, clinical symptoms and incidence of hyponatremia. There was a statistically significant decrease in the mean serum osmolality in hyponatremic patients as compared to non-hyponatremic patients. ($p < 0.001$) Among the hyponatremic cases distribution of cerebral salt wasting syndrome and SIADH are as follows.

Table 3: Causes Of Hyponatremia:

Disease	CSW	SIADH	Total
Pyomeningitis	2	3	5
TBM	4	6	10
VME	1	2	3
Others	1	2	3
Total	8	13	21

Of the 21 patients with hyponatremia, 13 (61.9%) were clinically euvolemic and 8 (38.1%) were hypovolemic All the13 euvolemic patients had SIADH. Of those with SIADH, 6 had tuberculous meningitis, 3 had pyomeningitis, 2 had viral meningoencephalitis and one each had transverse myelitis and status epilepticus.

All the 8 hypovolemic cases had CSW which was confirmed both clinically and lab wise including elevated hematocrit. Out of them 4 had tuberculous meningitis, 2 had pyomeningitis and one each had viral meningoencephalitis and Guillain-Barre syndrome.

V. Discussion

Among the 86 patients included during the study period, hyponatremia was detected in 21 patients (24.4%) with acute central nervous system disease. This percentage is comparable to Singhi S et al study which recorded hyponatremia in 29.8% of sick children.[2] In comparison with other studies, Bussmann et al [3] reported hyponatremia in 2 out of 23 (8.7%) patients with acute bacterial meningitis, partially treated meningitis and tuberculous meningitis, while Von-vigier et al described hyponatremia in 97 out of 300 (32.3%) patients with CNS infection. [4] The difference in percentage of hyponatremia among different studies may be related to the difference in both numbers of patients and diagnostic criteria. Mean age of the present study is similar to Singhi S et al, SubbaRao et al, Shan F et al, and Menon et al studies.[2, 5, 6, 7] Unlike many other studies only 15.11% of our patients were <1 year. This is probably because we have excluded neonates from our study.

Hyponatremia was detected in 21 of the 86 paediatric patients (24.4%) with acute CNS diseases studied.This is similar to Singhi S et al, VonVigier et al, SubbaRao et al, ShannF et al, PatwariAK et al, SinghBS et al, and Kanakriyeh M et al studies on acute CNS infections[2,4, 5, 6, 8, 9, 10,] where the incidence has

been quoted between 20-50% as most of the cases included in our study are also CNS infections. There was a strong correlation between hyponatremia and female sex. However there was no specific correlation between presence of hyponatremia and age. The symptoms and signs present also had no specific correlation with presence or absence of hyponatremia.The highest percentage of hyponatremia was found Tuberculous meningitis patients which was statistically significant (P=0.001). However due to small group of patients studied further studies are required before a definitive conclusion be draw. As shown in the table 3 CSW was as common as SIADH. SIADH was common in tuberculous meningitis.

Measurement of ADH levels either in serum or in urine is not useful in diagnosis of SIADH. This could be the cause for more frequent diagnosis of SIADH in MenonRK et al, KaplanSC, and FajardoJE studies. **(7, 11, 12)** Some studies did not consider the entity of CSW. Hence often all cases of hyponatremia in those studies were reported as SIADH. **(6)**

Our report of equal incidence of SIADH and CSW is similar to that of Bussmann et al. **(3)** Moreover this study was retrospective and included even all CNS disorders. Hence probably the incidence of SIADH and CSW were low in this study. Due to small sample size, analysis of each cause of hyponatremia in each of the clinical syndromes could not be done.

VI. Summary and Conclusions

1. SIADH and CSW. Monitoring of urine output in infants was difficult. Hyponatremia occurred in 24.4% of patients and is more common in tuberculous meningitis.
2. SIADH and CSW were found to cause hyponatremia in almost equal number of cases.
3. SIADH is more common in tuberculous meningitis.
4. Differentiation of SIADH and CSW is very important *as* in SIADH we need to restrict the fluids where as in CSW we need to correct the dehydration.

From this study, we conclude that hyponatremia is not uncommon in patients with acute CNS diseases. Total number of patients included in the study was only 86. A larger group of children need to be studied to validate the above results. Only children with CNS infection having hyponatremia were screened for SIADH and CSW..

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