Description Of Sodium Serum Levels Based On Severity Of Disease In Pediatric Meningitis Patients

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Abstract

Background

Children are more susceptible to infection. Meningitis is an inflammatory reaction of the meninges which is characterized by an increased leukocytes in the cerebrospinal fluid. The incidence of childhood meningitis is still high and mostly caused by bacteria with high case mortality and neurological sequelae. In tuberculosis (TB) endemic countries, the most common cause of meningitis is tuberculosis. The central nervous system plays a role in sodium and water regulation so in meningitis there are disruption of sodium homeostasis with the most is hyponatremia which associated with systemic complications, disease severity and death.

Material and Methods

The study was descriptive, retrospective from medical records of inpatients diagnosed with meningitis (ICD-10), children aged < 18 years and serum sodium results for the period 2019. Patients with a history of renal impairment and forced discharge were excluded.

Results

TB meningitis is the most common cause of meningitis in children. 68.8% of meningitis patients have hyponatremia with the most is mild hyponatremia (36%). In TB meningitis, the severity of the disease is not directly related to the degree of sodium disorder, while in non-TB meningitis it is related to the severity of the disease.

Discussions

Hyponatremia is associated with severity in non-TB meningitis. In normonatremia, sodium evaluation is still performed because hyponatremia can occur during treatment.

Conclusions and Recommendations

Meningitis is associated with hyponatremia and is associated with disease severity in non-TB meningitis. Sodium evaluation is necessary in tuberculous meningitis because hyponatremia can occur during the treatment.

Keywords: hyponatremia ; meningitis ; sodium

1. Introduction

Meningitis is an inflammatory reaction in the meningen lining the brain and spinal cord, which characterized by an increased number of leukocytes in the cerebrospinal fluid. Meningitis can be caused by bacterial, viral, or fungal infections or by head trauma that causes meningen tears. [1,2]

The World Health Organization (WHO) and Maternal and Child Epidemiology Estimation (MCEE) stated that in 2015 there were 142,841 cases of meningitis in children under 5 years old with a mortality rate of 21.28 per 100,000 children. Case fatality rate of meningitis reached 30% with neurologic sequelae between 30-70%. In tuberculosis endemic countries, M. tuberculosis is the leading cause of childhood meningitis compared to non-TB bacteria or viruses. In Indonesia, meningitis ranks 9th out of 10 most common diseases in pediatric with a mortality rate between 18-40% and neurologic sequelae between 30-50%. [3-8]

Hyponatremia is a serum sodium level <135 mmol/L, often occurring in patients with meningitis due to major role of the central nervous system's (CNS) in the regulation of sodium and water homeostasis, although its frequency and clinical course are not well known. Hyponatremia may reflect the severity of the disease, with the most severe leading to death. [9-12]

Hyponatremia in pediatric meningitis is caused by several mechanisms. First, syndrome of inappropriate antidiuretic hormone secretion (SIADH) with hypersecretion of antidiuretic hormone (ADH). Second, cerebral salt wasting syndrome with hypersecretion of natriuretic especially brain natriuretic peptide (BNP). [13-16]

Hyponatremia is categorized as severe hyponatremia when serum sodium levels are less than 125 mmol/L, moderate hyponatremia when serum sodium levels are 125-129 mmol/L and mild hyponatremia when serum sodium levels are 130-134 mmol/L. [13-16]

Hypernatremia is a serum sodium level of more than 145 mmol/L, may be associated with brain damage but is rare in meningitis. [17]

Hyponatremia in pediatric meningitis can reflect the severity of the disease where the more severe the degree of hyponatremia, the higher the systemic complications (shock, multiple organ dysfunction syndrome, and acute respiratory failure requiring ventilators). Therefore, monitoring sodium levels is hopefully able to assess the severity of the disease so that it can assist patient management and prevent systemic complications due to hyponatremia in pediatric meningitis. The results of this study are intended to provide additional information and guidance in the management of pediatric meningitis at Dr. Hasan Sadikin General Hospital, Bandung.

2. Materials and methods

The study was conducted at the Clinical Pathology Laboratory of Dr. Hasan Sadikin General Hospital with the population study was all patient data with a diagnosis of meningitis based on ICD-10 who were treated at Dr. Hasan Sadikin General Hospital in the period January to December 2019. The research was descriptive in approach with retrospective data collection. The inclusion criteria of subjects were (1) Pediatric patients aged < 18 years; (2) Performed an examination of serum sodium levels in the first 24 hours of admission to the hospital. While the exclusion criteria were (1) Pediatric patients with pre-existing kidney

disorders (based on pediatric Risk, Injury, Failure, Loss, and End Stage Renal Disease (pRIFLE) criteria with serum creatinine levels >1.05 mg/dL); (2) Pediatric patients who were discharged involuntarily.

Data searches were performed through medical record data tracking using ICD-10 codes (G00 - G04.9) for searching the characteristics of research subjects and laboratory information data, for the results of sodium and creatinine levels. The research variables measured in this study included (1) characteristics of the research subjects (age, gender, treatment room, length of hospitalization, nutritional status, presence or absence of convulsion, presence or absence of fever, etiology of meningitis). The categorization of the characteristics of the study subjects followed the categorization of hospital data; (2) serum sodium levels which are divided into categories of mild, moderate and severe hyponatremia; normonatremia and hypernatremia; (3) clinical outcomes that represent the severity of the disease which are divided into survive and death.

The results were presented in tables and graphs, with categorization into: (1) characteristics of study subjects, and (2) serum sodium levels in relation to clinical outcomes in etiological groups (TB and non-TB).

3. Results

During the period of data collection (January 1 - December 31, 2019), 197 children were diagnosed with meningitis based on ICD-10, and 125 children (63.5%) were included in the study population. The baseline characteristics of the research subjects are shown in Table 1 as follows.

Table 1. Baseline Characteristic Of Research Subject

Variable	Survive N=77		Death N=48		Total Subject N=125	
	N	%	N	%	N	%
Sex						
• Male	38	49.4	29	60.4	67	53.6
• Female	39	50.6	19	39.6	58	46.4
Age (years)						
• 0 – < 2	27	35.1	16	33.3	43	34.4
• 2 – 5	12	15.6	4	8.3	16	12.8
• 6 –10	12	15.6	9	18.8	21	16.8
• > 10 –18	26	33.7	19	39.6	45	36.0
Length of Hospitalization						
• ≤ 2 weeks	53	68.8	44	91.7	97	77.6
• > 2 weeks	24	31.2	4	8.3	28	22.4
Convulsion						
• Yes	40	51.9	26	54.2	66	52.8
• No	37	48.1	22	45.8	59	47.2
Fever						
• Yes	35	45.5	25	52.1	60	48.0
• No	42	54.5	23	47.9	65	52.0
Ward type						
• Intensive	5	6.5	10	20.8	15	12.0
• Non intensive	72	93.5	38	79.2	110	88.0
Nutritional Status						
• Normal	39	50.6	21	43.8	60	48.0
• Underweight	38	49.4	27	56.2	65	52.0
Etiology Meningitis						

• Tuberculosis	54	70.1	28	58.3	82	65.6
• Non TB	23	29.9	20	41.7	43	34.4
Hyponatremia						
• Mild	32	41.6	13	27.1	45	36.0
• Moderate	6	7.7	12	25.0	18	14.4
• Severe	11	14.3	12	25.0	23	18.4
Normonatremia	27	35.1	11	22.9	38	30.4
Hypernatremia	1	1.3	0	0.0	1	0.8

A total of 36% of pediatric patients with meningitis in this study had an age range of >10-18 years and the mortality rate in pediatric meningitis reached 38.4% of patients. Tuberculous meningitis was the most common etiology of meningitis in this study. Sodium disorders occur in meningitis where the most common in pediatric patients with meningitis is hyponatremia and the clinical outcome of mortality in mild, moderate and severe hyponatremia ranges from 25.0-27.1%. (Table 1).

Table 2. Overview Of Sodium Levels And Outcome In Meningitis Etiology Group

Sodium Level	Outcome				Total n=125		
	Survive n=77		Death n=48				
	TB n(%)	Non TB n(%)	TB n(%)	Non TB n(%)	TB n(%)	Non TB n(%)	Total n(%)
Hyponatremia							
• Mild	19 (24.7)	13 (16.8)	9 (18.8)	4 (8.3)	28 (22.4)	17 (13.6)	45 (36.0)
• Moderate	5 (6.5)	1 (1.3)	7 (14.6)	5 (10.4)	12 (9.6)	6 (4.8)	18 (14.4)
• Severe	8 (10.4)	3 (3.9)	5 (10.4)	7 (14.6)	13 (10.4)	10 (8.0)	23 (18.4)
Normonatremia	21 (27.3)	6 (7.8)	7 (14.6)	4 (8.3)	28 (22.4)	10 (8.0)	38 (30.4)
Hypernatremia	1 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	1 (0.8)

Note : TB : tuberculosis; Non TB : Non tuberculosis

This study shows that in meningitis, the mortality of mild, moderate and severe hyponatremia is 8.3-18.8%, and the most prevalent in meningitis with mild hyponatremia (TB 18.8%; non-TB 8.3%) In normonatremia, the mortalities were also found to be 8.3% and 14.6% in the TB and non-TB groups. Among TB meningitis, mortality was more prevalent in mild hyponatremia with a mortality rate in each sodium disturbance category of 10.4-18.8%. In non-TB meningitis, mortality was more prevalent in severe hyponatremia with a mortality rate in each sodium disturbance category of 8.3-10.4%. (Table 2)

The severity of the disease was not directly proportional to the degree of sodium disturbance in TB meningitis, whereas in mild and moderate hyponatremia, and even in normal sodium levels, there was higher mortality than in severe hyponatremia at 14.6-18.8%, while in non-TB meningitis the degree of severity of the disease was directly proportional to the degree of sodium disturbance. The mortality in severe hyponatremia is higher than in moderate and mild hyponatremia, which is 14.6%; 10.4% and 8.3% but in normal sodium levels also found as many as 8.3% mortality.

4. Discussions

In the pediatric meningitis, most patients had hyponatremia (65.6%) with the majority of pediatric meningitis having mild hyponatremia (36.0%). Hyponatremia is not linearly related to severity and mortality in TB meningitis where mortality is found to be highest in mild hyponatremia (32.1%). Truong et al. found no significant effect of serum sodium levels on mortality in TB meningitis but it was associated with length of stay, focal neurologic deficits, and the requirement for ventilator. [15,18]

In this study, mortality in pediatric patients with non-TB bacterial meningitis was directly related to the severity of hyponatremia with the highest mortality in severe hyponatremia (35%). Feixia Zheng et al stated that the severity of hyponatremia is related to the clinical severity of non-TB bacterial meningitis in relation to systemic complications (shock, multiple organ dysfunction syndrome, acute respiratory failure, ventilator requirements, and the most serious clinical outcome, death). [12,17]

In pediatric meningitis patients with normonatremia, the monitoring of sodium levels is required because hyponatremia can develop later during treatment and it was found that 8.3-14.6% of pediatric meningitis patients with normonatremia had a fatal outcome as shown in Zhang et al's study that hyponatremia can occur during treatment and is related to mortality in neurological critical illness. [18]

Evaluation of serum sodium levels is relatively rapid, widely available, relatively low cost and can provide useful information in the diagnosis of meningitis and assess disease prognosis in pediatric patients with non-TB bacterial meningitis and may help to reduce systemic and CNS complications, focal neurologic deficits, and the the need for mechanical ventilation in TB meningitis.

There were several limitations in this study. First, researchers were unable to examine issues that affect the results of sodium levels, such as comorbidities and treatment given by clinicians, because of the COVID-19 pandemic when searching for medical record data.

Second, the possibility of selection bias in the population where data obtained in this research was obtained from medical record data categorized as meningitis as the primary diagnosis, making it possible that the meningitis population categorized as secondary diagnosis was not included in process of tracing medical record data.

5. Conclusion

The most prevalent feature of serum sodium levels in pediatric meningitis is hyponatremia, which accounts in 65.6% of pediatric meningitis. The severity of the disease is not directly correlated with the severity of hyponatremia in children with TB meningitis, while in bacterial meningitis, the severity of the disease and mortality in meningitis were directly correlated with hyponatremia. Even in normonatremia, monitoring should still be performed as hyponatremia may occur during the treatments.

As suggestion, serum sodium levels can be used as a guide to assess the clinical severity of disease and mortality outcome in non-TB bacterial meningitis so that it is hopefully can help the management of pediatric meningitis cases, especially in evaluating prognosis, especially in pediatric patients with non-TB bacterial meningitis as well as meningitis in general.

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