ELECTROLYTE DISTURBANCES AND ABNORMAL URINE ANALYSIS IN CHILDREN WITH DENGUE INFECTION

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Abstract. Serum electrolytes and urine analysis results were retrospectively reviewed in children with either dengue fever (DF) or dengue hemorrhagic fever (DHF). Children who had positive serology for dengue infection and serum electrolytes determined before starting intravenous fluid were included in the study. During the years 2004-2007, 73 DF patients, age 9.29 ± 3.62 years, and 77 DHF patients, age 10.04 ± 3.64 years were enrolled in the study. The patients were admitted to the hospital on average on days 4.12 ± 1.1 and 4.25 ± 1.4 of febrile illness for DF and DHF, respectively. The prevalence of hyponatremia in patients with DF was 61% and DHF was 72% (p = 0.149). The mean serum sodium levels in patients with DF and DHF were 133.5 ± 3.52 and 133.5 ± 3.20 mEq/l (p = 0.938), respectively. The prevalence of hyponatremia in patients with mild (grade I), moderate (grade II) and severe (grade III-IV) DHF were 70, 77, and 78% (p = 0.729), respectively, and the mean serum sodium levels were 134.1 ± 3.05, 132.9 ± 3.33, and 132.5 + 3.28 (p = 0.189), respectively. The prevalence of hypokalemia in patients with DF was 14% and 17% in patients with DHF (p = 0.588). A high urine specific gravity reflecting dehydration was found in 63% of patients with DF and 60% of patients with DHF (p = 0.77). The prevalences of hematuria in patients with DF and DHF were 18% and 27% (p = 0.182), respectively and proteinuria were 15% and 27% (p = 0.072), respectively. The prevalences of hematuria and proteinuria were not different among patients with mild, moderate and severe DHF. No patients had gross hematuria or developed acute renal failure requiring dialysis. Mild hyponatremia is a common electrolyte disturbance and renal involvement is mild in patients with DF and DHF.

Key words: dengue fever, dengue hemorrhagic fever, electrolyte disturbance, urine analysis

INTRODUCTION

Dengue infection is one of the most common mosquito-borne infections caused by Flaviridae. Dengue hemorrhagic fever (DHF) is more serious than dengue fever (DF) due to capillary leakage. Dengue infection was initially described only in tropical areas, however over the past few decades has been found in many parts of the world. The World Health Organization has reported 2.5 billion people live in areas where dengue viruses can be transmitted (WHO, 2009).

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Electrolyte disturbances and renal dysfunction have been reported in dengue infection. Hyponatremia is common in DHF, especially in shock patients (Varavithya *et al*, 1973). Glomerular immune complex deposit is suspected as the pathogenesis of glomerulonephritis in DHF (Boonpucknavig *et al*, 1976). To date, there have been few studies comparing electrolyte disturbances and renal dysfunction between patients with DF and DHF (Futrakul *et al*, 1973; Samosorn, 1994). In the present study, we retrospectively compared the serum electrolyte and urine analysis results in children with DF and DHF.

MATERIALS AND METHODS

A retrospective review of the medical records of patients with dengue infection during the years 2004-2007 at the Department of Pediatrics, Phramongkutklao Hospital, Bangkok, Thailand was carried out. The study was approved by the institutional review board of Phramongkutklao Hospital. Patients with DF and DHF were graded using World Health Organization criteria (WHO, 1997). The diagnosis was confirmed by detection of dengue antibodies at the Armed Forces Research Institute of Medical Sciences (AFRIMS), Bangkok, Thailand. The inclusion criteria included all hospitalized children age 0-18 years who were diagnosed with DF or DHF in whom the results of serum electrolytes on admission before starting intravenous fluid were available. Children with a history of kidney disease were excluded from the study. DHF patients were classified into 3 groups: grade I as mild DHF, grade II as moderate DHF, and grades III-IV as severe DHF. Hyponatremia, hypokalemia and metabolic acidosis were defined as a serum sodium <135 mEq/l, a serum potassium less than 3.5 mEq/l and a serum bicarbonate less than 18 mEq/l, respectively. A urine specific gravity >1.020 without glucosuria was defined as dehydration. The presence of >5 red blood cells per high power field of centrifuged urine was defined as hematuria, and the presence of ≥2+ protein on a urine strip test in urine specimens with a specific gravity >1.015 was defined as proteinuria. Ketonuria was defined as the presence of ketones on a urine strip test.

The chi-square test was used to compare the prevalence of electrolyte disturbances, dehydration, hematuria and proteinuria between patients with DF and DHF. Comparison of mean parameters between patients with DF and DHF was carried out using an independent *t*-test. ANOVA analysis was done to compare mean parameters between patients with DF and DHF. A p-value <0.05 was considered statistically significant.

RESULTS

During 2004-2007, there were 73 DF patients with an average age of 9.29 ± 3.62 years and 77 DHF patients with an average age of 10.04 ± 3.64 years who were included in this study. Forty-two, 26, and 9 patients had mild, moderate, and severe DHF, respectively. On average, DF and DHF patients were admitted to the hospital on days 4.12 ± 1.1 and 4.25 ± 1.4 of febrile illness, respectively. Urinalysis was performed in 67/73 of DF patients and 73/77 of DHF patients. The mean serum electrolytes results, prevalences of electrolyte disturbances, hematuria, proteinuria and ketonuria in patients with DF and DHF are shown in Table1. Comparison of various parameters among patients with mild, moderate and severe DHF is shown in Table 2. Gross hematuria was not found

Table 1
Serum electrolytes and urinalysis in DF and DHF patients.

	DF	DHF	*p*-value
Serum electrolyte (mEq/l)			
Sodium	133.5 ± 3.52	133.5 ± 3.20	0.938
Potassium	3.89 ± 0.42	3.93 ± 0.52	0.565
Chloride	100.6 ± 3.94	99.8 ± 3.81	0.214
Bicarbonate	21.4 ± 2.71	21.4 ± 2.43	0.983
Prevalence of hyponatremia	61% (44/73)	72% (55/77)	0.149
Serum Na 130- <135 mEq/l	44% (32/73)	56% (43/77)	0.103
Serum Na 125-129 mEq/l	14% (10/73)	16% (12/77)	0.744
Serum Na 120-124 mEq/l	3% (2/73)	0% (0/77)	0.072
Prevalence of hypokalemia	14% (10/73)	17% (13/77)	0.588
Serum K 3.0-<3.5 mEq/l	14% (10/73)	14% (11/77)	0.918
Serum K 2.5-2.9 mEq/l	0% (0/73)	3% (2/77)	0.166
Serum K <2.5 mEq/l	0% (0/73)	0% (0/73)	-
Prevalence of metabolic acidosis	11% (8/73)	7% (5/77)	0.260
Urinalysis			
% Urine sp gr ≥ 1.020	63% (42/67)	60% (44/73)	0.770
% Hematuria	18% (12/67)	27% (20/73)	0.182
% Proteinuria	15% (10/67)	27% (20/73)	0.072
% Ketonuria	48% (32/67)	47% (34/73)	0.888

Table 2
Serum electrolytes and urinalysis results in each group of DHF patients.

	Mild	Moderate	Severe	*p*-value
Serum electrolyte (mEq/l)				
Sodium	134.1 ± 3.05	132.9 ± 3.33	132.5 ± 3.28	0.189
Potassium	3.90 ± 0.57	3.89 ± 0.41	4.22 ± 0.45	0.201
Chloride	100.2 ± 3.6	99.3 ± 3.90	99.7 ± 4.66	0.628
Bicarbonate	21.5 ± 2.2	21.4 ± 2.9	21.03 ± 1.81	0.880
Prevalence of hyponatremia	70% (29/42)	77% (20/26)	78% (7/9)	0.729
Serum Na 130- <135 mEq/l	60% (25/42)	54% (14/26)	56% (5/9)	0.837
Serum Na 125-129 mEq/l	10% (4/42)	23% (6/26)	22% (2/9)	0.295
Serum Na 120-124 mEq/l	0% (0/42)	0% (0/26)	0% (0/9)	-
Prevalence of hypokalemia	22% (9/42)	15% (4/26)	0% (0/9)	0.288
Serum K 3.0-<3.5 mEq/l	17% (7/42)	15% (4/26)	0% (0/9)	0.414
Serum K 2.5-2.9 mEq/l	5% (2/42)	0% (0/26)	0% (0/9)	0.416
Serum K 2.0-2.4 mEq/l	0% (0/42)	0% (0/26)	0% (0/9)	-
Prevalence of metabolic acidosis	10% (4/42)	4% (1/26)	0% (0/9)	0.444
Urinalysis				
% Urine sp gr ≥ 1.020	60% (24/40)	67% (16/24)	44% (4/9)	0.218
% Hematuria	28% (11/40)	33% (8/24)	11% (1/9)	0.444
% Proteinuria	30% (12/40)	25% (6/24)	22% (2/9)	0.849
% Ketonuria	43% (17/40)	54% (13/24)	44% (4/9)	0.657

in this study. All patients in both groups survived and none developed acute renal failure requiring dialysis.

DISCUSSION

Hyponatremia was the most common electrolyte disturbance seen in both patients with DF and DHF; mild hyponatremia, with a serum sodium 130-134 mEq/l, was seen in most hyponatremic patients. Serum sodium levels and the prevalence of hyponatremia in each group of patients with DHF were not significantly different from other studies (Varavithya *et al*, 1973; Mekmullica *et al*, 2005). A urine sodium less than 20 mEq/l was found in dengue infection, especially in shock patients, and may be a consequence of the depletion of intracellular volume and decreased renal excretion (Mekmullica *et al*, 2005). Most patients in our study were dehydrated, had starvation, a high urine specific gravity and the presence of ketonuria. The etiology of hyponatremia may be due to a decrease in salt intake, an increase in tubular reabsorption and an increase antidiuretic hormone secretion secondary to stress, fever or dehydration rather than impaired renal tubular function.

Mild hypokalemia, with a serum potassium between 3.0-3.5 mEq/l, and metabolic acidosis were present in some patients with DF and DHF. The causes of hypokalemia in this condition may be due to poor intake and an increase in renal excretion due to activation of renin, angiotensin and aldosterone system secondary to volume depletion. The etiology of metabolic acidosis may be starvation, ketoacidosis, lactic acidosis or compensation for respiratory alkalosis. A previous study showed metabolic acidosis and respiratory alkalosis were common in patients with DHF, especially in severe cases (Varavithya *et al*, 1973).

Hematuria and proteinuria was observed in our DF and DHF patients, similar to another study (Futrakul *et al*, 1973). Glomerular injury secondary to immune complex deposition from dengue antigens is recognized as the etiology of renal injury. Mild mesangial proliferation, deposition of IgG, IgM, and C3 and thickening of the glomerular basement membrane with dense spherical particle deposition were demonstrated in DHF patients (Boonpucknavig *et al*, 1976). Since the size of the immune complex is smaller than the glomerular diameter, the immune complex is mostly lost in the urine or cleared by the reticuloendothelial system (Wiwanitkit, 2005). The renal manifestations of DHF are usually mild. Severe renal injury, such as acute renal failure, has been reported with DHF; however, a lot of predisposing factors, such as shock, hemolysis and rhabdomyolysis, are common etiologies of renal failure in addition to immune complex deposition (Tanphaichitr *et al*, 2002; Davis and Bourke, 2004).

In conclusion, mild hyponatremia is a common electrolyte disturbance and renal involvement is mild in patients with DF and DHF. Careful monitoring electrolytes, acid-base status, and renal function are necessary. Future studies should include more severe cases, evaluate other electrolyte abnormalities, such as calcium, magnesium and phosphorus, assess renal tubular function and evaluate the quantity of proteinuria to assess renal function and the etiology of the electrolyte disturbance.

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