Original Article

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A study on Relation Between Disease and Hyponatremia in Hospitalized Children

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Abstract

Introduction: Diarrhea due to gastroenteritis is the most common cause of hypovolemic hyponatremia in children. Emesis causes hyponatremia if the patient takes in hypotonic fluid, either intravenously or enterally, despite the emesis. Most patients with emesis have either a normal sodium concentration or hypernatremia *Methodology:* All children (3 months to 12 years) who were admitted to pediatric ward, who required intravenous maintenance fluid therapy for at least 12 hours, with serum Na in between 135 and 150 meq per litre were included in the study *Results:* 25% of hyponatremic patients were in respiratory diseases group, so this is group at risk of developing hospital acquired hyponatremia. *Conclusion:* Duration of stay was increased (>5 days) in hyponatremic patients (p value 0.005), more so in hyponatremic group B patients (53% p value 0.001).

Keywords: Disease; Hyponatremia; Hospitalised Children.

Introduction

Classification of hyponatremia is based on the patient's volume status. In hypovolemic hyponatremia, the child has lost sodium from the body. The water balance may be positive or negative, but sodium loss has been higher than water loss. The pathogenesis of the hyponatremia is usually a combination of sodium loss and water retention to compensate for the volume depletion. The patient has a pathologic increase in fluid loss, and this fluid contains sodium. Most fluid that is lost has a lower sodium concentration than that of plasma. Viral diarrhea fluid has, on average, a sodium concentration of 50 m Eq/L. Replacing diarrheal fluid, which has a sodium concentration of 50 m Eq/L, with formula, which has only approximately 10 mEq/L of sodium, reduces the sodium concentration. Intravascular volume depletion interferes with renal water excretion, the body's usual mechanism for preventing hyponatremia. The volume depletion stimulates ADH synthesis, resulting in renal water retention in the collecting duct. Volume depletion also decreases the GFR and enhances water resorption in the proximal tubule, which reduces water delivery to the collecting duct [1].

Diarrhea due to gastroenteritis is the most common cause of hypovolemic hyponatremia in children. Emesis causes hyponatremia if the patient takes in hypotonic fluid, either intravenously or enterally, despite the emesis. Most patients with emesis have either a normal sodium concentration or hypernatremia. Burns may cause massive losses of isotonic fluid and resultant volume depletion. Hyponatremia develops if the patient receives hypotonic fluid. Losses of sodium from sweat are especially high in children with cystic fibrosis, aldosterone deficiency, or pseudohypoaldosteronism, although high losses can occur simply due to a hot climate. Third space losses are isotonic and can cause significant volume depletion, leading to ADH production and water retention, which can cause hyponatremia if the patient receives hypotonic fluid [2,3]. In diseases that cause volume depletion due to extrarenal sodium loss, the urine sodium level should be low (<10 mEq/L) as

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part of the renal response to maintain the intravascular volume. The only exceptions are diseases that cause both extrarenal and renal sodium losses: adrenal insufficiency and pseudohypoald osteronism [4].

Renal sodium loss may occur in a variety of situations. In some situations, the urine sodium concentration is >140 mEq/L; thus, hyponatremia may occur without any fluid intake. In many cases, the urine sodium level is less than the serum concentration; thus, the intake of hypotonic fluid is necessary for hyponatremia to develop. In diseases associated with urinary sodium loss, the urine sodium level is >20 mEq/L despite volume depletion. This may not be true if the urinary sodium loss is no longer occurring, as is frequently the case if diuretics are discontinued. Because loop diuretics prevent generation of a maximally hypertonic renal medulla, patients can neither maximally dilute nor concentrate the urine. The inability to maximally retain water provides some protection against severe hyponatremia. Patients receiving thiazide diuretics can concentrate the urine and are at higher risk for severe hyponatremia. Osmotic diuretics, such as glucose, during diabetic ketoacidosis, cause loss of both water and sodium. Urea accumulates during renal failure and then acts as an osmotic diuretic after relief of urinary tract obstruction and during the polyuric phase of acute tubular necrosis. Transient tubular damage in these conditions further impairs sodium conservation. The serum sodium concentration in these conditions is dependent on the sodium concentration of the fluid used to replace the losses. Hyponatremia develops when the fluid is hypotonic relative to the urinary losses [1,5].

Renal salt wasting [31] occurs in hereditary kidney diseases, such as juvenile nephronophthisis and autosomal recessive polycystic kidney disease. Obstructive uropathy, most commonly a consequence of posterior urethral valves, produces salt wasting, but these patients may also have hypernatremia due to impaired ability to concentrate urine and high water loss. Acquired tubulointerstitial nephritis, usually secondary to either medications or infections, may cause salt wasting, along with other evidence of tubular dysfunction. Central nervous system injury may produce cerebral salt wasting, which appears to be mediated by the production of a natriuretic peptide that causes renal salt wasting. In type II renal tubular acidosis (RTA), usually associated with Fanconi syndrome there is increased excretion of sodium and bicarbonate in the urine. Patients with Fanconi syndrome also have glycosuria, aminoaciduria, and hypophosphatemia due to renal phosphate wasting [6,7,8].

Methodology

Study Design

Study type: Randomized Control Trial

Study design: Allocation: Randomized.

Control: Active control

Intervention model: Parallel assignment

Sample Size

Based on literature review, the incidence of hyponatremia with standard intravenous fluid therapy is approximately 20%. In order to detect a difference of 10% at 7.5% level of significance (D) and power of 80% sample size was calculated by using the formula:

Sample size = Z^2 PQ/D^2.

Where Z is constant (1.96), Q is (1-P), P is the incidence.

Using this formula sample size was 109, we included 120 participants (60 in each group).

Inclusion Criteria

All children (3 months to 12 years) who were admitted to pediatric ward, who required intravenous maintenance fluid therapy for at least 12 hours, with serum Na in between 135 and 150 meq per litre were included in the study.

Exclusion Criteria

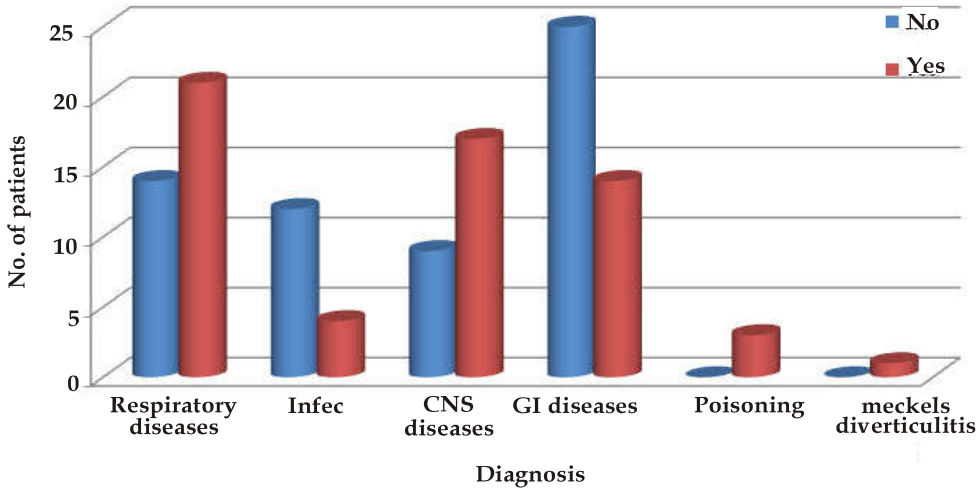
Children with illness that have primary fluid and electrolyte imbalance such as:

- Shock, Diarrhea with dehydration and Fluid Overload
- Abnormal serum sodium or Hyperglycemia at Presentation:
  - Hyponatremia: serum sodium < 135 mmol/ L^1.
  - Hypernatraemia: serum sodium >150 mmol/ L^1.
  - Hyperglycemia: blood glucose > 180 mg/ dl^2.
- Severe Protein Energy Malnutrition: Defined as grade III (50–59% of expected weight for age) and grade IV (less than 50% of expected weight for age) as per IAP classification [38].
- Child who is receiving drugs which cause abnormality in serum sodium such as diuretics, vasopressin.

Results

Primary diagnosis in both groups were comparable and is mentioned in Table 1 on baseline characters. Though most of the cases were respiratory and GI diseases, but both of them were in almost equal numbers in both groups. (P value 0.102).

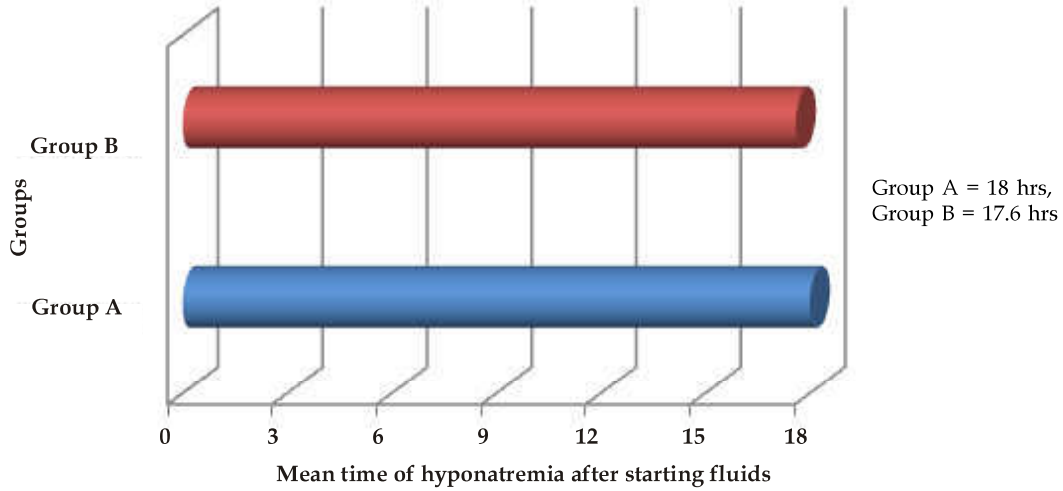
25% of hyponatremic patients were in respiratory diseases group, so this is group at risk of developing hospital acquired hyponatremia. (Table 1)



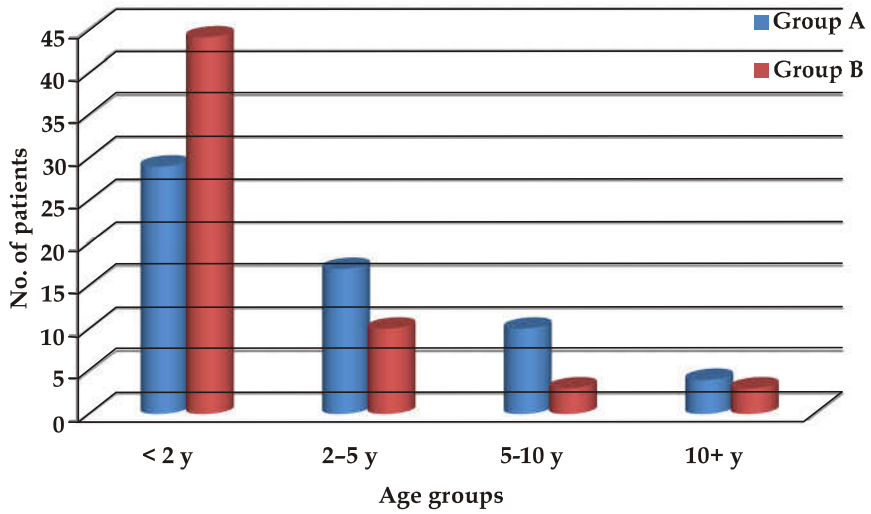
Graph 1: Diagnosis compared in both groups

Table 1: Diagnosis and Hyponatremia associated

			HYPON		Total
			No	Yes	
Full Diagnosis	Respiratory	Count	28	7	35
	Diseases	% of Full Diagnosis	80.0%	20.0%	100.0%
	Infectious diseases	Count	13	3	16
		% of Full Diagnosis	81.3%	18.8%	100.0%
	CNS diseases	Count	20	6	26
		% of Full Diagnosis	76.9%	23.1%	100.0%
	GI diseases	Count	38	1	39
		% of Full Diagnosis	97.4%	2.6%	100.0%
	Poisoning (kerosene,	Count	2	1	3
	Aluminium phosphide)	% of Full Diagnosis	66.7%	33.3%	100.0%
	Mickels diverticulitis	Count	0	1	1
		% of Full Diagnosis	.0%	100.0%	100.0%
	Total	Count	101	19	120
		% of Full Diagnosis	84.2%	15.8%	100.0%

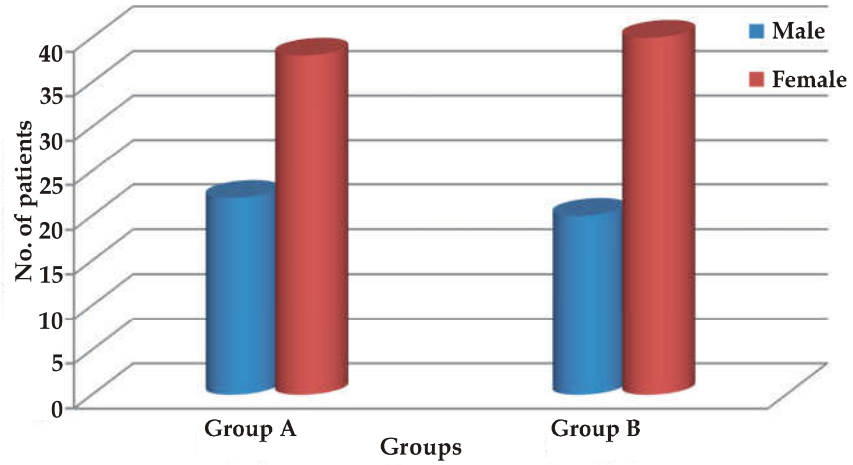


Graph 2: Mean time for hyponatremia to occur after starting IV Fluids



Graph 3: Age Group comparison in both groups

Both Groups Were Comparable (P Value 0.702)



Graph 4: Gender Group comparison in both groups

Both Groups Were Comparable (P Value 0.702)

Table 2. Hypon and duration of hospital stay

			HYPON		Total
			No	Yes	
DUUR	<5	Count	83	10	93
		% of HYPON	82.2%	52.6%	77.5%
	>5	Count	18	9	27
		% of HYPON	17.8%	47.4%	22.5%
Total		Count	101	19	120
		% of HYPON	100.0%	100.0%	100.0%

Duration of stay was increased (>5 days) in hyponatremic patients (p value 0.005), more so in hyponatremic group B patients (53% p value 0.001). (Table 2).

Discussion

This study shows that the incidence of hospital-acquired hyponatremia in patients who received maintenance fluids in accordance with the standard recommendations, in the form of multiple electrolytes and dextrose (hypotonic fluid) is high (30%) than those who received ringer lactate (6.66%).

This adds to the increasing body of evidence that suggests that hyponatremia associated with the use of hypotonic fluids is a common event and places children at risk for cerebral edema. The incidence of hyponatremia reported here is higher than the one recently described by Au et al. [9] and Kannan et al. [10] Au et al. studied retrospectively a cohort of postoperative critically ill children receiving hypotonic solutions and found that 12.9% had hyponatremia,

and Kannan et al RCT study included all paediatric patients who required IVF maintenance at least for 12hrs after fulfilling the inclusion criteria and reported the incidence to be 14.28%,but both studies defined as Na<130 mmol/L. The threshold we applied (Na <135 mmol/L)[1] was more conservative and could reasonably explain the higher occurrence rate found. The kind of design used, i.e., prospective and interventional, precluded opting for a different value because patient safety could have been compromised. Two patients in our study had fall in serum sodium (<130), one was dengue fever (129) and the other was Meckels diverticulitis (126). Both were intervened by replacing with ringer lactate and repeat serum sodium were 135 for dengue and 136 for Meckels diverticulitis. The importance of recognising mild hyponatremia as a frequent event is to alert paediatricians and provide the adequate time for appropriate interventions to avoid additional decreases in natremia and potential complications.

The incidence of hyponatremia reported is similar to the Pablo et al 2010 who studied the incidence of hyponatremia who received hypotonic saline (Na 40, K 20 meq/L) which was 21% at 12hrs and 31% at 24hrs of IVF.

Twenty five percent of hyponanatrmic cases constituted respiratory diseases (Pneumonia, bronchiolitis, WALRI) and may represent a group particularly at risk. There was fall in mean serum sodium by 1.35meq at 12hrs, 2.66 at 24hrs, 3.16 at 36hrs which were highly significant and hence degree of hyponatremia increases with time of infusion in group B. There was no fall in mean sodium with time in group A instead rose by 0.8 meq at 12hrs of infusion. Choong et al. studied a randomized controlled trial was to evaluate the risk of hyponatremia following administration of a isotonic (0.9% saline) compared to a hypotonic (0.45% saline) parenteral maintenance solution for 48 hours to postoperative pediatric patients and reported incidence of hyponatremia to be 40.8% in N/2 compared to 0.9% OF NS. Similarly Kristen et al reported an incidence of 30% in N/2 when compared to 10% of NS. Another RCT done by Montanana et al on paediatric ICU patients reported an incidence of 20.6% with hypotonic saline when compared to 5.1% of 0.9% saline (isotonic fluid) [11,12]. Our study provides further evidence that the use of multiple electrolytes and dextrose (hypotonic saline,) as suggested by Holliday and Segar's formula for maintenance fluids in postoperative management, is associated to a high occurrence rate of acute hyponatremia.

Conclusion

Twenty five percent of hyponanatrmic cases constituted respiratory diseases (Pneumonia, bronchiolitis, WALRI) and may represent a group particularly at risk.

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