

## Where did the salt go?

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Received: 6th January 2017, Accepted: 6th February 2017

**SUMMARY:** Paul SP, Hicks SS, Sanjeevaiah MK, Heaton PA. Where did the salt go? Turk J Pediatr 2017; 59: 345-348.

Bronchiolitis is a self-limiting viral respiratory-tract-infection seen commonly in infants. Some infants require hospitalization for feeding or respiratory support. A wide range of extra-pulmonary complications such as arrhythmias, myocarditis, central apneas, seizures, and hyponatremia are uncommonly known to occur with respiratory syncytial virus (RSV) infections. We present a 4-week-old-female infant admitted with RSV bronchiolitis for feeding support by nasogastric-tube. The infant suffered unexpected desaturations and seizure-like event 30-hours post-admission. Severe hyponatremia (sodium: 114 mmol/L) was detected although cause for this remained unexplained initially. Serum sodium improved following a bolus of 2.7% hypertonic-saline. The infant subsequently needed advanced respiratory support. Around time of transfer to PICU, the infant developed abdominal distension and continued to have bilious aspirate even after 6-days. An upper gastrointestinal contrast-study confirmed malrotation; improved following surgery. Co-existence of two serious pathologies may have accounted for the hyponatremia: malrotation (possible source of sodium loss into third-space) and severe bronchiolitis (inappropriate ADH-secretion). This case highlights the importance of determining origin of hyponatremia associated with acute bronchiolitis.

**Key words:** bronchiolitis, RSV, hyponatremia, seizures, malrotation.

Acute bronchiolitis is a clinical diagnosis due to viral infection of the lower respiratory tract of babies. It is most common in the winter months in temperate latitudes, and is an important cause of morbidity in infancy with a peak incidence noted between 2 and 6 months. Most cases seen in hospital that have a microbiological diagnosis are caused by respiratory syncytial virus (RSV), though other viruses may be responsible for a similar clinical presentation either alone or as co-infection with RSV and/or other viruses; these include: human metapneumovirus, influenza virus, parainfluenza virus, adenovirus and rhinovirus<sup>1</sup>. The diagnosis of acute bronchiolitis is based on history of upper respiratory tract symptoms followed by respiratory distress, characteristic dry cough, wheeze and fine inspiratory crackles (on auscultation). Admission is usually required when oxygen therapy and/or feeding support are needed; a minority of cases will require ventilatory support<sup>2,3</sup>. Risk factors for bronchiolitis include chronic lung disease of

prematurity, acyanotic congenital heart disease and immunodeficiency<sup>3</sup>.

A wide range of extra-pulmonary complications have been reported with severe RSV infections which include: arrhythmia, myocarditis and myocardial failure; central apnea and seizures; elevated transaminase concentrations; petechial rash; hyponatremia and raised anti-diuretic hormone (ADH) concentrations<sup>4</sup>. It remains uncertain the extent to which these observed extra-pulmonary features are the direct result of RSV infection at other sites or whether they are secondary to the respiratory tract infection and resulting respiratory compromise and release of inflammatory mediators<sup>5</sup>. This article presents a case of a 4-week old infant with RSV bronchiolitis who developed hyponatremic seizures.

### Case Report

A 4-week-old female infant was admitted with a 4-day history of cough and symptoms of an

upper respiratory tract infection. Her weight at admission was 4.09 Kg. She had been born prematurely at 35 weeks of gestation and had an uneventful neonatal period. She was previously feeding well on formula milk every 3 to 4 hours. Mother reported a 24-hour history of decreased feeding. At initial assessment, the respiratory rate was 54/min, oxygen saturation was 90% in air; she had mild chest wall recession, and bilateral scattered wheeze was audible on auscultation. Clinical diagnosis of bronchiolitis was made and the management plan included 2 hourly nasogastric tube-feeding at 100 ml/kg/day with formula feeds, and administration of supplemental oxygen as required. A nasopharyngeal aspirate (NPA) was reported as positive for RSV.

Sudden deterioration in clinical condition occurred around 30 hours post admission, when the oxygen saturation decreased to 78% following a nasogastric tube-feed from pre-constituted bottle with formula milk; no bolus of water had been given after the feed. Capillary blood gas analysis revealed a mixed respiratory and metabolic acidosis with a serum sodium concentration of 114 mmol/L (range 135 – 145 mmol/L); this was confirmed on a subsequent laboratory blood sample. As the infant had not required administration of any intravenous fluids the serum electrolytes were not measured previously, and urine output had not been specifically recorded. Whilst being assessed, she was noted as having cyclical movements of her upper arms; the clinical impression at this point was of a seizure with a possibility of aspiration of vomitus. Her stomach content was emptied via the

nasogastric tube and the infant was kept nil by mouth. Intravenous fluids with 0.9% sodium chloride and 5% dextrose were started at 60 ml/kg/day. The chest X-ray revealed a right upper lobe collapse/consolidation. Intravenous co-amoxiclav was started and further investigations were undertaken.

Laboratory blood and urine results sent at the time of deterioration showed: sodium 115 mmol/L, potassium 3.87mmol/L (range 3.5 – 5 mmol/L), serum creatinine <27  $\mu$ mol/L (60 -100  $\mu$ mol/L), urea 2.9 mmol/L (3.5 – 5.3 mmol/L), blood glucose 9.3 mmol/L (4-7 mmol/L), cortisol 253 nmol/L (130-690 nmol/L), serum osmolality 248 mmol/kg (260 – 290 mmol/kg), urine sodium 55 mmol/L, and urine osmolality 390 mmol/kg (280 – 850 mmol/kg). The laboratory results were considered to be consistent with respiratory illness causing inappropriate anti-diuretic hormone (ADH) secretion associated with severe hyponatremia and subsequent seizure activity.

The infant remained fluid restricted at 60 ml/kg/day, the hyponatraemia was treated with intravenous (hypertonic) 2.7% sodium chloride and a loading dose of intravenous phenytoin was administered; this was following a discussion with the PICU team. The serum sodium level gradually improved over the next 30 hours, but never reached the normal range (Fig. 1). There was no further seizure activity noted, however, her respiratory condition subsequently deteriorated and she required continuous positive airway pressure (CPAP) support. She also had a bilious vomit and was noted to have a full and distended abdomen. On the third day of admission, the oxygen requirement increased; she developed hypotension which necessitated intubation, inotropes and transfer to PICU. She remained intubated and ventilated for next 6 days and required dopamine and noradrenaline support to maintain blood pressure during this time.

As she continued to have intermittent bilious aspirates from the nasogastric tube even after 9 days following her initial presentation, an upper gastrointestinal contrast study was performed. This revealed a malrotation which was surgically corrected with a Ladd's procedure. She has subsequently been reviewed in the outpatient clinic and was found to be

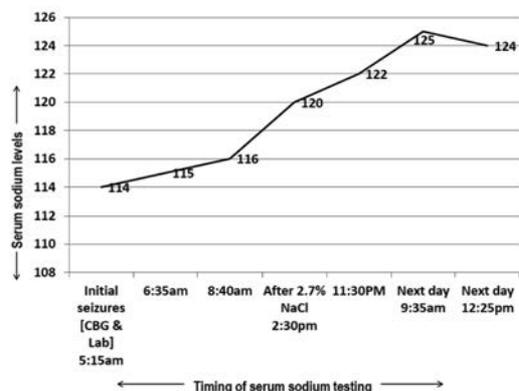


Fig 1. Serial serum sodium levels [normal 135 – 145 mmol/L]

thriving and developing normally. Participation involved informed consent.

### Discussion

The unexpected hyponatremia was initially attributed to “inappropriate ADH secretion” caused by the patient’s respiratory illness, though its severity seemed initially difficult to explain given that her bronchiolitis was relatively mild at initial presentation until the time of deterioration and the infant had not received any hypotonic oral or intravenous fluids, or excessive volumes of fluid. In retrospect, her co-existing malrotation, with signs of gastrointestinal compromise in the form of bilious vomiting, was likely to have contributed to the low sodium concentrations that were observed. This previously undiagnosed gastrointestinal pathology most probably accounted for a possible source of sodium loss into the third space, thus contributing to the severity of hyponatremia and seizures.

Causes of hyponatremia in an infant include: iatrogenic causes (most commonly seen in hospitalized patients receiving intravenous administration of hypotonic fluids or non-electrolyte osmotically active substance such as glucose, and use of diuretics), adrenocortical insufficiency, renal disease, severe hypothyroidism, and falsely low sodium due to severe hyperglycaemia. These other causes were either not applicable (the infant has not received IV fluids or diuretics at the time of deterioration), or were ruled out with laboratory testing: she had normal renal function, only mild raised blood glucose possibly secondary to stress response, and an appropriately raised cortisol concentration (infant also had normal female genitalia). Her newborn heel prick test revealed a normal TSH concentration and she had no other clinical features of hypothyroidism.

Increased ADH concentrations are known to be associated with respiratory pathologies including bronchiolitis<sup>6,7</sup>. ADH acts to conserve body water by increasing the permeability of the distal renal tubule and collecting duct<sup>8</sup>. The trigger(s) for increased ADH release in bronchiolitis are yet to be proven but 3 possible mechanisms have been suggested:

(1) stimulation of atrial baroreceptors either due to atrial compression by hyperinflated lungs

or due to decreased venous return secondary to increased pulmonary vascular resistance

(2) stimulation due to hypoxaemia

(3) stress causing central hypothalamic stimulation<sup>6,7</sup>. There is also now emerging evidence for the role of the inflammatory mediator interleukin-6 in the non-osmotic release of ADH<sup>9</sup>.

Hyponatremia has been known to be associated with bronchiolitis, there appears to be a particular risk when intravenous fluids are administered. One study reported the phenomenon in 33% of patients admitted to a paediatric intensive care unit with RSV infection, and 4 out of those 33 patients (4.4%) had seizures prior to admission to PICU<sup>10</sup>. Three of these 4 infants had received hypotonic intravenous fluids at 100–150 ml/kg/day before referral to PICU and all four were managed successfully with 3% hypertonic saline, followed by fluid restriction, resulting in immediate termination of seizure activity and normalization of serum sodium values over 48 hours<sup>10</sup>.

Seizures followed by coma and respiratory arrest are severe features of symptomatic hyponatremia; other features include weakness and vomiting. Not every case has shown an association between increased ADH concentrations and hyponatremia, a possible explanation for this is concurrent hyperreninaemia and secondary hyperaldosteronism<sup>7</sup>. Nevertheless, the known increase in ADH secretion associated with bronchiolitis puts those infants at risk of developing hyponatremia, particularly if concurrently receiving standard hypotonic intravenous fluids such as 0.18% or 0.45% sodium chloride<sup>4,5</sup>. Hyponatremia-related seizures have been described in infants with bronchiolitis either at initial presentation or subsequently while being on high-volume intravenous fluids<sup>11</sup>. Errors in judgment in fluid administration has been known to occur due to recording of infant’s weight in English system (pounds and ounces) and inadvertently using the same value for calculating fluid requirements for the infant in metric system (kilograms)<sup>12</sup>.

In conclusion, this case highlights the significance of determining correctly the origin hyponatremia, seen here in the course of acute bronchiolitis. The electrolyte abnormality may

need both clinical and laboratory investigation to clarify whether the pathophysiological explanation is fundamentally one of fluid overload, or sodium depletion, or a combination of the two. When two or more potential serious pathologies co-exist this may represent a diagnostic challenge. Patients who are receiving intravenous fluids for whatever reason remain at increased risk of hyponatremia compared to patients who are not having intravenous fluids.

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