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Brief report

Salt depletion and dehydration in hypertensive preterm infants

J. B. Gouyon, S. Bernardini, D. S. Semama, and M. Françoise

Service de Pédiatrie 2, Hôpital d'Enfants, 10 Boulevard Maréchal de Lattre de Tassigny, F-21034 Dijon Cedex, France

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Abstract. Three preterm infants presented with both severe or moderate arterial hypertension and dehydration due to increased water and sodium urinary excretion. In patient 1, water and sodium wasting were extremely severe and peaked at 575 ml/kg per day and 73 mEq/kg per day, respectively. In all infants, urinary water and sodium excretion dramatically decreased when hypertension resolved. The overall clinical data suggest a pressure natriuresis phenomenon.

Key words: Preterm infant – Hypertension – Dehydration

Introduction

Systemic arterial hypertension is rare in neonates. The incidence of hypertension in neonatal intensive care units varies from 0.7% to 3.2% [1, 2]. Renal artery thrombosis, a complication of umbilical artery catheterization, has been the leading cause for neonatal hypertension in many studies [1–3]. Recently, administration of corticosteroids, as a treatment of bronchopulmonary dysplasia, has been associated with a high incidence of arterial hypertension, which was observed in up to 67% of dexamethasone-treated preterm infants [4]. Arterial hypertension may cause a wide range of non-specific clinical symptoms in neonates, including water and sodium wasting [3]. Increased water and sodium urinary losses may led to severe dehydration, which have previously been reported in only two term neonates with renovascular hypertension [5, 6]. We report three preterm infants, free of diuretic therapy, in whom arterial hypertension caused hyponatremic dehydration due to polyuria and increased natriuresis.

Correspondence to: J. B. Gouyon

Case reports

According to Adelman [7], neonatal hypertension was defined as persistent systolic blood pressure levels exceeding 90 mmHg and diastolic levels 60 mmHg in term neonates and 80 mmHg and 50 mmHg in preterm infants. Blood pressure was measured with an automatic oscillometric monitoring device (Dinamap, Critikon). Water and sodium intakes were always calculated according to the changes in body weight, protidemia, and natremia.

Case 1

This boy was born at 36 weeks' gestation weighing 2,365 g. He was delivered by cesarean section because of a retroplacental hematoma. His mother was 29 years old. Cardiorespiratory resuscitation was required at birth and the Apgar score was 3, 5, and 10 at 1, 5, and 10 min, respectively. The infant developed an immediate respiratory distress syndrome treated with natural surfactant (Curosurf, Serono), high-frequency oscillation for 4 days, and conventional mechanical ventilation for 9 additional days. An umbilical artery catheter (UAC) was inserted on day 1 and was removed on day 6. The tip of the UAC was at the level of the 9th thoracic vertebra on chest X-ray.

Arterial hypertension was first noticed on day 10 (Fig. 1). On day 15, systolic and diastolic blood pressure reached 126 and 90 mmHg, respectively and nicardipine infusion (1.17 μg/kg per min) was started. This allowed blood pressure to normalize completely on day 20. A renal Doppler study found no perfusion of the left kidney. A radionuclide scan with 99m technetium-dimercaptosuccinic acid also failed to demonstrate left renal function. Plasma renin activity (5,200 ng/l, normal range 168–284 ng/l) and aldosterone (7,375 ng/l, normal range 217–1231 ng/l) were markedly elevated on day 12. The plasma creatinine levels ranged from 3 to 6 mg/l. Plasma bicarbonate and potassium were measured daily and always remained in the normal range. Hematuria and proteinuria were not detected and the urine was sterile. These findings suggested renovascular hypertension due to left renal artery occlusion.

On day 12, the infant was found to be dehydrated. From day 10 to day 12, the plasma protein level increased from 54 to 71 g/l, while the body weight decreased by 7.4% (from 2,175 to 2,015 g) (Fig. 1). Despite a high fluid and sodium intake (672 ml/kg per day and 52 mEq/kg per day on day 17, respectively) the dramatic urinary water and sodium losses led to hyponatremic (129 mEq/l) dehydration (Fig. 1). On days 17–18, diuresis and natriuresis peaked at 575 ml/kg per day and 73 mEq/kg per day, respectively (Fig. 1).

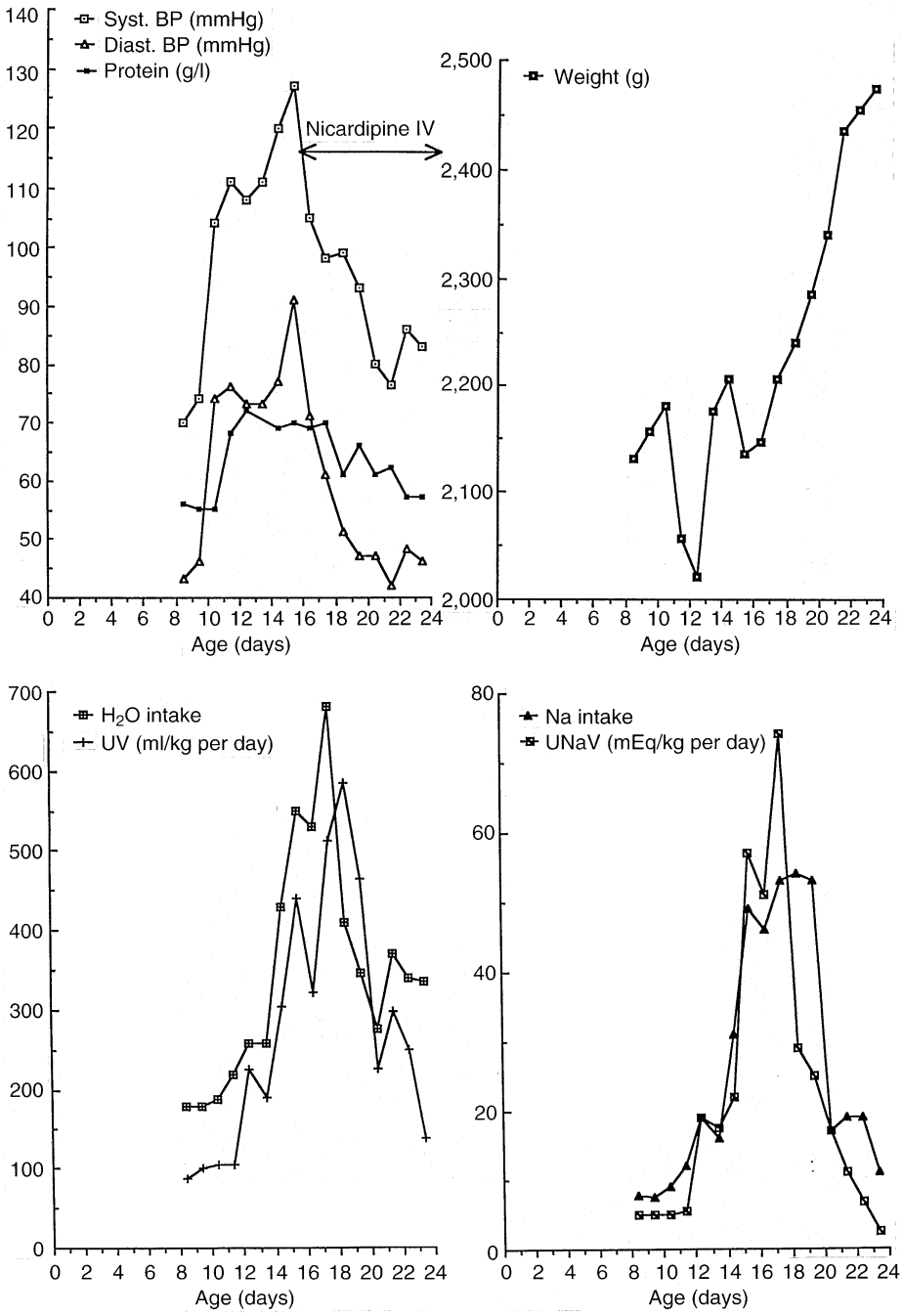

Fig. 1. Systolic (*Syst. BP*) and diastolic blood pressure (*Diast. BP*), plasma protein level (g/l), weight changes, diuresis (*UY*) and water (H_2O) intake (ml/kg per day), natriuresis (*UNaV*) and sodium (*Na*) intake (mEq/kg per day) in one hypertensive neonate (patient 1)

On day 16, urinary fractional excretion of β_2-microglobulin (14%) was increased. Fractional excretion of sodium was measured daily and ranged from 2.9% to 4.1% during the hypertensive period. Concomitantly, the arginine vasopressin plasma level (32 pg/l) and the urine osmolality (326 mosmol/kg) were elevated. The urine/plasma osmolality ratio was moderately increased (1.1) and an intranasal DDAVP administration (10 μg) was performed to assess the renal concentrating ability. This was associated with a further urinary osmolality increase from 326 to 450 mosmol/kg. Urine levels of amino acids were in the normal range. The plasma 17-hydroxyprogesterone level (0.14 μg/l) was normal.

Nicardipine infusion allowed a progressive decrease in blood pressure which was associated with a concomitant decrease in the serum protein level and a sharp decline in urinary excretion of water and sodium, thus allowing a dramatic reduction in water and sodium intake (Fig. 1).

Fractional excretion of sodium was 0.9% on day 23. Throughout the study, natriuresis, diuresis, and creatinine clearance were measured daily from day 10 to day 23. Diuresis and creatinine clearance (range 1.3–13.8 ml/kg per min) were closely correlated by regression analysis over the periods with ($r^2 = 0.98$, $P < 0.001$) and without ($r^2 = 0.96$, $P < 0.001$) nicardipine treatment. Natriuresis and creatinine clearance were closely correlated by regression analysis over the periods with ($r^2 = 0.91$, $P < 0.001$) and without ($r^2 = 0.99$, $P < 0.001$) nicardipine treatment. The outcome at 5 months was favorable, but the patient still needed antihypertensive treatment.

Case 2

This boy was born at 27 weeks' gestation, with a birth weight of 1,165 g, by vaginal delivery at home. His mother was 28 years old. The

infant presented with a respiratory distress syndrome treated with high-frequency oscillation and surfactant (Curosurf). The pulmonary disease was complicated by bronchopulmonary dysplasia. According to Cummings et al. [8], dexamethasone (0.5 mg/kg per day) was administered intravenously for treatment of bronchopulmonary dysplasia from day 18, while his weight was 1,120 g, plasma protein level 50 g/l, diuresis 108 ml/kg per day, and blood pressure 75/45 mmHg.

Arterial hypertension was observed on day 19, peaked at 93/60 mmHg on day 21, and resolved on day 25, i.e., the day after the corticosteroid treatment was stopped. Hypertension was associated with a hyponatremic dehydration due to a marked increase in diuresis and natriuresis. The serum protein level increased from 50 g/l on day 18 to 59 g/l on day 24, and his weight decreased concomitantly from 1,135 g to 1,085 g (–4.4%). Plasma sodium fell from 137 mEq/l on day 18 to 130 mEq/l on day 24. Urinary water and sodium excretion peaked at 144 ml/kg per day and 6 mEq/kg per day respectively on day 24, while water and sodium intakes were 230 ml/kg per day and 9 mEq/kg per day. Plasma bicarbonate, potassium, and creatinine levels were 20 mEq/l, 4.7 mEq/l, and 5 mg/l, respectively on day 19 and subsequently remained in the normal range.

Blood pressure normalized on day 25 and this was followed by a sharp decrease in diuresis (72 ml/kg per day on days 26 and 27, respectively), natriuresis (1.3 mEq/kg per day on day 27), and plasma protein level (42 and 40 g/l on day 26 and 27, respectively). From day 26, water and sodium intakes were rapidly reduced, while diuresis and natriuresis decreased. The outcome was favorable.

Case 3

This boy was born at 27 weeks' gestation with a birth weight of 860 g. He was delivered by emergency cesarean section because of acute fetal distress. His mother was 36 years old. The Apgar score was 4, 10, and 10 at 1, 5, and 10 min, respectively. This infant was free of any respiratory symptoms, but severe apneas of prematurity, refractory to caffeine and nasal continuous positive airway pressure (CPAP), justified tracheal intubation for tracheal CPAP. The outcome was complicated by bronchopulmonary dysplasia. According to Cummings et al. [8], dexamethasone (0.5 mg/kg per day) was administered intravenously for treatment of bronchopulmonary dysplasia from day 20, while his weight was 905 g, plasma protein level 39 g/l, plasma sodium 140 mEq/l, diuresis 89 ml/kg per day, natriuresis 1.4 mEq/kg per day and systolic blood pressure 52/28 mmHg.

The systolic and diastolic blood pressure progressively increased and the patient became hypertensive on day 25. Thereafter, the systolic blood pressure ranged from 85 to 90 mmHg, until dexamethasone was stopped on day 31. Blood pressure normalized on day 33. With the hypertension, the patient became dehydrated and hyponatremic. His body weight fell from 975 g on day 24 to 910 g (–6.7%) on day 28. On day 28, the plasma protein level peaked at 56 g/l and the plasma sodium level fell at 131 mEq/l. This was due to a marked increase in urinary excretion of water and sodium which peaked at 159 ml/kg per day and 5.5 mEq/kg per day, respectively on day 29, while water and sodium intakes reached 230 ml/kg per day and 6.5 mEq/kg per day. Plasma bicarbonate, potassium, and creatinine levels were daily measured and always remained in the normal range.

Blood pressure normalized on day 33, followed by a dramatic fall in diuresis, natriuresis, and plasma protein level (50 ml/kg per day, 1.5 mEq/kg per day and 46 g/l, respectively on day 34). From day 31, water and sodium intakes could be rapidly reduced. His clinical condition was satisfactory at 17 months of age.

Discussion

Our study demonstrates that arterial hypertension of renal or non-renal origin may result in increased natriuresis, polyuria, and subsequent dehydration in preterm infants. This has previously been observed in adults and in two full-term neonates with severe arterial hypertension [5, 6]. The first newborn infant presented with severe dehydration and hyponatremia with marked hypertension (systolic blood pressure 180–210 mmHg) due to unilateral thrombosis of the renal artery. This infant died of intractable hypertension [5]. The second baby presented with polyuria, severe renal salt loss, dehydration, hyponatremia, and hypertension (130/60 mmHg) due to unilateral stenosis of the renal artery. Blood pressure settled to within the normal range only after nephrectomy [6]. High plasma renin activity [5, 6] and aldosterone concentrations [5] were found in these two infants. Observations in our patients confirm and extend these data.

The close temporal relationship between hypertension, dehydration (as assessed by the plasma protein level and weight changes), water and sodium loss suggested that the immature kidney may respond to moderate (patients 2 and 3) or severe (patient 1) hypertension by polyuria and natriuresis. This hypothesis was confirmed by the reversibility of polyuria and natriuresis when hypertension was resolved. Kidneys involved in this response were normal, as the kidney with arterial occlusion was not functional in patient 1 and hypertension was not of renovascular origin in patients 2 and 3.

Dehydration, which was the sole clinical symptom in these patients, may be particularly severe, as in patient 1, when polyuria and natriuresis reached 575 ml/kg per day and 73 mEq/kg per day, respectively. This patient was characterized by hypertension of renovascular origin with marked activation of the renin-angiotensin system, as observed in two-kidney-one-clip hypertension [9]. In this patient, the marked increase in renin secretion might have been due to both the initial renal ischemia and the subsequent sodium depletion. Indeed, previous studies have shown that the renin-angiotensin system of preterm infants can be physiologically stimulated by a negative sodium balance [10].

The hypertension-induced natriuresis and polyuria observed in our neonates may suggest the so called pressure-natriuresis phenomenon, whose mechanism remains unclear. In animals, the fact that diuresis and natriuresis increased when blood pressure was raised, despite a stable glomerular filtration rate, suggested that increasing the renal perfusion pressure was responsible for a decrease in tubular water and sodium reabsorption [11, 12]. It has been suggested that suppression of tubular sodium reabsorption was due to an interstitial hydrostatic pressure increase associated with changes in papillary hemodynamics [11, 12]. However, the close relationship between diuresis and creatinine clearance in patient 1 may support the hypothesis that polyuria and natriuresis in this immature kidney were, at least partly, due to an increase in glomerular filtration.

In conclusion, arterial hypertension may induce severe natriuresis, polyuria, and dehydration in preterm infants. Our data illustrate that blood pressure measurement is mandatory in neonates with insufficient weight gain or overt dehydration, even if other symptoms of hypertension are lacking. The high incidence of hyponatremia (30%) reported by Skalina et al. [13] in hypertensive neonates suggests that this phenomenon could have been underestimated in preterm infants. Further clinical and experi-

mental data are mandatory to assess the incidence and mechanism of this clinical condition in neonates.

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Literature abstract

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Primary vesicoureteric reflux – how useful is postnatal ultrasound?

J. M. Tibballs and R. De Bruyn

The presence or absence of pelvicalyceal dilatation on postnatal ultrasound continues to appear within diagnostic algorithms to select patients for micturating cystourethrography (MCU) in the investigation of antenatally diagnosed hydronephrosis. Postnatal ultrasound findings were assessed in a population diagnosed as having antenatal hydronephrosis due solely to primary vesicoureteric reflux (VUR) to see whether this is justified.

The postnatal ultrasound and MCU findings in 177 patients with primary VUR detected as antenatal hydronephrosis were reviewed retrospectively. A total of 132 (75%) were boys. Reflux was unilateral in 103 cases and bilateral in 74 (42%). Altogether 37% of boys and 33% of girls with a renal pelvic diameter of ≤10 mm had grade III–V VUR. Calyceal and/or ureteric dilatation had specificities of 87–96% for grade III–V VUR, but sensitivities of only 37–54%. Fifty eight per cent of male and 75% of female renal units with grade III VUR and 17% of male units with grade IV–V VUR were normal on ultrasound. Approximately 25% of ultrasonically normal renal units had grade III–V VUR on MCU.

Postnatal ultrasound criteria correlate poorly with the presence and degree of VUR in children with antenatally diagnosed hydronephrosis and should not be used to direct the use of cystography.