

# Nonoliguric hyperkalemia in a late preterm infant with severe birth asphyxia

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**Abstract:** Nonoliguric hyperkalemia (NOHK) is common during the first days after birth in premature infants with gestational age <28 weeks. It was rarely reported in term or late preterm infants. We present a case of a 3 hours baby at 34 weeks and 3 days' gestational age who was delivered of severe birth asphyxia by cesarean section for failing to vaginal delivery. Serum potassium reached to 8.3 mmol/L at 12 hours age, with normal urinary output and serum urea and creatinine. Abnormal ECG of tall peaked T waves was developed. Marked fall in serum Ca<sup>2+</sup> of 0.6 mmol/L and total calcium of 1.13 mmol/L was also noted. Cerebral lesions in the head MRI demonstrated extensive periventricular white matter injury.

**Keywords:** Nonoliguric hyperkalemia; late preterm; asphyxia

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Although hyperkalemia is a common and serious complication among preterm neonates, it is usually in extremely premature infants. Nonoliguric hyperkalemia (NOHK) has been defined as serum potassium 7 mmol/L during the first 72 hours of life in the presence of urinary output of >1 mL/kg-h (1). It was reported that more than 80% of babies with NOHK were ELBW infants with gestational age below 28 weeks (2). Few cases have been reported in late preterm infants with NOHK who were born at 34 0/7 to 36 6/7 weeks' gestation. We therefore report a case of a 3-hour-old late preterm infant who was born with severe birth asphyxia and developed NOHK at 12 hours age. The neuroimaging finding of the infant was showed as well.

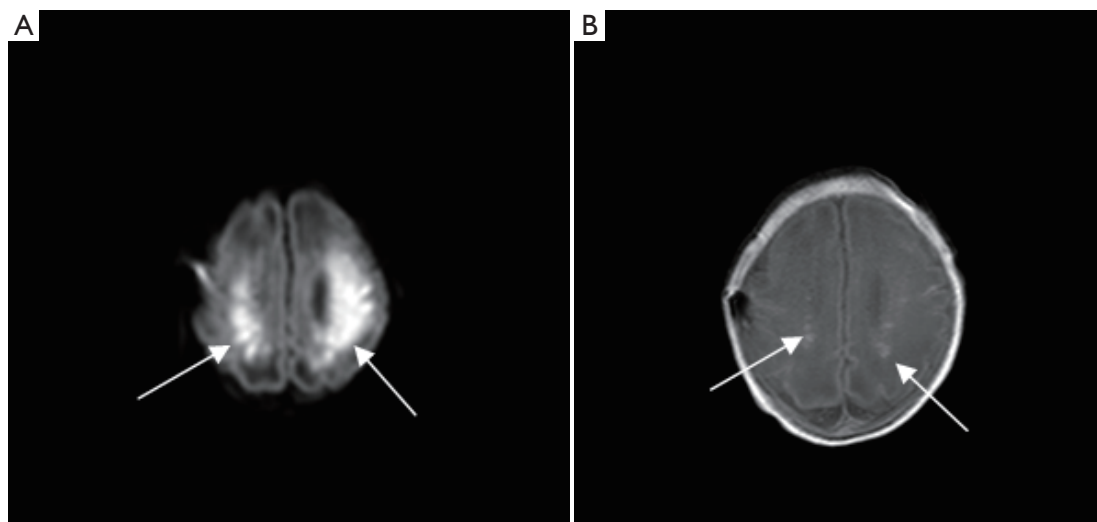
## Case report

A premature baby boy was delivered at 34 weeks and 3 days' gestational age. He was delivered by cesarean section for failing to vaginal delivery. Apgar scores were 4 and 5 at 1 and 5 minutes, respectively. No abnormal placenta,

umbilical cord and amniotic fluid were found. Birth weight was 2,210 g. The baby developed grunt and cyanosis right after birth and was no any relief after oxygen inhalation. No seizures were noticed. No blood transfusion or medications was received. He was transported to our hospital 3 hours later. Body temperature was 36.5 °C on admission. His pulse and respiratory rates were 150 beats and 66 per minute, respectively. Oxygen saturation (SpO<sub>2</sub>) was 70% without oxygen. He was awake but hyporeactive with irritability and sharp crying, tachypnoea and mild flaring of the alae nasi. Anterior fontanel was normotensive. There was a cephalohematoma (5 cm × 5 cm) on the right top of the head. The respiratory movements were fast and shallow. Lungs were clear to auscultation. The heart rate was regular and no murmurs were heard. The heart sound was strong. The abdomen was soft on palpation, and no hepatosplenomegaly. Borborygmus and umbilical cord were normal. He showed poor peripheral perfusion with chilly and capillary refilling time 4 seconds. Muscle tension was reduced on the upper limbs and normal on the lower limbs. Hugging and holding reflexes were incomplete,

**Table 1** Blood gas and electrolytes at different time after birth (in arterial blood samples)

Hours of age	pH (-)	BE (mmol/L)	PCO <sub>2</sub> (mmHg)	PO <sub>2</sub> (mmHg)	K <sup>+</sup> (mmol/L)	Na <sup>+</sup> (mmol/L)	Ca <sup>2+</sup> (mmol/L)
3	7.21	-6.60	55.30	44.20	5.40	136.70	1.32
12	7.34	-3.70	41.90	54.30	8.30	133.00	0.83
24	7.34	-0.80	48.80	39.20	7.19	130.00	0.86
28	7.34	1.00	51.40	119.30	6.40	132.30	0.76
37	7.35	0.30	48.50	140.40	5.34	132.90	0.60
45	7.32	0.40	54.70	79.30	5.37	134.10	0.56
69	7.41	0.80	41.20	229.40	3.42	141.70	0.80
100	7.53	4.60	32.00	78.00	4.00	144.00	0.99

**Figure 1** MRI brain performed on day 5. A. Diffusion-weighted imaging (DWI, axial section) with abnormal high signal in periventricular white matter (arrows); B. T1 weighted image (axial section) showing abnormal high signal around the lateral ventricles of the same section (arrows).

whilst foraging, sucking and swallowing reflexes were all disappeared. Gestational age assessment was 34 weeks.

The baby was sedated with phenobarbital in the first day after admission. Oxygen was administered by face mask at 1 L/min in the first two days for the relief of cyanosis. Serum potassium reached to 8.3 mmol/L at 12 hours age, and meanwhile the baby developed abnormal ECG of tall peaked T waves with 134 bpm of the heart rate. Calcium gluconate 10%, 1 mL/kg diluted 10 folds with glucose 5%, i.v. bolus at 1 mL/min was employed. Insulin and glucose (1 unit to 4 g) were infused at 0.05 units/kg·h. Urinary output was monitored closely which was between 2.41 to 2.64 mL/kg·day and blood glucose was normal during hospitalization. Serum potassium came down gradually below 6.5 mmol/L at 28 hours age. Laboratory findings showed normal white blood cells, and  $247 \times 10^9/L$  of platelets, no anemia. Two serum urea and creatinine were

3.89 mmol/L and  $74.5 \mu\text{mol/L}$ , 4.32 mmol/L and  $70 \mu\text{mol/L}$ , respectively. C-reactive protein  $<1.00 \text{ mg/L}$ . TORCH-IgM were negative and blood culture was sterile. Marked fall in serum Ca<sup>2+</sup> of 0.6 mmol/L and total calcium of 1.13 mmol/L (Table 1) at age of 37 hours was noted, accompanied by weak heart sound and bradycardia (115/min). Serum inorganic phosphorus was 3.91 mmol/L, 0.78 mmol/L of magnesium (0.67-1.15 mmol/L) and 158 U/L of alkaline phosphatase. A 10% solution of calcium gluconate (2 mL/kg) was infused at the same dilution as above. Ionized calcium increased to 1 mmol/L on the 5<sup>th</sup> day after birth. Parathyroid hormone (PTH) was 145.0 pg/mL. Blood gas and electrolytes at different time of age were listed as Table 1. Chest X-ray showed mild decreased densities with patchy opacity areas in both lung fields. The head magnetic resonance imaging (MRI) findings were shown (Figure 1).

The baby was sedated with phenobarbital for 24 hours

after admission. Oxygen was administered by face mask at 1 L/min in the first two days for the relief of cyanosis. The serum potassium increased to 8.3 mmol/L at 12 hours age, and abnormal ECG of tall peaked T waves was noted. The heart rate was 134 bpm. Calcium gluconate 10%, 1 mL/kg diluted 10 folds with glucose 5%, i.v. bolus at 1 mL/min was employed. Insulin and glucose (1 unit to 4 g) were infused at 0.05 units/kg·h. Blood glucose was normal during hospitalization. Urinary output was monitored closely which was between 2.41 to 2.64 mL/kg·day. Serum potassium came down gradually below 6.5 mmol/L at 28 hours of age. Laboratory findings showed normal white blood cells, and  $247 \times 10^9/L$  of platelets, no anemia. Two serum urea and creatinine were 3.89 mmol/L and 74.5  $\mu\text{mol/L}$ , 4.32 mmol/L and 70  $\mu\text{mol/L}$ , respectively. C-reactive protein < 1.00 mg/L. TORCH-IgM were negative and blood culture was sterile. Marked fall in serum  $\text{Ca}^{2+}$  of 0.6 mmol/L and total calcium of 1.13 mmol/L (Table 1) at age of 37 hours was noted, accompanied by weak heart sound and bradycardia (115/min). Serum inorganic phosphorus was 3.91 mmol/L, 0.78 mmol/L of magnesium (0.67-1.15 mmol/L) and 158 U/L of alkaline phosphatase. A 10% solution of calcium gluconate (2 mL/kg) was infused at the same dilution as above. Ionized calcium increased to 1.0 mmol / L on the 5<sup>th</sup> day of age. Parathyroid hormone (PTH) was 145.0 pg/mL. Blood gas and electrolytes at different time of age were listed as Table 1. Chest X-ray showed a mild decreased densities with patchy opacity areas in both lung fields. The head magnetic resonance imaging (MRI) findings were shown (Figure 1). Extensive brain damage was showed with abnormal high signal in periventricular white matter. The baby was stable in the following days and discharged at the age of 18 days.

## Discussion

In 1977, Perkkiö and Rähä reported a single episode of hyperkalemia at the age of 17 hrs in an otherwise healthy premature infant, representing the first description of a clinical entity now referred to as nonoliguric hyperkalemia of the premature infants (3,4). Nonoliguric hyperkalemia (NOHK) has been defined as serum potassium >7.0 mmol/L during the first 72 hours of life in the presence of urinary output of >1 mL/kg·h. It is more common in extremely low birth weight infants than term infants and the reported incidence varies widely between 11% and 52%. This reversible condition does not appear to be related to renal failure, increased potassium intake, or excessive

bruising (1,2,5,6). It was significantly associated with fetal distress, early metabolic acidosis, early hyperglycemia, and absence of antenatal steroid administration (2). A study by Yaseen *et al.* (2) and Kazuo *et al.* (7) demonstrated that more than 80% of babies with NOHK were extremely low birth weight infants with gestational age <28 weeks, because the potassium balance for premature infants with gestational age 33 to 36 weeks was more stable than those under 33 weeks. In this paper, we reported a late preterm infant with NOHK which were no reports before. Late preterm is the recommended definition for infants born at 34 0/7 to 36 6/7 weeks' gestation. The baby was born with severe birth asphyxia and developed hyperkalemia at 12 hours age. Urinary output as well as serum urea and creatinine were all at normal levels.

The mechanism of NOHK is suggested mainly an immature function of Na/K ATPase activity in severe prematurity resulting in an internal potassium from intracellular to plasma. Fetal distress, low Apgar scores, and early neonatal acidosis or glucose and insulin abnormality were all significantly associated with the high incidence of potassium transport towards the intracellular space decreased and intracellular potassium into the extracellular space by leaking or shifting (6,8,9). Some people found that the complete inactivation of aldosterone could result in hyperkalemia, which was frequently accompanied by hyponatremia (10). Kazuo *et al.* (7) thought that *in vivo* the shift or leakage of potassium was the main factor causing NOHK and was negatively associated with gestational age and postnatal age.

We found in our case a decreased serum calcium as serum potassium decreased which did not change at the same time, and higher serum phosphorus was also noted. Thayyil *et al.* (11) found that the abnormality of serum calcium was earlier than that of serum potassium in very low birth weight infants with NOHK. Fukuda *et al.* (12) found that hypocalcemia was more common in preterm infants who had serum potassium >7 mmol/L. The pathogenesis of combination of hypocalcemia and increased serum phosphate may raise the possibility of a transient hypoparathyroidism (2). Whereas PTH was at normal level in our case. We think that it is unlikely that all biochemical abnormalities were merely a coincidence. Associated risk factors for NOHK in late preterm infants have not been identified. In this case, the baby had no extra potassium intake and blood transfusion before the onset of hyperkalemia. Serum sodium was at normal level. Severe birth asphyxia was the only factor for the development of

NOHK in this case (13). We think that the biochemical abnormalities in this baby were due to decreased potassium transport towards the intracellular space resulted from birth asphyxia, but in a study by Thayyil *et al.* (11), no any association with Apgar scores or gestation with hyperkalemia was found. Asphyxia might also influence the activity of calcium related enzyme on cell membrane. This has not previously been reported in the literature and might be useful in recognizing late preterm infants likely to be developing NOHK.

Neonatal hyperkalemia could result in cardiac arrhythmias and has been associated with the development of periventricular leukomalacia, brain hemorrhage and sudden death (7). The head MRI (*Figure 1*) showed abnormal high signal in periventricular white matter, and it was much more obvious in DWI than in T1WI which predicts poor outcome. Rutherford *et al.* (14) recommended that DWI is a clinically useful for the early identification of ischaemic tissue in the neonatal brain.

As neonatal hypoxia and neonatal hypoglycemia all contribute to brain injury, one should separate the injuries of the two factors on the basis of the imaging appearance. Barkovich *et al.* (15) found that the pattern of brain damage in neonatal hypoglycemia was mainly localized primarily to the parietal and occipital cortex of the brain, whereas the common types of injury in the preterm brain from ischemia are intraventricular hemorrhage (IVH) and periventricular white matter injury. As no hypoglycemia was recorded, we speculate that abnormal neurologic activities on admission and brain MRI findings of the baby were due to severe birth asphyxia which resulted in the disturbance of electrolytes in the following days.

The treatment of hyperkalemia in infants varies among institutions and limited information from small studied of uncertain quality on therapeutic for intervention of NOHK. The treatment indication for preterm infants with NOHK is not unified at present. Chevalier (16) thought that therapy should be initiated when serum potassium was greater than 7 mmol/L in a non-hemolysed arterial or venous blood sample, because the risk of cardiac arrhythmia in non-oliguric hyperkalemia of premature infants increased substantially at this level. Serum potassium below 7 mmol/L in the presence of characteristic electrocardiogram changes was also an indication for therapy. Whilst most clinical experience suggests that serum potassium above 6.5 mmol/L should begin treatment regardless of the electrocardiogram changes. Based on our experience, insulin with glucose in the absence of arrhythmia was used if serum potassium

was greater than 6.5 mmol/L. Calcium gluconate was admitted if characteristic electrocardiogram developed. Mildenberger *et al.* (6) preferred causal treatment rather than administration of sodium bicarbonate for the relief of metabolic acidosis. The limitations of this report were that the creatinine clearance and functional excretion of Na and K were not calculated to understand the renal function.

Concerning for the prevention of NOHK, it was reported that antenatal glucocorticoid could promote Na/K-ATP enzyme maturation and could effectively prevent premature with NOHK (17,18), whilst it was unclear in infants resulted from birth asphyxia.

In conclusion, NOHK mainly affects very low birth weight or extremely low birth weight infants and is associated with other electrolyte disturbances with high morbidity and mortality. NOHK in term or late preterm infants was rarely reported. A future study with larger samples is needed.

### Acknowledgements

None.

### Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

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