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Case Report

Nursing Care of an Extremely Preterm Infant with Sodium Taurocholate Cotransporting Polypeptide Deficiency: A Case Report

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Abstract: Sodium taurocholate cotransporting polypeptide (NTCP) is a protein encoded by the solute carrier family 10 member 1 gene and expressed in the basolateral membrane of the hepatocyte to uptake conjugated bile acids from the plasma. This study reported an extremely premature infant (EPI) with NTCP deficiency (NTCPD). The patient presented with jaundice, persistently elevated total bile acids, 25-(OH)-VitD deficiency, and cleft palate. Nursing care mainly focused on disease surveillance, jaundice care, nutrition, kangaroo mother care, and psychological care. In response to 5 months of the nursing care, the infant's weight reached 3.324 kg, the jaundice was alleviated, and the infant gained the ability to suck milk. However, his TBA levels were abnormally elevated, and 25-(OH)-VitD was still deficient when the patient was discharged from hospital. The nurses taught the patient's parents the importance of monitoring liver function and trace elements during a routine outpatient visit. Telephone follow-up 1 year later showed that the patient was in good health with no obvious clinical manifestations. This article reports our experiences in caring for an EPI with NTCPD. To the best of our knowledge, this is the first case report worldwide in NTCPD nursing care.

Keywords: Extremely Preterm Infant (EPI), Sodium Taurocholate Cotransporting Polypeptide (NTCP), Care, *SLC10A1*

1. Introduction

Sodium taurocholate cotransporting polypeptide (NTCP) is the transmembrane transporter to uptake mainly conjugated bile salts in the basolateral membrane of hepatocytes. NTCP serves a key role in the primary transporter of conjugated bile from the portal venous circulation into hepatocytes [1-3]. In 2015, Vaz [4] *et al* reported the first NTCP deficiency (NTCPD) in a patient who presented extremely elevated total bile acids (TBA) in plasma, mild hypotonia, growth retardation, and delayed motor milestones. Subsequently, several patients with NTCPD have been reported, with the primary manifestation of persistently elevated TBA [3, 5-14]. By March 2020, a total of 43 patients with NTCPD were reported. However, there was as yet no nursing research on the care of NTCPD patients.

The patient in this article was an extremely premature infant (EPI) on admission. During hospitalization, the patient exhibited persistent and marked hypercholanemia and cholestatic jaundice for 2 months. Thus, solute carrier family 10 member 1 (*SLC10A1)* gene analysis was performed. As a result, the patient was found to be a homozygote of the variation c. 800C > T (p. Ser267Phe). Special care for EPI with NTCPD was provided, including jaundice care, surveillance, nutrition, kangaroo mother care (KMC), and psychological care.

2. Case Description

The patient was delivered via caesarean section in the Third Affiliated Hospital of Southern Medical University at the gestation age of 27 weeks and 5 days. The Apgar score was 8 points at 1 minutes, and 10 points at 5 minutes after umbilical ligation, with a birth weight of 1.02 kg, length of 39 cm, and head circumference of 28 cm. The patient was apneic soon after birth, and was given continuous positive airway pressure, mechanical ventilation, and curosurf via a tracheal tube. For further treatment, the patient was transported into the First Affiliated Hospital of Jinan University by ambulance when aged 82 minutes. As the first child of a non-consanguineous couple, his parents reported no knowledge of a family history of hereditary or infectious diseases.

On physical examination on admission, the patient had a body temperature (T) of 36.8°C, heart rate (HR) of 139 beats/min, respiratory rate (RR) of 65 beats/min, blood pressure (BP) 37/15 mmHg, weight (WT) 1.02 kg, and height 39.0 cm. A cleft palate was noticed. There was no abdominal distention, and his liver and spleen were not enlarged.

After admission, he was immediately connected to a ventilator for Synchronized Intermittent Mandatory Ventilation mode assisted ventilation, and his oxygen saturation (SPO_2) was maintained between 90% and 95%. Umbilical artery and vein catheterization were performed, normal saline was given (10 mL at 20 mL/h for static drip expansion), and dopamine 5 μg/kg/min was given to improve and maintain normal circulation. Appropriate measures were taken to keep the infant warm and prevent hypothermia. At age 2 days, jaundiced skin and sclera were noticed, and the jaundice progressed. A liver function test found that the serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), γ-glutamyl transpeptidase (GGT), alkaline phosphatase (ALP), total bilirubin (TBIL), direct bilirubin (DBil), and indirect bilirubin (IBIL) were increased, indicating cholestatic jaundice (Table 1). Intravenous levocarnitine (26 mg/kg/d) and oral ursodeoxycholic acid (11 mg/kg/d) were used to relieve cholestasis. As a result, his jaundice was alleviated gradually, but his liver function remained abnormal (Table 1), especially marked and intractable TBA elevation, the highest level 145.2 μmol/L (reference range: 0-10 μmol/L) (Table 1). Therefore, at 2.5 months, *SLC10A1* analysis was performed to evaluate the possibility of NTCPD. Sanger sequencing of the *SLC10A1* gene demonstrated that the patient and his father were both homozygotes of the variant c. 800C > T (p. Ser267Phe). The serum level of total 25-(OH)-VitD 14 ng/mL (reference range: 30-100 ng/mL) was observed, and D3 drops (10 unit/d) and Moss vitamin D_3 drops (0.25 μg/d) were given to the patient. On the 124th day after birth, a special nipple was used to exercise the infant's sucking function. The patient was discharged at the age of 5 months, when physical examination showed the patient's T 37.1°C, HR 123 beats/min, RR 34 beats/min, BP 95/46 mmHg, WT 3.324kg, and milk volume 62 mL/3h, including oral feeding 30 mL/3h. His liver function improved, with a serum TBA of 114.7 μmol/L and 25-(OH)-VitD of 7.95 ng/mL. During the subsequent follow-up over 20 months, the patient showed normal neurobehavioral and anthropometric development. The patient continues in follow-up to determine long-term outcome.

Table 1. *Biochemical indices of the patient.*

Biochemical Indices	1D	11D	25D	41D	63D	77D	92D	105D	148D
ALT (5-40 U/L)	7	4	25	213	459	107	62	106	89
AST (5-40 U/L)	85	38	81	279	306	179	141	241	141
GGT (8-50 U/L)	397	127	93	164	104	86	80	78	100
Alb (35.0-55.0 g/L)	38.2	32.3	33.3	30.5	34.5	32.3	31.6	45.2	38.6
Tbil (2-19μmol/L)	46.1	241	206.2	256.1	382.5	352.7	387.1	540.8	181.2
Dbil (0-6μmol/L)	10.5	57.9	133.8	180.6	285	183.6	196.6	394.1	108.3
Ibil (2.56-20.9μmol/L)	35.6	183.1	72.4	75.5	97.5	169.1	190.5	146.7	72.9
TBA (0-10μmol/L)	5.8	36.7	73.5	103.5	102.6	145.2	69.6	123.4	114.7

D, days; ALT, alanine transaminase; AST, aspartate transaminase; GGT, gamma-glutamyl transpeptidase; Alb, albumin; Tbil, Total bilirubin; Dbil, direct bilirubin; Ibil, indirect bilirubin; TBA, total bile acids; not tested.

3. Nursing Management

An EPI has a 30% to 50% higher risk for death and disability [15]. EPI is a complicated disease, and our management of patients was constantly changing as symptoms changed. EPI results in numerous physiologic changes and increased physical demands on the body that could complicate the chronic disease state. High rates of temperature instability, respiratory distress, jaundice, feeding difficulties, and apnea make the daily tasks of routine care for an EPI with NTCPD more difficult to complete. For an EPI with NTCPD, it is crucial to be aggressive with needed treatments and interventions to promote positive outcomes for the neonate. During the hospitalization of this patient, we gained nursing experience of the care of an EPI with NTCPD. The purpose of the following case report is to present an overview of the nursing care of an EPI with NTCPD.

3.1. Surveillance

The infant was an EPI with rapid changes in his condition and incomplete respiratory function; thus, it was very important to constantly observe the patient's condition.

Auscultation was performed every 2 hours to determine whether the breath sounds in both lungs were symmetrical and the fluctuation of the bilateral thorax was consistent. The respiratory monitor was used to monitor the breathing

condition of the infant at any time. We set up a special assessment form to observe the vital signs, reaction, complexion, skin color, suckling, vomiting, limb movement, and limb temperature of the infant once every 15 minutes and record them. The day-to-day record could provide a summary of the patient's medical treatment. These records could also serve as a database to understand more about whether the patient's response to therapy was relative to patients with NTCPD. If the infant's vital signs were abnormal, corresponding nursing measures were immediately taken, and the physician was informed in a timely manner. In addition, rescue articles and medicines such as a vacuum aspirator, oxygen, and simple breathing apparatus were always kept on standby.

3.2. Jaundice Care

Jaundice care is directed toward the prevention and treatment of nuclear jaundice. First, phototherapy is essential components of jaundice care throughout the treatment. Protection of the infant's eyes and the nurse chose a suitable eye mask for the infant is very important. Secondly, The patient was often given glycerin enemas to facilitate meconium evacuation and alleviate jaundice. Thirdly, the patient was closely monitored whether extinction of xanthochromia in sclera and skin, the colour of sclera and urine, and the serum levels of IBIL, liver function and other biochemical indicators were turned to normal. These were essential components of care throughout the jaundice care period.

3.3. Maintaining Body Temperature

To prevent the patient with EPI from becoming hypothermic, a temperature probe was placed on the abdomen to monitor his temperature. The patient's body was covered with a polyethylene warming blanket, and the patient wore a hat to prevent heat loss from the head. Until the patient's condition was stable, he remained in the warming box, and a humidity meter was placed to monitor the temperature and humidity in real time. The warming box was set at 35°C, with 60%-80% humidity, and the skin temperature probe is maintained at 36°C-36.5°C. When the air temperature changes due to opening of the warming box, the premature infant has to adapt to the new environment for at least 30 to 60 minutes to reach a thermal balance [16]. Thus, it is very important to try to keep the temperature constant by avoiding frequent opening of the warming box.

3.4. Nutrition

Nutrition is an essential aspect when caring for an EPI. Nutrition is also important for patients with NTCPD, because there are affected by varying degrees of hepatic insufficiency, which results in malabsorption of fat-soluble vitamins A, D, E, and K. However, a cleft palate adds an additional challenge to providing adequate nutrition. With an estimated increased need for nutrition, adequate nutrition was achieved through enteral feeds, parenteral nutrition, oral feeding, and medication.

The nursing staff assessed the serum level of fat-soluble vitamins and supplemented as needed. The patient had 25-(OH)-VitD deficiency; thus, vitamin D supplementation was necessary. Medicine was used to strictly control the patient's 25-(OH)-VitD deficiency.

An indwelling oral-nasal gastric tube was placed. The patient had a large amount of residual gastric juice in the stomach 1 to 4 days after birth; thus, feeding was suspended and the nutrient solution was injected through the vein. Sixteen days after birth, the residual amount of gastric juice in the stomach was reduced and began to feed milk. Nasal feeding via a gastric tube was performed as follows: 1-5 mL every 2-3h. Before the patient was fed, the residual quantity of milk in the stomach was extracted through the gastric tube. If the residual quantity was greater than 1/3 of the last feeding quantity, the feeding was stopped for 1 time. When the feeding amount was more than 47 mL/h, the residual amount in the stomach was less than 5 mL, and no reflux occurred, the infant used a special nipple to feed. At 123 days after birth, a special nipple for infants with cleft palate was used for sucking function exercises, once every 3-4 hours. It is usual for the infant to demonstrate evidence of dysphagia (eg, coughing, choking, difficulty swallowing, desaturation with oral feedings), and such signs should be considered while feeding. Therefore, Nurses monitored the color of the skin and mucous membrane, as well as the infant's SpO_2, and observed the respiratory rate and rhythm. When the patient sucked too fast, he was as risk for hypoxia and respiratory distress. In that case, the nurse immediately stopped feeding, pulled out the nipple, and let the patient rest. After continuous oral feeding training, the sucking ability of the patient gradually improved, his non-nutritive suckling volume increased from 5 mL/3h to 30 mL/3h, and his SpO_2 was above 85% without dyspnea. On discharge from the hospital, a nurse instructed his parents on how to use the special nipple and told the patient's family to take him to the oral surgery department for follow-up.

3.5. KMC

At present, KMC as an effective method of nursing that has been gradually promoted in China. Before the implementation of kangaroo care, the patient was evaluated to determine whether he was stable and could be held. The patient's endotracheal tube was removed and informed consent for KMC was obtained from the family. We prepare the ward by having only quiet voices, and the room temperature is maintained at 25°C -28°C. The lights are adjusted to reduce infant stimulation. The mother or father can request music to relax the body and mind. The infant is placed on the exposed chest and abdomen of the mother or father. The infant is kept in an upright position with his head turned to one side. The parent should gently touch and whisper to the infant, so that he can feel his parent's temperature, breathing, and voice, to promote parental bonding. During KMC, the condition of the newborn was observed at all times, and attention was paid to observe whether the patient had lip cyanosis. If cyanosis was found, the KMC was stopped immediately, and the patient was

given an oxygen mask.

3.6. Psychological Care

With the constant change of nursing concepts, medical staff and parents of premature infants are fully aware of the importance and necessity of psychological care. NTCPD is caused by a genetic defect that the infant will have for life. Further, because there is little reported about NTCPD, the family members of the patient may became very anxious and isolated, worried about the prognosis of the infant, which may even result in an unnecessary operation [12]. In addition, financial difficulties may arise as a result of the EPI-related health issues. Therefore, it is necessary for nurses to assess all aspects of the psychological care of the patient's parents. When meeting with the patient's parents, we patiently listen to their concerns and offer help and guidance. We provide information about NTCPD to alleviate their anxiety. The primary manifestations of NTCPD are persistently high TBA [10], neonatal jaundice [12], and fat-soluble vitamin deficiency [4]. In addition, some female patients will have increased TBA during pregnancy [7]. A full understanding of the clinical manifestations of the disease remain is still being investigated, and new evidence must be observed and accumulated. The treatment lacks a definite plan. Thus, the patient should attend follow-up every year to check for changes of liver function.

4. Discussion

The World Health Organization (WHO) regards neonates born before 28 weeks of gestation as EPIs. It is well known that with technological advances and the collaboration of neonatologists, EPIs now have increased survival and improved outcome [15]. In this case, so far as we know, this patient was the youngest patient with NTCPD recorded to date. He presented with hypercholanemia in the neonatal period. And, the elevated serum levels of IBil and TBil suggested that the patient had cholestatic jaundice (Table 1). Furthermore, the patient was noted to have a cleft palate and 25-(OH)-VitD deficiency. Therefore, specialized and individualized care of this EPI was initiated immediately.

Any change in the patient's condition should be noted as soon as possible. Concentrating on improved monitoring, particularly respiratory parameters, can help in the recognition of a deteriorating patients [16]. This patient was an EPI, and his alveolar development was immature, requiring tracheal intubation to assist ventilation. Thus, a timely, accurate record of the changes in vital signs could prevent a decline in the patient's condition and help to identify early risk signals, such as carbon dioxide retention.

In the enterohepatic circulation, bile acids are synthesized in the hepatocyte, excreted into the biliary tree, and enter the intestine, where 5% of the bile acids are excreted with feces and 95% of the bile acids are reabsorbed from the intestine and then transported back to the liver via the portal venous circulation. The bile salt cycle is called enterohepatic circulation [17]. Due to the impaired function of sodium-dependent bile acid in hepatocytes of patients with NTCPD; thus, these patients could have plasma bile acid is increased and jaundice [10, 14]. In this case, the patient appeared jaundiced after birth.

Appropriate temperature intervention strategies can effectively prevent the occurrence of early hypothermia in premature infants, improve the quality of life of premature infants, and reduce early complications [18]. The 2015 neonatal resuscitation guidelines clearly suggest that premature infants should avoid overheating during resuscitation or when keeping warm [19]. Therefore, nursing staff must know the physiological characteristics of premature infants and the possible problems in the process of keeping infants warm. Nurses should take timely and effective scientific measures to reduce the risk of complications caused by hypothermia and promote the recovery of premature infants.

The main physiological function of bile acids is to promote the absorption of lipids and fat-soluble vitamins A, D, E, and K in the intestine [20]. The high content of bile acids in the blood of the patients could decrease bile acids in the intestinal circulation, which results in weak absorption of lipids and fat-soluble vitamins in the intestinal tract. Therefore, some NTCPD patients develop fat-soluble vitamin deficiency. However, The patient was still 25-(OH)-VitD deficiency until discharge. Therefore, for this patient, 25-(OH)-VitD deficiency cannot be ignored.

Cleft palate is a congenital malformation caused by errors in the fusion process of the embryonic face. Changes in the anatomy of the infant lead to impaired swallowing and feeding difficulties. Thus, the growth and development of an infant with a cleft palate was lower than the standard [21]. Furthermore, the early feeding of children with cleft palate is correlated with the success of surgery and the patient's prognosis [22]. Therefore, it is very important to master the correct feeding method to maintain the normal growth and development of patients. The infant required a special feeding device because he could not generate adequate negative intraoral pressure to suck milk. Until the infant grows up, palatoplasty is important for the development of normal speech in children who have cleft palate. As with every infant with cleft palate, the first year of life means frequent visits to the pediatrician to decide when to perform surgery. Therefore, focus should be placed on the patient's nutrient intake to maintain normal growth and development.

KMC is a term used for skin-to-skin contact between an infant and caregiver; it is a low-cost alternative to incubator care [23]. According to articles, KMC can improve and stabilize the vital signs of newborns, reducing the risk of increased morbidity and mortality [24]. However, Virginie Andres *et al* [25] reported six cases of newborn infants who died of asphyxiation due to respiratory obstruction while undergoing KMC. For this patient, because he had a cleft palate, he could not coordinate sucking and swallowing. Thus, the contact he could not get from breast feeding was replaced by the skin-to-skin contact of KMC. Therefore, it is very important to do a good job of neonatal assessment before the

implementation and strengthen the monitoring during the implementation of KMC.

5. Conclusion

In this case report, we demonstrated the care plan of an EPI with NTCPD. The management of the patient was based on his individual presentation and condition. Surveillance, body temperature nursing, jaundice care, nutrition, and KMC are vital to patient outcomes. For the family members of the patient, it is crucial to provide psychological care, which is helpful to ease their anxiety. At present, there have been limited reports of patients with NTCPD. All nursing staff and medical staff need to do their best to fight this disease.

Conflict of Interest

All the authors do not have any possible conflicts of interest.

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