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Progress in Nursing Care of Neonatal Bilirubin Encephalopathy

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Abstract: Bilirubin encephalopathy (BE) is the most serious complication of hyperbilirubinemia, which can cause neurological damage and even death in children. With the development of neonatal medicine, people have a certain degree of understanding and recognition of BE, and the damage caused by BE has been paid more and more attention. In order to prevent or reduce the degree of damage to the nervous system caused by BE, research can be conducted through the pathogenesis of the disease, early diagnostic methods and interventions, etc. Therefore, this article introduces an overview of BE and elaborates on the mechanisms of BE, risk factors, and nursing care, etc., so as to provide references for healthcare professionals to carry out nursing care practices for the prevention of BE in the future and to carry out research related to BE, so as to reduce the hazards of the disease on newborns, improve the quality of life of newborns.

Keywords: Bilirubin encephalopathy; Risk factors; Nursing measures

Introduction

Neonatal hyperbilirubinemia NH is characterized by elevated unconjugated bilirubin. Without timely and effective intervention and treatment, plasma bilirubin can cross the blood-brain barrier and be deposited in the central nucleus accumbens, leading to bilirubin encephalopathy (BE), with 2/3 of survivors having permanent neurological sequelae or even life-threatening. permanent neurologic sequelae and even life-threatening. Neonatal BE is the most serious complication of NH, with high mortality and disability rates, poor prognosis, and one of the most prominent public health problems worldwide. Reports have shown that BE is among the top 3 causes of neonatal disability and death[1] . The incidence of neonatal BE is not high in developed regions abroad; the incidence of BE in Europe and the United States is (7-45)/100,000, and studies in Canada have shown that it is even higher[2-3]. In China, especially in certain economically and medically underdeveloped areas, the lack of a comprehensive follow-up mechanism for neonatal NH has led to a high incidence of BE. 2012, the Neonatology Group of the Chinese Medical Association's Pediatrics Branch analyzed the clinical characteristics, treatment, and prognosis of 348 children with BE in 28 tertiary hospitals across China, and concluded that BE is still not uncommon in China[4].DIALA[5] suggested that The high incidence of BE is largely due to delays in seeking treatment. Delayed diagnosis and intervention may put neonates at risk for neurologic dysfunction, which may lead to chronic or permanent neurologic damage and sequelae, especially in neonates who are susceptible to hearing damage[6-7]. Some studies have shown that sepsis, metabolic acidosis, peak total bilirubin (TSB), and total bilirubin/albumin (bilimbin/albumin, B/A) are the main causes[8]. With the development of society and the advancement of medical technology, more and more attention has been paid to BE, and more advanced diagnostic techniques and more effective care measures are expected to appear. In this paper, we will review neonatal BE around the relevant concepts, occurrence mechanisms, risk factors and nursing measures of neonatal BE, which will provide reference for healthcare professionals to carry out the prevention of BE in the future.

1.Overview of neonatal BE

1.1The concept of neonatal BE

Neonatal BE, also called neonatal kernel jaundice, refers to acute brain damage in newborns brought about by the toxic effects of bilirubin, resulting in severe neurological sequelae and even causing death of the child[9]. Survivors usually also suffer from neurological sequelae such as oculomotor disorders, hearing loss, mental retardation, and cerebral palsy[10].The main clinical manifestations of BE are typical encephalopathic symptoms, and the lesions of BE mainly focus on basal ganglia region lesions, and the most typical pathological changes are symmetric bilateral pallidum involvement. Therefore, early recognition and prevention are of great significance for the recovery and prog-

nosis of BE, which has a high incidence in the neonatal population and seriously affects the growth and development of newborns, and often imposes a huge mental and economic burden on the children themselves and their families, as well as adversely affecting the quality of the population[11].

1.2 Diagnostic criteria for neonatal BE

① Magnetic resonance imaging (MRI) is a non-invasive technique that is very reliable as a diagnostic tool for brain diseases, providing excellent soft tissue contrast and high-resolution anatomical details of the brain, comprehensive brain function metabolism, and multi-parameter information without radiation, and has the advantages of non-invasiveness, safety, and high diagnostic value in the diagnosis of neonatal central nervous system disorders[12-13].MRI examination can be used in the early monitoring of BE, which helps early diagnosis, early treatment, and prevention of sequelae.BE is most likely to involve the pallidum, especially the posterior part of the pallidum. Sahoo et al[14] concluded that the occurrence of symmetric T1WI high signal in the bilateral pallidum has a close relationship with the level of jaundice, and Wu et al[15] examined the pallidum visually by T1-weighted imaging (T1WI) images, standardized T1WI sequence Semi-quantitative method of the ratio of signal intensity values of the superior pallidum, the underlying thalamus and the frontal lobe and the use of deep learning methods based on the Res Net 18 framework of deep convolutional neural networks, the study showed that artificial intelligence can improve the accuracy of image feature extraction and the accuracy of disease diagnosis, according to the signal intensity of the T1WI and T2WI, as well as having a characteristic manifestation in conventional MRI, which can be used as a method for early diagnosis and judging the According to its T1WI and T2WI signal intensity and its characteristic manifestation in conventional MRI, it can be used as a non-invasive means of early diagnosis and prognosis, which is of great significance in reducing the occurrence of sequelae. ② Detection of unbound serum bilirubin (UB)， Since BE is caused by elevated UB, the detection of UB in serum is a simple and economical test. Studies have shown that UB can be measured by high-performance liquid chromatography-ultrasensitive thermal lens spectroscopy and capillary electrophoresis, but these two methods cannot be applied to the clinic at present[16-17].Iman et al[18] proposed that the B/A ratio is a better estimator of BE than UB, and the American Academy of Pediatrics guideline recommends this method for the prediction of BE[19]. Because only UB can penetrate the blood-brain barrier and neuronal cell membranes to produce neurotoxicity, it is crucial to monitor UB levels. A study by Khairy et al[20] suggests that those with abnormal cord blood B/A ratio, total bilirubin, and albumin indices need to be alerted to the occurrence of BE. There are many domestic studies applying this method of prediction, and it is believed that the occurrence of BE is related to the B/A ratio, and the higher its ratio, the higher the possibility of BE, which is positively correlated[21]. At present, there is no uniform standard for the B/A ratio in China, and a foreign study showed that when B/A≥8.9 mg/g, it can indicate a higher risk of developing BE[22].

2. Mechanisms and risk factors of neonatal BE occurrence

2.1 Mechanisms of neonatal BE

The pathogenesis of BE is not yet clear, but it is clear that bilirubin neurotoxicity is mainly caused by free unconjugated bilirubin. ① In neonates, unconjugated bilirubin (UCB) is produced after the destruction of erythrocytes, and most of it binds to plasma albumin to form a bilirubin-albumin complex, which is transported to the liver and transformed into conjugated bilirubin after a series of metabolism, but some of the UCB does not bind to albumin and is free in intravascular and extravascular tissues, i.e., free bilirubin. binds to albumin and remains free in intravascular and extravascular tissues, i.e., free unconjugated bilirubin (Bf)[23]. Normally, this state is balanced, but in some pathological conditions, the UCB content exceeds the plasma albumin binding capacity, and an imbalance occurs, and the main mechanism of its damage is to reduce the activity of synaptic membrane Na ＋ -K ＋ -ATP ase of neuronal cells, and the Na ＋ pump function fails, resulting in a decrease in the level of cellular energy metabolism, which in turn will have a toxic effect on the central nervous system. ② Oxidative stress, gene expression regulation and excitotoxicity are recent hot spots in the study of the mechanism of neonatal BE. Oxidative stress means that the body's ability to produce reactive oxygen species or reactive nitrogen species exceeds the antioxidant defense capacity. The physiological level of bilirubin in the body is a potent antioxidant that prevents lipid peroxidation, while high concentrations of UCB through the blood-

brain barrier can induce oxidative stress, which can cause cerebellar DNA damage, and can cause neurological damage[24]. ③ For the study of gene expression regulation, Vianello et al[25] found that gene expression changes caused by acetylation/deacetylation of gene promoters may cause neurological dysfunction leading to brain damage in an animal model of hyperbilirubinemia. The gene regulation theory is a new theory of bilirubin neurotoxicity in recent years, and due to the difficulty of the study, there is less research data. ④ Excitotoxicity refers to neuronal excitotoxicity, which leads to neurological damage in BE patients. Because neuronal cells are rich in myelin, which binds strongly with bilirubin, neuronal cells are more susceptible to damage by bilirubin, and become the target of bilirubin toxicity. Calcium plays a more important role in this, so maintaining intracellular calcium homeostasis is crucial for neuronal survival.

2.2 Risk factors for neonatal BE

Risk factors for neonatal BE are broadly categorized into 4 groups: infection, metabolic acidosis, sepsis, and others. ① Infection: neonates are susceptible to infectious diseases, which often lead to dysfunction of the blood-brain barrier as well as severe jaundice, resulting in oxygen deficiency and decreased activity of bilirubin metabolizing enzymes in the affected children. In this case, neonatal bilirubin is highly susceptible to penetrate the blood-brain barrier, thus inducing BE[26]. Lin Yanping[27] showed that infection can destroy the immature blood-brain barrier, but also affect the rate of bilirubin production, energy metabolism of brain tissue, which will further aggravate the susceptibility to brain injury. Liu Fang et al[28] suggested that the risk of BE in full-term children with severe hyperbilirubinemia due to infectious factors increased by 8.7-15 times. ② Metabolic acidosis: it can cause increased regional cerebral blood flow, increased opening of the blood-brain barrier, and hypoxia can also inhibit the binding of UB to albumin and increase the level of UB, and bilirubin can easily cross the blood-brain barrier, which can cause neurological damage[29]. ③ Sepsis: as a risk factor for neonatal BE because pathogens cause oxidative stress in the body and affect liver enzyme activity. In addition, the infection can damage the blood-brain barrier and increase the permeability of the blood-brain barrier, and free bilirubin enters the brain tissue through the blood-brain barrier, aggregates and deposits in the brain cells, causing BE[30]. Some studies have found that neonatal combined sepsis can be a risk factor for BE[31]. ④ Others: peak total bilirubin, neonatal hemolytic disease, G-6-PD deficiency, and craniocerebral hematoma also increase the incidence of neonatal BE[32-35].

3. Neonatal BE care measures

① Prevention of infection: neonates have immature organ and system development, are susceptible to pathogens, and have a higher probability of infection[36-37], so it is important to strengthen the cleanliness and disinfection of the ward environment, keep the air in the ward fresh, and disinfect and clean the floors, instruments, and supplies in the ward. It has been reported that the proportion of nosocomial infections caused by poor hand hygiene is high[38]. It is necessary to strengthen the hand hygiene management of healthcare personnel, strictly implement the hand hygiene system, and strictly implement the indication of hand washing or hand disinfection. In addition, strict compliance with the principle of aseptic technical operation, good skin, umbilical cord, oral cavity, eye special care, gentle movements, avoid damage to the skin and mucous membranes, to reduce the risk of infection[39]. Tu Yangyang[40] pointed out that strengthening breastfeeding education and guidance is conducive to the prevention of BE, improve the immunity of newborns, breastfeeding as early as possible, and enhance the nutrition of newborns. ② Metabolic acidosis: informed that if mothers feed their preterm infants with casein-based cow's milk or formula, the phenylalanine and methionine content of casein can increase the concentration of phenylalanine and methionine in the blood, and blood urea nitrogen and blood ammonia are also significantly increased, which can lead to the formation of acidosis[41]. Therefore, it is necessary to feed the children reasonably, closely observe the children's response and milk consumption, and when applying sodium bicarbonate to correct acidity, if the overdose can lead to metabolic alkalosis, which is manifested as shallow and slow respiration, pulse irregularity, and convulsions of the hands and feet. ③ Touch care: early implementation of rehabilitative nursing interventions is of great significance in reducing bilirubin levels and improving prognostic outcomes in children[42]. Before contacting the child, the operator should wash and warm the hands, and then stroke the child's buttocks, back, limbs, head, chest and abdomen in turn, and the method can be taught to the child's parents, so that it is easy for the child to carry out stroking massage at home after discharge from the hospital, and Fang Fengmei[43] found that stroking can promote the metabolism of newborn babies, accelerate intestinal peristalsis, and reduce the reabsorption of bilirubin.

4. Summary

At present, the danger of BE to newborns has attracted more and more attention from all walks of life, and more and more studies on the prevention of BE have been conducted in recent years. Since neonates are not yet well developed, UB can easily cross the blood-brain barrier and cause diseases, and there are many related risk factors, so it is necessary to consider the medical region and the individual differences of the children, and combine with the wishes of the children's families to provide appropriate care measures for the children. By increasing the knowledge of neonatal parents about neonatal BE, early detection and treatment can be realized to reduce the neurological damage of the disease and promote the recovery of the children.

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