Influencing Factors and Countermeasures of Neonatal Brain Injury

Danfeng Li, Wenqing Kang, Yinsen Song, Yaodong Zhang, Lei Zhao*

ABSTRACT

This study probes into the occurrence of neonatal brain injury, explores the influencing factors of neonatal brain injury and puts forwards relevant suggestions, with a view to providing scientific basis for clinical effective preventive measures. The study selects 225 neonates admitted to Neonatal Intensive Care Unit (NICU) from March 2016 to May 2017 in Zhengzhou Children's Hospital and collects the related clinical data and the results of cranial magnetic resonance imaging (MRI) for single factor chi-square test and binary logistic regression analysis using SPSS statistical software. The incidence rate of neonatal brain injury is 37.8%. Chorioamnionitis in pregnant women, mechanical ventilation during the neonatal period, and neonatal infection are independent risk factors for neonatal brain injury, while cesarean delivery is its protective factor (P<0.05). Risk factors for brain injury include chorioamnionitis in pregnant women, mechanical ventilation in the neonatal period, and neonatal infections, thus it is necessary to pay attention to the high-risk neonates before, during and after delivery, and take intervention measures to reduce the incidence rate of brain injury so as to improve the life quality of neonates.

Key Words: Neonate, Brain Injury, Influencing Factor, Countermeasure.

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Introduction

In recent years, the survival rate of neonates has been on the rise with the improvement of medical technology and treatment capabilities. However, the incidence rate of neurological sequelae such as brain injury, cerebral palsy, and mental retardation caused by various reasons before and during or after delivery is also gradually increasing (Longo and Hankins, 2009). Neonatal brain injury is one of the major diseases causing neonatal death and pediatric disability in China, which imposes a heavy burden on families and society. How to detect and reduce the incidence rate of neonatal brain injury early and improve the quality of life of neonates has become an urgent issue in public health. Therefore, this study investigates the incidence rate of neonatal brain injury in Zhengzhou City and screens its relevant influencing factors in order to provide a basis for effective prevention and treatment in clinics for medical staff. The report is provided as follows.

Methods

Subjects

The neonates admitted to Neonatal Intensive Care Unit (NICU) from March 2016 to May 2017 in Zhengzhou Children's Hospital are selected as subjects. Selection criteria: age of 0-28 days; informed consent of legal guardians; exclusion of neonates with congenital metabolic diseases, bilirubin encephalopathy, and gastrointestinal malformations. A total of 224 neonates are selected as subjects.

Corresponding author: Lei Zhao
Address: Henan Key Laboratory of Childhood Genetic Metabolism, Children's Hospital Affiliated to Zhengzhou University, Zhengzhou 450018, China
e-mail ✉ 869719212@qq.com
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Research methods

The clinical data are collected by a unified trained investigator of the department of neonates by referring to case files, mainly including:

(1) Basic information of neonates: sex, gestational age, birth weight, etc.;

(2) Prenatal status: parity (multiparity/primiparity), single/multiple pregnancy, with or without chorioamnionitis in pregnant women, premature rupture of membranes, etc.;

(3) Delivery status: Delivery mode (natural delivery /cesarean delivery), with or without amniotic fluid contamination, etc.;

(4) Post-natal status: with or without apnea, neonatal infection, whether to carry out mechanical ventilation or not, etc.;

(5) Diagnosis of children with brain injury based on cranial MRI findings of neonates.

Statistical methods

SPSS 17.0 software is used for statistical analysis, the statistical description of the enumeration data is represented by the rate and the comparison between the rates of the different groups is performed using the chi-square test. All the statistically significant variables in the single factor analysis are included in a binary logistic regression model to screen for related factors affecting neonatal brain injury. The difference of $P < 0.05$ is statistically significant.

Results

General situation

Among 225 neonates, there are 115 males (51.1%) and 110 females (48.9%), with a male to female ratio of 1:0.96; there are 89 full-term infants(39.6%); the average gestational age is (34.1±1.5) weeks, and birth weight ranges from 0.9 to 3.1kg, with an average birth weight of (1.8±0.5) kg; there are 132 cases of primiparity (58.7%), 40 cases of multiparity (17.8%), 168 cases of cesarean delivery (74.7%) and 57 cases of natural delivery (25.3%). The other information is detailed in Table 1.

Comparison of the incidence rate of brain injury in neonates with different characteristics

Among 225 neonates, there are 85 cases of brain injury, accounting for 37.8%. The incidence rates of brain injury in neonates with different characteristics, including gestational age, birth weight, parity, chorioamnionitis in pregnant women, premature membrane rupture, delivery mode, amniotic fluid contamination, mechanical ventilation and neonatal infection, is different, and the difference is statistically significant ($P<0.05$). Details are shown in Table 2.

Table 1. General information of research subjects (n=225)

Variables	Number of cases(n)	Percentage (%)
Sex		
Male	115	51.1
Female	110	48.9
Gestational age (weeks)		
<32	45	20.0
32~34	53	23.6
34~37	38	16.8
>37	89	39.6
Birth weight (g)		
<1500	54	24.0
1500~2000	74	32.9
>2000	97	43.1
Parity		
Primiparity	132	58.7
Multiparity	93	41.3
Multiple pregnancy	40	17.8
Chorioamnionitis in pregnant women	108	48.0
Premature membrane rupture	132	58.7
Cesarean delivery	168	74.7
Amniotic fluid contamination	135	60.0
Apnea	128	56.9
Mechanical ventilation	31	13.8
Neonatal infection	72	32.0

Multivariate logistic regression analysis of factors affecting brain injury in neonates

Taking the occurrence of neonatal brain injury as a dependent variable, the variables with statistical significance in Table 2 are included in the multivariate logistic regression model. As the results show, chorioamnionitis in pregnant women(*OR*=2.91, 95% *CI*=1.19-7.13, and *P*<0.05), mechanical ventilation during the neonatal period(*OR*=3.03, 95% *CI*=1.13-8.09, and *P*<0.05), and neonatal infection(*OR*=3.30, 95% *CI*=1.14-9.57, and *P*<0.05) are independent risk factors for neonatal brain injury, while cesarean delivery is its protective factor (*OR*=0.21, 95% *CI*=0.09-0.53, and *P*<0.05). The details are shown in Table 3.

Discussions and Suggestions

As an important cause of neonatal death and chronic nervous system injury, neonatal brain injury has become a focus of attention in pediatrics in recent years. The pathogenesis of neonatal brain injury is complex, and lack of specific clinical manifestations at the early stage, which makes it easy to be misdiagnosed, so it is of great necessity to carry out relevant research.

Table 2. Comparison of the incidence rate of brain injury in neonates with different characteristics (n=225)

Variables		Group with brain injury (n=85)	Group without brain injury (n=140)	χ^2 value	*P* value
Sex	Male	46 (40.0)	69 (60.0)	0.494	0.482
	Female	39 (35.5)	71 (64.5)		
Gestational age(weeks)	<32	27 (60.0)	18 (40.0)	12.811	0.005
	32~34	20 (37.7)	33 (62.3)		
	34~37	11 (28.9)	27 (71.1)		
	>37	27 (30.3)	62 (69.7)		
Birth weight (g)	<1500	31 (57.4)	23 (42.6)	14.861	0.001
	1500~2000	29 (39.2)	45 (60.8)		
	>2000	25 (25.8)	72 (74.2)		
Parity	Primiparity	57 (43.2)	75 (56.8)	3.968	0.046
	Multiparity	28 (30.1)	65 (69.9)		
Multiple pregnancy	Yes	12 (30.0)	28 (70.0)	1.252	0.263
	No	73 (39.5)	112 (60.5)		
Chorioamnionitis in pregnant women	Yes	51 (47.2)	57 (52.8)	7.881	0.005
	No	34 (29.1)	83 (70.9)		
Premature membrane rupture	Yes	58 (43.9)	74 (56.1)	5.158	0.023
	No	27 (29.0)	66 (71.0)		
Delivery mode	Cesarean	76 (45.2)	92 (54.8)	15.702	<0.001
	Natural	9 (15.8)	48 (84.2)		
Amniotic fluid contamination	Yes	61 (45.2)	74 (54.8)	5.031	0.025
	No	29 (30.5)	66 (69.5)		
Apnea	Yes	59 (46.1)	69 (53.9)	8.735	0.003
	No	26 (26.8)	71 (73.2)		
Mechanical ventilation	Yes	18 (58.1)	13 (41.9)	6.492	0.011
	No	66 (34.2)	127 (65.8)		
Neonatal infection	Yes	48 (66.7)	24 (33.3)	37.593	<0.001
	No	37 (24.2)	116 (75.8)		

Table 3. Multivariate logistic regression analysis of factors affecting brain injury in neonates

Variables	Partial regression coefficient	*Wald* value	*OR* value	95% *CI*	*P* value
Chorioamnionitis in pregnant women	1.06	5.47	2.91	1.19-7.13	0.019
Cesarean delivery	-1.55	10.86	0.21	0.09-0.53	0.001
Mechanical ventilation	1.11	4.88	3.03	1.13-8.09	0.025
Neonatal infection	1.20	4.85	3.30	1.14-9.57	0.027

Some studies show that compared with CT, MRI has better sensitivity and specificity for diagnosis of neonatal brain injury, and also a higher detection rate (Xin, 2014). According to the results of MRI, the incidence rate of neonatal brain injury is 37.8%, which is higher than that reported by Li Lei *et al*. (2013). The incidence rate of neonatal brain injury remains to be high, suggesting that clinical staff shall be highly concerned with high-risk children and provide them with timely diagnosis and early intervention.

This study finds that the incidence rate of brain injury in neonates with different gestational age and birth weight is different, and brain injury commonly occurs in infants with gestational age<32 weeks and birth weight<1500 g, which is consistent with the research results of Huang Puyan (2017) and Kidokoro *et al.* (2014). It is agreed that premature labor is the most important risk factor for neonatal brain injury, especially for permanent nerve injury-related brain injury. It is now widely recognized that immature brain development is the leading cause of neonatal brain injury. The smaller the gestational age, the lighter the birth weight, indicating that the neonates' development is not completed, thus their ability to adapt to the outside world is weaker, and their regulatory function is not sound, thus they are more likely to have impaired neurodevelopment.

Multivariate regression analysis show that pregnant women with chorioamnionitis, mechanical ventilation during the neonatal period, and neonatal infection are risk factors for neonatal brain injury, while cesarean delivery is its protective factor (P<0.05). Clinical medical staff shall get to know and identify the risk factors that cause neonatal brain injury, and actively carry out intervention measures in advance in order to reduce the incidence rate of brain injury and neurological sequelae and improve the quality of life of neonates.

Studies have shown that exposure to a number of adverse factors during fetal period, particularly intrauterine infection, is closely associated with neonatal brain injury and nervous system dysfunction (Mwaniki *et al*., 2012). Chorioamnionitis, as a specific clinical feature of

intrauterine infection in pregnant women, is an acute inflammation of placental villi or fetal membranes. Numerous studies have shown that pregnant women with chorioamnionitis can not only increase the incidence rate of brain injury of preterm infants (Ma *et al.*, 2016; Qiu *et al*., 2017; Xu *et al.*, 2012; Chau *et al.*, 2014), but can also increase the incidence rate of brain injury in full-term infants by 4.5 times (lume *et al*., 2008). A meta-analysis shows that chorioamnionitis is closely associated with periventricular leukomalacia of preterm infants, and cerebral palsy of preterm and full-term infants (Wu and Colford, 2000). This study finds that the risk of neonatal brain injury in pregnant women with chorioamnionitis increases by 2.91 times, which is similar to the research results of Zhao Lizhen *et al.* (2016). Its pathogenesis may be related to cytokine- mediated inflammatory reaction that directly damage nerve cells and the synergistic effect of hypoxia and ischemia on brain injury. In the event of intrauterine infection, the pathogenic microorganism is recognized by the corresponding receptors in the pregnant mother and fetus to activate the immune system, inducing an inflammatory reaction that produces a large number of inflammatory cytokines, which can damage the fetal and neonatal neurons through direct injury or stimulation of nitric oxide synthesis, thus leading to neonatal brain injury. Therefore, it is suggested that the medical staff shall pay more attention to the prevention of intrauterine infection during pregnancy, encourage the pregnant women to strengthen prenatal care, conduct pathogenic screening for high-risk pregnant women, as well as further strengthen clinical and basic research so as to explore more effective intervention and treatment measures.

Neonatal infection is often a continuation of intrauterine infection, which is found to be one of the risk factors affecting brain injury in the present study. Bacterial endotoxin can cause aggregation of inflammatory cell and up-regulate mRNA expression of inflammatory mediators in infection, leading to cerebral blood flow fluctuations. Bacterial toxins can seriously affect the cardiovascular function in children with infection, resulting in decreased cerebral blood flow (Heep *et al*., 2003). Therefore, it is suggested that medical staff shall actively control infections in their clinical work and performs disinfection and isolation to avoid cross-infection in clinical operations, examinations, and care of neonates. At the same time, they shall try to find abnormalities through related auxiliary examination so as to reduce the occurrence of brain injury through timely intervention, and active and effective treatment.

The results show that mechanical ventilation is an independent risk factor for brain injury, which is consistent with the results of Zhao Lizhen *et al.* (2016). Neonates under mechanical ventilation may have impaired cerebral blood flow regulation. The increase of air flow is directly transmitted to the skull, affecting the reflux of the superior vena cava and resulting in fluctuations in blood pressure, thus the blood flow imposes great impact to the blood vessel wall to cause variceal bleeding. Therefore, it is suggested that the medical staff shall strictly grasp the indications for the use of the ventilator, monitor the blood gas in a timely manner, and adjust the parameters of the ventilator smoothly, thus to avoid abnormal fluctuations in blood pressure and blood gas due to frequent and rapid adjustment of parameters. In addition, gentle movement during mechanical ventilation is also needed to prevent pain, severe fluctuations in neonatal blood pressure and brain injury caused by invasive operations such as tracheal intubation and suction.

This study also finds that the mode of delivery is associated with the occurrence of neonatal brain injury and cesarean delivery has a protective effect on neonatal brain injury, which is consistent with previous studies. During the process of natural delivery, the fetal skull will be compressed and the intracranial venous pressure will increase obviously, which may easily cause capillary rupture, and also lead to transient hypoxic ischemia in the brain. In addition, indications for cesarean delivery can improve the successful delivery rate of preterm infants with intrauterine infection and intrauterine distress, and reduce the influence of intrauterine abnormalities on preterm infants. However, some scholars have found that the incidence rate of craniocerebral injury in preterm infants born by cesarean delivery is higher than that of preterm infants born by natural delivery, and the prognosis is poor (Yang and Chen, 2013). They believe that infants born by cesarean delivery are not squeezed through the birth canal, thus their lung fluids cannot be eliminated in time and in large amount, which raises the incidence rate of neonatal respiratory distress syndrome, aspiration pneumonia, etc., and increases the use of mechanical ventilation and antibiotics, leading

to abnormalities in the normal respiratory mechanics in neonates which then cause abnormalities in the nervous system. In a study on pregnancy related factors of 256 cases of full-term infants with neonatal brain injury, it is found that the occurrence of brain injury has no significant relationship with the mode of delivery. At present, there is no unified conclusion about whether different modes of delivery affect the neurological development of neonates, and the relationship between different modes of delivery and brain injury still needs further study.

In summary, neonatal brain injury is a complex result of the interaction of multiple factors. Therefore, clinical medical staff shall actively learn the relevant risk factors, and strengthen the monitoring of high-risk children before, during and after delivery, so as to realize early detection and diagnosis, and take effective intervention measures to avoid the occurrence of poor prognosis.

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