·Clinical Research·

A survey of high risk factors affecting retinopathy in full-term infants in China

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Abstract

• AIM: To investigate the possible relationship between the influencing factors occurring before and during birth in full-term infants and the outcome of retinopathy.

• METHODS: Totally 816 full-term infants admitted in the neonate intensive unit of Boai Hospital of Zhongshan between 1 May, 2008 and 30 June, 2011 were included in the study. Fundus examination was performed and evaluated individually on them at the age of 48 hours after delivery, 2 weeks and 1 month. Some possible risk factors happening prenatally or during delivery such as pregnant related hypertension, placenta previa, placental abruption etc, as well as some neonatal risk factors such as neonatal asphyxia, hypoxic-ischemic encephalopathy (HIE), low birth weight etc, were recorded and evacuated. Then the effect of the risk factors of full-term infants on retinopathy was studied.

• RESULTS: The incidence of retinal hemorrhage of full-term infants with prenatal pregnant related hypertension (PRH) of the mother (43.6%) was significantly higher than that of full-term infants without (8.0%). (P<0.001). The incidence of retinal hemorrhage of full-term infants with neonatal asphyxia and /or hypoxic-ischemic encephalopathy (HIE)(29.3%) was significantly higher than that of those without (15.7%), but correlation was not found between the severity of retina hemorrhage and the degree of hypoxic disease. A pale color of optic disc was associated with a low birth weight of full-term infant. Full-term infants with birth weigh less than 2500g had a significant higher incidence of retinopathy than those with birth weight equal or more than 2500g(P<0.001).

• CONCLUSION: The main influencing factors which lead to retinopathy of high risk full-term infants are prenatal factors such as PRH, and some neonatal risk factors such as asphyxia, hypoxic-ischemic encephalopathy, and low birth weight.

• KEYWORDS: full-term infant; high risk factor; retinopathy
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INTRODUCTION

High risk full-term infants are defined as full-term newborn babies who are in high risk situations or probably will be in high risk situations in the future. Some researches[1] have suggested that those full-term infants with high risk factors such as hypoxic-ischemic encephalopathy (HIE) and neonatal asphyxia may be at risk of developing retinopathy. Cases of retinopathy of prematurity-mimicking retinopathy have been reported in full-term babies who did not require supplementary oxygen [2]. But most of those researches concentrated on screening of retinopathy of prematurity (ROP) which had a formed fix procedure, so the majority of pediatricians know very little about the retinopathy of full-term infants. In order to find the possible retinopathy of full term infants in the early stage and investigate the possible relationship between influencing factors and retinopathy, fundus screening was performed on every full-term newborns in intensive unit (NICU) of Boai hospital of Zhongshan during 1 May, 2008 to 30 June, 2011.

PATIENTS AND METHODS

Patients A total of 816 full-term infants admitted in the neonate intensive unit of Boai hospital of Zhongshan between 1 May, 2008 and 30 June, 2011 were included in the study. All the babies had been born at full term with gestational age more than 37 weeks. Among them, 435 cases were male and 381 cases were female and they did not differ significantly from each other in range of social class, employment status of parents, or environment of inhabitation.

Methods Collection of clinical materials: All of the infants' parents or guardians returned questionnaires giving details of any medical problems that the baby's mother had

Table 1 Comparison of the potential risk factors for retinal hemorrhage and optic disc paleness in full-term infants

Risk factor	Retinal hemorrhage				Optic disc paleness			
	Retinal hemorrhage (*n*=165)	No retinal hemorrhage (*n*=651)	χ^2	Significance (*P* value)	Pale optic disc(*n*=176)	Normal optic disc (*n*=640)	χ^2	Significance (*P* value)
X_1 PRH	130	246	89.06	<0.001	89	287	1.82	0.21
X_2 Placenta praevia	28	81	2.33	0.13	31	78	3.51	0.061
X_3 Placental abruption	11	31	0.98	0.32	14	28	3.62	0.06
X_4 BW< 2500g	45	123	5.65	0.02	124	44	341.30	<0.001
X_5 Oxygen therapy given	36	106	2.80	0.09	28	114	0.35	0.56
X_6 Presence of jaundice (maximum bilirubin>220umol)	48	199	0.14	0.71	56	191	0.26	0.61
X_7 Phototherapy given	44	182	0.11	0.74	50	176	0.05	0.81
X_8 Positive result of cerebral ultrasound scanning and/or CT	28	76	3.32	0.07	23	79	0.07	0.79
X_9 Neonatal asphyxia and/or HIE	79	190	20.81	<0.001	64	205	1.17	0.28
X_{10} Meconium aspiration	22	59	2.68	0.1	19	62	0.19	0.66

experienced during the whole period of pregnancy and delivery, such as pregnant related hypertension (PRH), placenta praevia, placental abruption etc. For all patients, details of their neonatal history and subsequent medical care were extracted from hospital and pediatricians' notes. Extensive details were recorded, including birth weight (BW), Apgar scores, number of days on oxygen therapy, presence of jaundice, and maximum bilirubin level, number of days phototherapy given, and length of stay on the neonatal unit, records of cerebral ultrasound scanning and/or CT etc.

The fundus examinations of all patients were performed respectively on 48 hours, two weeks and 1 month after birth. Half an hour before the examination , compound tropicamide eye drops were used every 5-10mins for 5 times to dilate the pupils and then after applying Alcaine eye drops for surface anesthesia, the fundus examinations were performed and recorded .

Statistical Analysis By using the statistic program for social sciences (SPSS), χ^2 test and correlation analysis were performed to analyze the data.

RESULTS

Risk Factors Some of the patients were associated with maternal risk factors before birth, such as 109 cases with placenta praevia, 42 cases with placental abruption and 376 cases with pregnant related hypertension. Some of them are associated with neonatal risk factors during birth or after birth, such as 248 cases with neonatal asphyxia (mild asphyxia 136 cases, severe 112 cases); 175 cases with HIE (mild 84cases, moderate 70 cases, severe 21 cases); 81 cases with meconium aspiration; 168 cases are small for gestational age with birth weight less than 2500g.

Retinal Findings Of the 816 patients, 531 (65.1%) had normal retinal findings and the rest of 285 (34.9%) patients has abnormal retinal findings. Among the abnormal ones, 165cases had retinal hemorrhage, 176 cases had pale optic disc as well as 29 cases had retinal edema, 43 cases had retinal vessel tortuosity, 5 cases had optic nerve edema. Among the retinal findings of our survey, the major types of retinopathy of full-term infants are retinal hemorrhage and pale optic disc and some types of retinopathy such as retinal edema, optic nerve edema were mostly transient and not so convinsible.

Relationship between Retinopathy and High Risk Factors of Full-term Infants The statistical analysis of every single potential risk factor revealed that PRH (X_1), neonatal asphyxia and/or HIE (X_9) are major risk factors of retinal hemorrhage; BW< 2500g (X_4) related to pale optic disc; and BW< 2500g(X_4) related to both of them (Table 1).

An assay for the relation between retinal hemorrhage and PRH, neonatal asphyxia and/or HIE Retinal hemorrhage of full-term infants related to PRH, neonatal asphyxia and/or HIE. Among the full-term infants whose mothers had PRH,130 of 376 (43.6%) cases developed retinal hemorrhage, but among those whose mother didn't have PRH, only 35 of 440 (8.0%) cases developed retinal hemorrhage afterwards and the difference is significant (χ^2=89.06, P<0.001). Among those with postnatal neonatal asphyxia and/or HIE, 79 of 269 (29.3%) cases developed retinal hemorrhage, while 86 of 547 (15.7%) cases without postnatal asphyxia or HIE between developed retinal hemorrhage and the difference is significant (χ^2 =20.81, P<0.001).

Correlation was not found between the severity of retinal hemorrhage and the degree of hypoxic disease (neonatal asphyxia and/or HIE). (Table 2).

Table 2 Relation between the severity of retinal hemorrhage and the degree of asphyxia and HIE

Severity of retinal hemorrhage	Degree of asphyxia		Degree of HIE		
	Mild(n=136)	Severe(n=112)	Mild(n=84)	Moderate(n=70)	Severe(n=21)
Mild retinal hemorrhage	25	17	11	18	5
Moderate hemorrhage	13	16	10	13	4
Large area of flame-shaped hemorrhage	19	5	14	3	2

A pale optic disc related to a low birth weight of full-term infant. In our study, there were 176 cases with pale optic disc, including 52 cases whose birth weight were equal or more than 2500g and 124 cases whose birth weight were less than 2500g. The incidence of pale optic in full-term infants with birth weight less than 2500g (73.8%) is much higher than that of infants with birth weight equal or more than 2500g (8.0%). The difference between them is significant (χ^2 =341.30, P<0.001).

Incidence of retinopathy of high risk full-term infants related to low birth weight. Among the full-term infants with birth weigh less than 2500g, 145 of 168 cases had retinopathy (86.3%), while among those with birth weight equal or more than 2500g, 140 of 648 cases had retinopathy (21.6%). The incidence of retinopathy of full-term infants with BW less than 2500g, is much higher that of which with BW equal or more than 2500g, and the difference is significant (χ^2 =245.76 , P <0.001).

In our study, no significant link was found between the outcome of retinopathy and some risk factors such as oxygen therapy given, and number of days on oxygen therapy, presence of jaundice, and maximum bilirubin level, phototherapy given, and number of days phototherapy given, and length of stay on the neonatal unit. These negative findings are difficult to interpret since the number of subjects is not big enough.

DISCUSSION

In our study ,the commonest type of retinopathy is retinal hemorrhage , locating in central area of the fundus, which presented many forms of hemorrhage such as spotted, patchy, and flame-shape. Other forms of retinopathy revealed pale optic disc, retinal edema, tortuosity of retinal vessels and optic disc edema etc. Compared to pre-term infants, the development of the retinal vessels of full-term infants has become mature, so the location and appearance of retinal hemorrhage of full-term infants are different from that of preterm infants. The retinal hemorrhage of preterm infants is characterized by appearing in the peripheral area of the fundus at the beginning and then extending to the central area, while that of full-term infants occurred mostly in the central area characterized by patchy or flame-shape hemorrhage which is similar to that of patients with retinal vein occlusion. Below is the analysis of the risk factors of retinal hemorrhage.

The pregnant with PRH might suffer from spasm of small arteries, decrease of blood volume, concentration of blood and then decrease of blood supply of organs in whole body eventually, which will lead to decrease of blood supply in the fetus. The study of Zhang *et al* [3] revealed that acute arteriosclerosis existing in the placenta with PRH cause widely embolism and necrosis of villas tissue of placenta which may decrease the intake of oxygen in fetus. Lack of oxygen supply in fetus may cause congestion of retinal vein as well as increase of blood viscosity which may result in retinal hemorrhage after birth.

There is a close relationship between the outcome of retinopathy of full-term infants and neonatal hypoxic disease (neonatal asphyxia or/and HIE). In our study, the incidence of retinal hemorrhage of full-term infants with postnatal neonatal asphyxia or/and HIE is much higher than that of infants without. Neonatal asphyxia or/and HIE cause hypoxia and ischemia of brain tissue which resulted in dilation of blood vessels of brain and even increase of intracranial pressure (ICP) in some severe cases. Increase of ICP may cause retinal edema and optic disc edema. On the other hand, neonatal asphyxia or/and HIE cause block of venous return ,obstruction of central retinal vein and rupture of capillary vessels which leaded to retinal hemorrhage. Our study revealed that the incidence of retinal hemorrhage of infants with neonatal asphyxia or/and HIE increased significantly, but the degree of hypoxic disease (neonatal asphyxia and/or HIE) was not paralleled to severity of retinal hemorrhage. We found that some cases with severe asphyxia had very mild retinal hemorrhage while large area of flame-shaped retinal hemorrhage occurred in some cases with very mild asphyxia. Similar result was found in infants with HIE. Flame-shaped retinal hemorrhage may be caused by obstruction of central retinal vein which was affected by multiple factors and not just asphyxia or HIE. But the quantity of samples in our study is not enough to cover most of the situations which might cause bias in the result, so we need further research to confirm our conclusion.

Low birth weight is one of the most important influencing factors of developing retinopathy in full-term babies. Our

study revealed pale optic disc is related to low birth weight in full-term babies. The color of optic disc in newborns ranging from pink to mild pale is lighter than that of older children. The research of Rimermer *et al*[4] revealed that the collagen tissue left on surface of optic disc cause small and pale optic disc in newborn and with the development of babies, the collagen tissue is degenerating little by little and the capillary vessels on the surface of optic disc increase, which result in optic disc turning red. In our study, full-term infants with low BW is more likely to have pale optic disc which is caused by the delay development of optic nerve together with delay systemic development. Besides that, full-term infant with low birth weight is prone to develop retinopathy than that with normal birth weight.

No significant link was found between the outcome of retinopathy and some risk factors such as number of days on oxygen therapy, presence of jaundice, and maximum bilirubin level, number of days phototherapy given, and length of stay on the neonatal unit. These negative findings are difficult to interpret since the number of subjects is not big enough, so further prospective studies are needed to investigate the relation between retinal outcome and risk factors.

In a word, these results suggest that for full-term babies who had associated high risk factors such as PRH, neonatal hypoxic disease (neonatal asphyxia or/and HIE) and low BW, the presence of retinopathy should be ascertained postnatally by fundus screen.

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