Biomedical Research 2017; 28 (1): 58-60 *ISSN 0970-938X*
www.biomedres.info

Effect of the early intervention on neonate with hyperbilirubinemia and perinatal factors.

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Abstract

OBJECTIVE: Neonatal hyperbilirubinemia (N-HB) usually resulted in bilirubin encephalopathy even death in children. The present study was designed to investigate the prevention and intervention initiatives for N-HB.
MATERIALS AND METHODS: Case-control method was used to study the effects of early intervention on neonate with hyperbilirubinemia and perinatal factors. A total of 412 N-HB cases (209 were boys and 203 were girls) in Weihai Municipal Hospital were divided into intervention group and control group and five important perinatal factors were observed including intrauterine pneumonia, neonatal asphyxia, cephalohematoma, polycythaemia and maternal diabetes. The effectiveness of early intervention by greater or fewer than 75% position was determined.
RESULTS: The results showed that the interventions with enema containing glycerol and saline significantly reduced the bilirubin levels in serum from birth to 96 hours after birth compared with control group (P<0.05). In addition, five factors showed the significance between two groups respectively (P<0.05).
CONCLUSIONS: Early intervention significantly decreased the hyperbilirubinemia incidence of neonate. These measures were easy to be taken.

Keywords: Hyperbilirubinnemia, neonate, early intervention.

Accepted on April 8, 2016

Introduction

Neonatal hyperbilirubinemia is a common problem in new born nurseries and manifests clinically as jaundice. Nearly 25-50% of new-borns and a higher percentage of premature babies develop hyperbilirubinemia [1,2]. Significant hyperbilirubinemia is defined as plasma total bilirubin (TB) concentrations in the high risk zone ($\geq 95^{th}$ percentile) as defined by the age specific Bhutani nomogram [3]. These new-borns are at high risk for kernicterus and accordingly they are eligible for phototherapy. Nowadays, many hospitals use an early postnatal discharge policy for medical and socio-economic reasons, with the risk of readmissions for neonatal hyperbilirubinemia in the first week of life [4-6]. Recently, it was found that the significant increase in serum bilirubin not only influences on the development of central nervous system, but also causes damages of heart, liver, kidney and blood vessel as well as immune system [1,2]. It is of great importance to seek the cause of disease and make early intervention [7]. The present study was designed to investigate effect of the early intervention on neonate with hyperbilirubinemia and perinatal factors.

Methods and Patients

N-HB cases were enrolled in Weihai Municipal Hospital from January 2010 to March 2013. Ethical approval for human subjects was obtained from the research ethics committee of Weihai Municipal Hospital of Shandong Province and informed consent was obtained from each child parent. This study excluded these conditions of premature delivery, birth weight under 2500 g, neonatal haemolytic disease and feeding intolerance. 412 N-HB cases were randomly divided into intervention group of 211 cases and control group of 201 cases. Each group was re-divided into five perinatal factors groups as shown in Table 1. Their primary diseases were actively cured well firstly. Then the intervention methods followed that: anal injected (with enema of 7.5 ml physiological saline and 7.5 ml glycerol) every 12 hours and breastfed with Neonatal milk every 2 hours, while the control group was breastfed every 4 hours without enema injection. The intervention process continued to 96 hours after birth. During that time, the changes of bilirubin levels were detected in serum every 24 hours.

Intrauterine pneumonia can lead to intravascular hemolysis and red blood cell damage, consequently causing excessive bilirubin formation and increasing the level of unconjugated bilirubin. Neonatal asphyxia can inhibit the activity of uridine diphosphate glucuronyl transferase (UDPGT) in liver,

consequently increasing the level of unconjugated bilirubin. Cephalohematoma or ecchymosis can lead to extravascular hemolysis, consequently increasing the level of bilirubin. Polycythemia can lead to red blood cell damage, consequently causing excessive bilirubin formation and increasing the level of unconjugated bilirubin. Maternal Diabetes can stimulate the production of erythropoietin in kidney due to fetal intrauterine hypoxia, consequently increasing the number of red blood cells and the level of unconjugated bilirubin.

Table 1. The comparative study of control group and treatment group

Perinatal factors		Total	Bilirubin levels in serum		P value
			<75% position	>75% position	
Intrauterine Pneumonia	Control group	48	35 (72.9%)	13 (27.1%)	0.018
	Intervention group	54	49 (90.74%)	5 (9.26%)	
Neonatal Asphyxia	Control group	31	22 (71.0%)	9 (29.0%)	0.041
	Intervention group	33	30 (90.9%)	3 (9.1%)	
Cephalohematoma or Ecchymosis	Control group	46	33 (71.7%)	13 (28.3%)	0.041
	Intervention group	51	45 (88.2%)	6 (11.8%)	
Polycythemia	Control group	29	20 (69.0%)	9 (31.0%)	0.031
	Intervention group	39	35 (89.9%)	4 (10.1%)	
Maternal Diabetes	Control group	47	32 (69.1%)	15 (31.9%)	0.035
	Intervention group	34	30 (88.2%)	4 (11.8%)	

These perinatal factors are closely related to the neonatal hyperbilirubinemia.

Results

The results showed that the interventions with enema containing glycerol and saline significantly reduced the bilirubin levels in serum from birth to 96 hours after birth compared with control group ($P<0.05$). In addition, five factors including intrauterine pneumonia, neonatal asphyxia, cephalohematoma, polycythaemia and maternal diabetes which are closely related to the neonatal hyperbilirubinemia showed the significance between two groups respectively ($P<0.05$).

Discussion

Neonatal jaundice is a common phenomenon in hospitalized neonates and almost 20% hospitalized neonates suffer from hyperbilirubinemia. Due to the immature blood-brain barrier of neonates, severe hyperbilirubinemia is fatal or leads to severe and permanent nervous system sequelae. Although the prognosis of normal pathologic jaundice was quite well by removal of aetiology and treatment of blue light irradiation, these treatments is time-spending and cost-consuming. So much better therapy of prevention and early intervention might be used [8,9].

Neonatal bilirubin metabolism is significantly different from that of adult, as the neonatal enterohepatic circulation with different from adult. The intestinal micro flora of new born is not well established and hence the urobilinogen is not generated. In this situation, the β-glucuronidase in intestinal epithelial cell can efficiently remove the glucuronic group of conjugated bilirubin to convert it to fat-soluble unconjugated bilirubin which will be excreting by intestine. The meconium exists in neonatal enteric cavity contains about 80-120 mg of bilirubin, which is 5 to 10 fold of bilirubin generated by a neonate one day. The burden of enterohepatic circulation of bilirubin and reabsorbed of bilirubin would be significantly increased if the meconium excretion was delayed by 12 hours [10]. Early laxative treatments and increase of feeding frequency reduce the enterohepatic circulation of bilirubin, which leads to decrease of neonatal serum bilirubin level.

The dynamic study of bilirubin was of great importance because high-risk factors are main causes of hyperbilirubinemia of in-hospital neonates. In 1999, Bhutani et al. studied an hour-specific total serum bilirubin percentile nomogram [10]. Ding et al. studied total serum bilirubin percentile nomogram of new-borns with different day-old in China, which is clinically used generally [11]. However, this nomogram cannot be used to test the bilirubin dynamic tendency because it counts the level of bilirubin only at one time every 24 hours. It is suggested, by APS in 2004 [12], that the combination analysis of hour-specific bilirubin percentile and high-risk factors is important to test the neonatal aurigo risk. It was also highlighted in a 2008 Israel guidelines [13], that the value of bilirubin should be tested at regular time and the management should refer to tendency of the nomogram. It was recommended that the light therapy should be considered when the bilirubin level was higher than 75 percentile together with significant jaundice or the bilirubin level was higher than 95 percentile together with high-risk of hyperbilirubinemia

In this study we tested the total serum bilirubin levels of new-borns in 96 hours after birth. It showed that the number of mature new-borns with high-risk factors whose total serum bilirubin levels increased to 75 percentile or higher 96 hours after birth was significantly lower in early intervention group compared with control groups. The differences between 5 groups are all statistical significant. The early intervention was worthy to clinical applicant as it is convenient, cost-saving and painless. For the new-borns with ABO/Rh haemolysis required early light-therapy, the progression of them was faster than normal new-borns which may lead to bilirubin encephalopathy and was not included in this study. Premature infants were also excluded as the immaturity of blood-brain barrier might lead to nervous toxicity of bilirubin. We also noticed that the sample size of this study was small and large-scale study is required for further research.

In conclusion, the present study showed that the interventions with enema containing glycerol and saline significantly reduced the bilirubin levels in serum.

Acknowledgments

This study was supported by Weihai Science and Technology Bureau (2012GNSO40).

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