

The influence of continuous glucose monitoring of high-risk neonate on guiding perinatal complications and one-year follow-up results

P.-W. SHANG, G.-Z. LU, X. SUN, Z.-M. BIAN, Z.-Y. SHANG, J. LI

Neonatal Department of Internal Medicine, Xuzhou Children's Hospital, Xuzhou, Jiangsu, China

Abstract. – OBJECTIVE: To investigate the value of micro blood glucose monitoring of high risk neonate on guiding perinatal complications and one-year follow-up results.

PATIENTS AND METHODS: A total of 268 cases that were diagnosed as high-risk neonates by our Obstetrics Department from June 2010 to June 2014 were enrolled. After measuring their micro blood glucose instantly, 6h, 12h, 24h, 1d, 2d and 3d after delivery, divided them into two groups: hypoglycemic group (n = 54) and normal group (n = 214). And then the differences of perinatal complications and their one-year follow-up results were compared.

RESULTS: The occurrence of perinatal complications in hypoglycemic group was significantly higher than that in normal group ($p < 0.05$); the faster the hypoglycemia occurred, the longer the duration was, and the severer the complications were. Hypoglycemia often occurred prior to the complications. The mental development index (MDI) and the physical development index (PDI) of hypoglycemic group were significantly lower than those in the normal group and differences were statistically significant ($p < 0.05$).

CONCLUSIONS: Continuous blood glucose monitoring of high-risk neonate was of great significance in guiding perinatal complications at one-year follow-up.

Key Words:

High-risk neonate, Micro blood glucose monitoring, Perinatal complication, Bayley scale.

intelligence and development levels of the neonates were delayed than their peers^{2,3}. In our study, we have further investigated the value of micro blood glucose monitoring of high-risk neonate on guiding perinatal complications and one-year follow-up.

Patients and Methods

General Materials

A total of 268 cases, diagnosed as high risk neonates by the Obstetrics Department from June 2010 to June 2014 were enrolled in the study. All were high risk neonates as confirmed by the diagnostic standards⁴: (1) Mothers had diseases, such as hypertension, diabetes mellitus etc.; (2) Preterm birth, low birth weight, fetal macrosomia, multiple pregnancy, IVF, hypothermia, cesarean section, birth trauma, asphyxia; (3) Neonatal hypoxic ischemic encephalopathy, hyperbilirubinemia, aspiration pneumonia, respiratory distress, Apgar score < 7 and so on.

Exclusion standards: (1) The mother with severe systemic lupus erythematosus, hematological diseases, viral hepatitis and infectious diseases etc; (2) Birth defects, congenital heart disease, genetic diseases etc.

Research Methods

After obtaining the approval of the hospital Ethics Committee and the informed consent of the parents/guardians of the neonates, immediately measuring the neonates' micro blood glucose instantly, 6h, 12h, 24h, 1d, 2d and 3d after delivery, then dividing them into two groups: hypoglycemia group (n = 54) and normal group (n = 214). Hypoglycemic group: 32 cases of male and 22 cases of female, gestational age from 33-42 weeks, on average (38.6 ± 3.4) weeks; weight from 2.2-4.3 kg, on average (2.7 ± 0.5) kg. Normal group: 113 cases of male and 101 cases of

Introduction

Hypoglycemia in high-risk neonates has aroused great attention of Obstetrics Department and neonatologists. Many articles have pointed out that prevalence of hypoglycemia in high risk infants is between 10-20%¹. Hypoglycemia results in early irreversible ischemia anoxic encephalopathy and even death in some cases. Follow-up results have indicated that even if the hypoglycemia was mild or quickly corrected, the

female, gestational age from 37-40 weeks, on average (39.2 ± 1.3) weeks; weight from 2.8-3.7 kg, on average (3.2 ± 0.7) kg. Difference on gender between the two groups had no statistical significance ($p > 0.05$); the gestational age and body weight in hypoglycemia group were significantly lower than those in normal group and difference had statistical significance ($p < 0.05$).

Detection Method

Blood glucose was measured and recorded by Abbot micro amount blood glucose detector. A drop of blood from the neonate's blood capillary of the right heel was assessed onto the test paper. Diagnostic criteria for hypoglycemia: term infant < 1.7 mmol/L, 3d later < 2.2 mmol/L; low birth weight premature infants < 1.1 mmol/L; 3d later < 2.2 mmol/L.

Treatment Method

As for the hypoglycemic high risk neonates with gestational weeks > 35 weeks, birth weight > 1.8 kg, Apgar score at 5 min after birth > 6 points, good sucking and swallowing ability and without other neonatal diseases, are immediately treated with oral administration or nasal feeding of 3-6 mg/kg 5-10% glucose, then feed them once every 2-3 hours till colostrums secretion is there. As for the hypoglycemic high risk neonates with gestational weeks < 35 weeks, birth weight < 1.8 kg, Apgar score at 5min upon birth < 6 points, and accompanied with respiratory distress syndromes, severe aspiration pneumonia and other disease, immediately treated them with carbohydrate supplementation via vein and other symptomatic treatments.

Observation Index

Observed the differences between the two groups of neonates on the occurrence of complications, their onset time and duration of hypoglycemia; differences on Bayley* scale mental development index (MDI) and psychomotor development index (PDI). *Bayley scale was completed by professional training personnel. Development index ≥ 80 points were classified as good, 70-79 as critical state, ≤ 69 as development retardation.

Statistical Analysis

Statistical software package SPSS 20.0 (SPSS Inc., Chicago, IL, USA) was applied to process the data; measurement data was presented by

means $\pm$ standard deviation; t -test was applied in comparisons between groups; enumeration data was presented by percentage (%); χ^2 test was applied in comparisons between groups; Logistic test was applied in multi factor regression analysis; $p < 0.05$ was considered with statistical significance.

Results

Comparison on the Prevalence of Perinatal Complications

The Apgar score of the hypoglycemic group was 3-9 points, on average (7.2 ± 1.6) points. 4 cases of the neonates had choking, 5 cases had hypoxic ischemic encephalopathy, 2 cases had aspiration pneumonia, 1 case had intracranial hemorrhage and 1 case had respiratory distress; the prevalence of perinatal complications was 24.07% (13/54). The Apgar score of the normal group was 8-10 points, on average (9.3 ± 0.7) points. 6 cases of the neonates had choking, 6 cases had hypoxic ischemic encephalopathy, 4 cases had aspiration pneumonia, 3 cases had intracranial hemorrhage and 3 case had respiratory distress; the prevalence of perinatal complications was 10.28% (22/214). The Apgar scores in hypoglycemic group were significantly lower than that in normal group and the occurrence of perinatal complications in hypoglycemia group was significantly higher than that in normal group and differences had statistical significance ($t = 5.627$, $p = 0.034$; $\chi^2 = 7.226$, $p = 0.007$).

Implemented the logistic multivariate regression analysis on the gestational age, body weight, Apgar score, with or without hypoglycemia, occurrence time and duration of hypoglycemia and the results showed: with or without hypoglycemia, occurrence time and duration of hypoglycemia were the independent risk factors of perinatal complications; the faster the hypoglycemia occurred, the longer was the duration of complications and the severer the complications. Hypoglycemia often occurred earlier than the complications (Table I).

Comparisons on Bayley Scale

The mental development index (MDI) and the physical development index (PDI) of hypoglycemic group were significantly lower than those in the normal group and differences were statistically significant ($p < 0.05$) (Table II).

Table I. Logistic multivariate regression analysis on perinatal complication.

Factor	β	Wald	<i>p</i>	OR	95% CI
With or without hypoglycemia	0.124	4.623	0.037	1.324	0.758-2.103
Occurrence time of hypoglycemia	0.136	4.957	0.034	1.827	1.127-3.215
Duration	0.201	5.134	0.029	2.317	1.957-3.624

p value < 0.05 statistically significant; OR: Odds Ratio; CI: Confidence Interval.

Discussion

Causes of Hypoglycemia in High-Risk Infants

Firstly, the neonate of high-risk mother, such as the mother with diabetics, at birth the constant supply of hyperglycemic blood is removed while the hyperinsulinemia remains and hypoglycemia ensues. Glucohomeostatic mechanisms are inadequate to reverse the rapid drop in blood sugar. Then, the high level of insulin in the body might result in sudden hypoglycemia⁵. Secondly, high stress and high consumption at delivery, insufficient energy storage of the infants, the obstructed gluconeogenesis or increased glucose utilization, increased energy consumption at choking, ARDS, sepsis, and scleroderma and the insufficient or even interrupted gluconeogenesis would also lead to hypoglycemia^{6,7}. Thirdly, late or insufficient intake of colostrum would also lead to hypoglycemia. Meanwhile, the necessary adjuvant therapy of high risk neonates, such as neonatal intensive care unit, would disturb the normal energy intake and metabolism^{8,9}. Glucose supplement by oral or other exogenous methods would lead to the risk of hyperglycaemia and hypoglycemia can happen again after the interruption of treatment^{10,11}.

Harms of Hypoglycemia

High risk neonatal hypoglycemia was not only the accompanying symptom of perinatal

complications but also an important factor in inducing and aggravating perinatal complications^{12,13}. The results of our study pointed out that the appearance of perinatal complications in hypoglycemia group was significantly higher than that in normal group. From logistic multivariate regression analysis, we have come to: with or without hypoglycemia, occurrence time and duration of hypoglycemia were the independent risk factors of perinatal complications; the faster the hypoglycemia occurred, the longer the duration was, and the severer the complications were. Hypoglycemia often occurred earlier than the complications. Few researches in the past has focused on the relationship between hypoglycemia and perinatal complications. From the study results of our study, we could see that the occurrence of hypoglycemia may play an important role in the occurrence of perinatal complications, and the mechanism of hypoglycemia should be further explored.

Neonatal hypoglycemia would lead to irreversible damages to the brain development and brain function of neonates, including mental retardation, cerebral palsy and even death, thus causing remarkable potential damages to the family and society^{14,15}. Through following up the Bayley scale for one year, our study has discovered: the mental development index (MDI) and the physical development index (PDI) of hypoglycemia group were significantly lower than those in the normal group.

Innovation and Shortcoming of Our Research

Based on the previous studies, in our study, we have tried to monitor the micro amount blood sugar of high risk neonates dynamically and consecutively, so the measurement time was less, the instrument was more flexible¹⁶, and the diagnostic criteria of hypoglycemia was more accurate¹⁷, rather than merely relying on the criteria of less than 2.2 mmol/L.

Table II. Comparisons on Bayley scale.

Group	MDI	PDI
Hypoglycemia group	65.4 ± 10.2	63.2 ± 8.7
Normal group	86.3 ± 12.3	87.4 ± 15.2
T value	6.328	6.758
<i>p</i> value*	< 0.001	< 0.001

**p* value < 0.001 highly significant.

Conclusions

Our study was focused on studying the relationship between the occurrence of hypoglycemia and perinatal complications and further compared the intelligence and motor development levels through 1-year follow-up. Besides, the number of our samples was relatively large, so the research results were quite reliable. Our study did not make any further investigation on whether the results would be improved after the hypoglycemia children completed treatment.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

References

- 1) FAUSTINO EV, HIRSHBERG EL, BOGUE CW. Hypoglycemia in Critically Ill Children. *J Diabetes Sci Technol* 2012; 6: 48-57.
- 2) DUNING T, VAN DEN HEUVEL I, DICKMANN A, VOLKERT T, WEMPE C, REINHOLZ J, LOHMANN H, FREISE H, ELLGER B. Hypoglycemia aggravates critical illness-induced neurocognitive dysfunction. *Diabetes Care* 2010; 33: 639-644.
- 3) FAUSTINO EV, BOGUE CW. Relationship between hypoglycemia and mortality in critically ill children. *Pediatr Crit Care Med* 2010; 11: 690-698.
- 4) GARCIA BRANCO R, TASKER RC, RAMOS GARCIA PC, PIVA JP, DIAS XAVIER L. Glycemic control and insulin therapy in sepsis and critical illness. *J Pediatr* 2007; 83: S128-S136.
- 5) HIRSHBERG E, LARSEN G, VAN DUKE H. Alterations in glucose homeostasis in the pediatric intensive care unit: hyperglycemia and glucose variability are associated with increased mortality and morbidity. *Pediatr Crit Care Med* 2008; 9: 361-366.
- 6) PREISSIG C, RIGBY M. Glycaemic control in paediatric critical care. *Lancet* 2009; 373: 1423.
- 7) RIGBY MR, PREISSIG CM. Management of hyperglycemia in the pediatric intensive care unit. *Pediatr Crit Care Med* 2010; 11: 163.
- 8) VLASSELAERS D, MILANTS I, DESMET L, WOUTERS PJ, VANHOREBEEK I, VAN DEN HEUVEL I, MESOTTEN D, CASAER MP, MEYFROIDT G, INGELS C, MULLER J, VAN CROMPHAUT S, SCHETZ M, VAN DE BERGHE G. Intensive insulin therapy for patients in paediatric intensive care: a prospective, randomised controlled study. *Lancet* 2009; 373: 547-556.
- 9) OGNIBENE KL, VAWDREY DK, BIAGAS KV. The association of age, illness severity, and glycemic status in a pediatric intensive care unit. *Pediatr Crit Care Med* 2011; 12: e386-e390.
- 10) NAYAK P, LANG H, PARSLAW R, DAVIES P, MORRIS K. Hyperglycemia and insulin therapy in the critically ill child. *Pediatr Crit Care Med* 2009; 10: 303-305.
- 11) SALHAB WA, WYCKOFF MH, LAPTOOK AR, PERLMAN JM. Initial hypoglycemia and neonatal brain injury in term infants with severe fetal acidemia. *Pediatrics* 2004; 114: 361-366.
- 12) ADAMKIN DH. Postnatal glucose homeostasis in late-preterm and term infants. *Pediatrics* 2011; 127: 575-579.
- 13) BALION C, GREY V, ISMAILA A, BLATZ S, SEIDLITZ W. Screening for hypoglycemia at the bedside in the neonatal intensive care unit (NICU) with the Abbott PCx glucose meter. *BMC Pediatr* 2006; 6: 28.
- 14) BELLINI C, SERRA G, RISSO D, MAZZELLA M, BONIOLI E. Reliability assessment of glucose measurement by HemoCue analyser in a neonatal intensive care unit. *Clin Chem Lab Med* 2007; 45: 1549-1554.
- 15) WINTERGERST KA, BUCKINGHAM B, GANDRUD L, WONG BJ, KACHE S, WILSON DM. Association of hypoglycemia, hyperglycemia, and glucose variability with morbidity and death in the pediatric intensive care unit. *Pediatrics* 2006; 118: 173-179.
- 16) BEARDSALL K, VANHAESBROUCK S, OGILVY-STUART AL, VANHOLE C, PALMER CR, VAN WEISSENBRUCH M, MIDGLEY P, THOMPSON M, THIO M, CORNETTE L, OSSUETTA I, IGLESIAS I, THEYKENS C, DE JONG M, AHLUWALIA JS, DE ZEGHER F, DUNGER DB. Early insulin therapy in very-low-birth-weight infants. *N Engl J Med* 2008; 359: 1873-1884.
- 17) ISHIGURO A, NAMAI Y, ITO YM. Managing "healthy" late preterm infants. *Pediatr Int* 2009; 51: 720-725.