Clinical Trial/Experimental Study

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Characteristics and risk factors for extrauterine growth retardation in very-low-birth-weight infants

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Abstract

Background: To investigate the characteristics and risk factors for extrauterine growth retardation (EUGR) in very-low-birth-weight infants (VLBWIs).

Methods: The medical records of 137 VLBWIs admitted to the neonatal intensive care unit between June 2015 and December 2017 were retrospectively reviewed. The patients were divided into EUGR (n = 92) and non-EUGR (n = 45) groups. This study collected data on demographic and clinical characteristics and analyzed the risk factors for EUGR with multivariate logistic regression.

Results: Gestational age (OR = 0.573, $P < .01$), SGA (OR = 3.887, $P = .022$), feeding intolerance (OR = 4.632, $P = .002$), and calories supplied by amino acids at the 7th day (OR = 0.786, $P = .006$) were high-risk factors for EUGR.

Conclusion: Feeding intolerance reduction and amino acid nutrition support should be applied to prevent delayed extrauterine growth for VLBWIs.

Abbreviations: EUGR = extrauterine growth retardation, NEC = necrotizing enterocolitis, NRDS = neonatal respiratory distress syndrome, PDA = patent ductus arteriosus, PVL = periventricular leukomalacia, SGA = small for gestational age, VLBWIs = very-low-birth-weight infants.

Keywords: extrauterine growth retardation, nutrition, premature infant, very-low-birth-weight infant

1. Introduction

The survival of very-low-birth-weight infants (VLBWIs) has improved with the development of technologies on perinatal and neonatal intensive care and respiratory and nutrition support.[1,2] However, weight growth in VLBWIs is usually difficult because of delayed maturation of various organs and underlying diseases. Besides, the newborns energy expenditure shifts from weight growth to survival support, resulting in extrauterine growth restriction (EUGR). EUGR is defined as growth values ≤10th percentile of intrauterine growth expectation based on estimated postmenstrual age in premature.[3] EUGR has been recognized as an important issue for VLBWIs in the clinic. The incidence of EUGR in VLBWIs is strikingly high.[4–6] In China, the incidence of EUGR achieves to 56.8%.[7] In VLBWIs, inadequate nutrient intake, especially energy intake, aggravated the occurrence of EUGR.[8]

Early and aggressive introduction of parenteral nutrition and enteral feeding leads to better growth.[10] Energy intake during the first 7 days after birth is associated with growth until the corrected age of 2 years for extremely preterm (<28 weeks gestation) neonates.[9] According to the nutrition program theory, EUGR has an irreversible long-term negative effect on neurodevelopment and adult body height.[10,11] Evidence has demonstrated that an early aggressive nutrition plan can reduce the incidence of EUGR in VLBWIs.[12,13] However, the risk factors for EUGR still need to be further explored. This study was designed to investigate the characteristics and risk factors for EUGR in VLBWIs to determine the optimal postnatal nutrition mode to prevent growth retardation.

Editor: Vasile Valeriu Lupu.

XZ and LD, contributed equally in this work.

This project was funded by the General Program of the National Natural Science Foundation of China (81771626; 81971423), Jiangsu Provincial Key Talent Program for Women's and Children's Health (FRC201731), Suzhou Science and Technology Development Program (SS201428), Diagnosis and Treatment Technology Project of Clinical Key Diseases in Suzhou province (LCZX201612), Minsheng Technology - Key Technology Application Research Project (SS201644), Jiangsu Provincial Social Development Project (No. H201316), and Suzhou Key Laboratory Fund for Brain Development Injury (SZS201108).

The study was approved by the Ethics Committee of the Children's Hospital of Soochow University.

The authors declare that they have no conflict of interest.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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How to cite this article: Zhao X, Ding L, Chen X, Zhu X, Wang J. Characteristics and risk factors for extrauterine growth retardation in very-low-birth-weight infants. Medicine 2020;99:47(e23104).

Received: 19 February 2020 / Received in final form: 14 July 2020 / Accepted: 11 October 2020

http://dx.doi.org/10.1097/MD.0000000000023104

2. Methods

2.1. Patients and research design

This study retrospectively reviewed the medical records of VLBWIs admitted to the neonatal intensive care unit at the Children's Hospital of Soochow University between June 2015 and December 2017. The inclusion criteria were infants with gestational age ≤32weeks and hospital stays ≥28 days. The exclusion criteria included the age more than 24 hour upon admission to the NICU, and/or incomplete clinical data, congenital abnormalities or inborn errors, poor milk consumption and unstable vital signs at discharge, which refers to abnormalities of blood pressure, respiration, body temperature, pulse, and oxygen saturation.

2.2. Feeding strategy

The feeding principals are that enteral feeding, minimal feeding, and even non-nutritive sucking should be initiated as soon as possible within postnatal 24hours. Positive and individualized principals should be addressed either in enteral or parenteral nutrition administration.

1. As donated breast milk is unavailable in our unit, we encourage mothers to feed their babies with expressed breast milk (EBM). If the EBM is unavailable, we feed infants with formula.
2. If feeding intolerance occurs, we will switch to minimal feeding and/or non-nutritive sucking instead of suspending feeding. Once the related symptoms are improved, the feeding will be continued. The choices of formula types, such as hydrolyzed protein formula, low lactose formula, or lactose addition formula, are based upon patients clinical conditions. And the caloric notch will be supplemented through parenteral nutrition.
3. The speed of feeding advancement is 20 to 25 ml/kg/d.
4. When the amount of breastfeeding reaches 50 to 80 ml/kg/d, we begin to add breast milk fortifier to breast milk, and then fortify by half the amount.

If the infant was intolerant, we reduce the proportion or even fortify by 1/3–1/4, and then gradually increase the dose according to the clinical situation.

2.3. Demographic and clinical parameters

Data on VLBWIs gender, gestational age, birth weight, age at admission, and small for gestational age (SGA) were collected. The occurrence of neonatal respiratory distress syndrome (NRDS), neonatal pneumonia, or asphyxia was recorded. The following parameters were compared between the EUGR and non-EUGR groups: antibiotic, hospital stay, duration of intravenous nutrition support, initiation time of lactation, feeding intolerance rate, time of minimum weight, weight loss, time of return to birth weight, initiation time of amino acid application, initiation time of fat emulsion, age of oral calorie intake reaching 120 kcal/kg/d, fluid intake at the 3rd and 7th days, total calories supplied intravenously, calories supplied by intravenous amino acids, calories provided by intravenous fat emulsion, and weight changes.

Records including nutritional intake, weight gain, underlying diseases, complications, length of hospital stay, and physical development at discharge were collected. Informed consent was obtained from the guardian of each patient. The study was approved by the Ethics Committee of the Children's Hospital of Soochow University.

2.4. Evaluation criteria

EUGR group was defined as infants whose body weight at discharge is below the 10th percentile of the corresponding growth curve of gestational age. Feeding intolerance in the preterm infant is defined as follows:[14] Experiencing difficulty with the ingestion or digestion of formula or breast milk that disrupts the current enteral feeding plan. The manifestation of the clinical symptoms is gastric retention with more than 50% the volume of the previous feed, abdominal distention and/or vomiting.

Postnatal weight loss (%) = (birth weight – minimum weight) / birth weight × 100%,

Weight gain rate (g/kg/d) = (body weight at discharge – birth weight) / (length of hospital stay × birth weight).

2.5. Statistical analysis

Data were analyzed using IBM SPSS statistics software version 17.0. Data were expressed as the mean ± standard deviation for normally distributed variables, or as the median (P25, P75) for non-normally distributed data. The *t*-test and the *z*-test were performed to examine the differences between groups for continuous variables. Pearsons χ^2 test or Fishers exact test was performed to examine the differences between groups for categorical variables. Logistic regression analysis was applied to evaluate the risk factors for EUGR. The variables with statistical significance by univariate analysis were included in a multivariate analysis. All reported *P* values were two-tailed. A *P* value <.05 was considered statistically significant.

3. Results

3.1. Demographic and clinical characteristics

Among the 137 VLBWIs included in this study, 62 were males and 75 were females. The number of SGA infants was 30 (21.9%). Of the 137 cases, 9 were on breast milk and 128 were on formula. All patients received total parenteral nutrition through an intravenous line. A total of 92 (67.2%) infants had EUGR at discharge. In the EUGR group, there were 42 males and 50 females. A comparison between the EUGR and the non-EUGR group indicates no significant difference in gender, age at admission, the incidence of NRDS, neonatal pneumonia, and asphyxia. The gestational age of the EUGR and the non-EUGR group ranged from 26 weeks^{+3} to 32 weeks and 25 weeks^{+6} to 32 weeks, respectively. The average gestational age of the non-EUGR group was significantly greater than that of the EUGR group (30.50 ± 1.41 weeks vs 29.67 ± 1.44 weeks, $P = .002$). Similarly, the birth weight of the non-EUGR group was substantially greater than that of the EUGR group (1294.78 ± 170.15 g vs 1206.90 ± 182.30 g, $P = .008$). The number of patients with SGA in the EUGR group was significantly greater than that of the non-EUGR group [25 (27.5%) vs 5 (11.1%), $P = .030$] (Table 1).

The length of hospital stay and the duration of intravenous nutrition were significantly longer in the EUGR group than in the non-EUGR group ($P < .05$). The initiation time of lactation was earlier in the non-EUGR group than in the EUGR group

Table 1

Comparisons of demographic, nutrition-related characteristics and complications between the groups.

Variable	EUGR group (n = 92)	non-EUGR group (n = 45)	*P* value
Baseline			
Male	42 (45.7)	20 (44.4)	.894
Birth weight (g)	1206.90 ± 182.30	1294.78 ± 170.15	.008
Gestational age (w)	29.67 ± 1.44	30.50 ± 1.41	.002
vAge at admission (h)	2.00 (1.50, 3.75)	3.00 (2.00, 6.00)	.128
SGA	25 (27.5)	5 (11.1)	.030
NRDS	42 (45.7)	16 (35.6)	.261
Neonatal pneumonia	77 (83.7)	8 (84.4)	.911
Neonatal asphyxia	29 (31.5)	12 (6.7)	.560
Carbapenems antibiotics	18 (19.6)	7 (15.6)	.568
Antibiotics upgrade	62 (67.4)	36 (80.0)	.125
Nutrition-related characteristics			
Hospital stay (d)	59.5 ± 20.13	48.91 ± 15.21	.003
Feeding intolerance	41 (44.6)	8 (17.8)	.002
Time of minimum weight (d)	5.00 (3.00, 7.00)	5.00 (4.00, 7.00)	.295
Weight loss rate (%)	6.49 ± 4.78	5.53 (2.60, 8.02)	.186
Weight gain rate (g/kg/d)	15.01 ± 3.91	16.47 ± 4.55	.550
Time of return to birth weight (d)	10.07 ± 4.65	10.55 ± 4.25	.566
Initiation time of amino acid application (d)	2.00 (1.00, 2.00)	2.00 (1.00, 2.00)	.905
Initiation time of fat emulsion (d)	3.00 (3.00, 4.00)	3.00 (3.00, 3.50)	.089
Initiation time of lactation (d)	3.00 (2.00, 6.00)	3.00 (2.00, 4.00)	.017
Time to reach oral calorie intake of 120 kcal/kg/d (d)	36.00 (28.00, 49.75)	35.00 (26.00, 52.00)	.689
Duration of intravenous nutrition (d)	45.00 (38.00, 59.00)	41.00 (32.00, 51.00)	.040
Complications			
Hypebilirubinemia	89 (96.7)	41 (91.1)	.160
Septicemia	11 (12.0)	5 (11.1)	.885
Anemia	77 (83.7)	34 (75.6)	.254
Intracranial bleeding	17 (18.5)	12 (26.7)	.270
PVL	6 (6.6)	5 (11.1)	.565
Intracranial infection	6 (6.5)	2 (4.4)	.921
Pulmonary hemorrhage	5 (5.4)	0 (0.0)	.172*
Neonatal hypoglycemia	20 (21.7)	4 (8.9)	.063
Liver dysfunction	7 (7.6)	2 (4.4)	.483
NEC	5 (5.4)	0 (0.0)	.172*
PDA	15 (16.3)	3 (6.7)	.117

* *P* value was analyzed by Fishers exact test.

Data are presented as No. (%), mean ± standard deviation, or median (interquartile range).

SGA = small for gestational age, NRDS = neonatal respiratory distress syndrome, PVL = periventricular leukomalacia, NEC = necrotizing enterocolitis, PDA = patent ductus arteriosus.

(*P* = .017). The incidence of feeding intolerance was significantly higher in the EUGR group than in the non-EUGR group (*P* = .002). However, characteristics including the usage rate of the antibiotics of the carbapenem, requirement of upgrading antibiotics, age of minimum weight, weight loss, age of birth weight recovery, initiation time of amino acid application, initiation time of fat emulsion, and time of oral calorie intake reaching 120 kcal/kg/d were not significantly different between the 2 groups (Table 1).

3.2. Comparison of complications between the EUGR and non-EUGR groups

The incidence of complications, including hyperbilirubinemia, septicemia, anemia, intracranial bleeding, periventricular leukomalacia, intracranial infection, pulmonary hemorrhage, neonatal hypoglycemia, liver dysfunction, necrotizing enterocolitis (NEC), and patent ductus arteriosus (PDA), was compared between the EUGR and non-EUGR group. There were no significant differences in these complications between the 2 groups (all $P > .05$) (Table 1).

3.3. Nutritional status and changes in body weight during the hospital stay

There were no significant differences in the total fluid intake or calories supplied by intravenous nutritional therapy or fat emulsion day on both the 3rd and the 7th day between the EUGR and the non-EUGR group (all $P > .05$). The calories supplied by amino acids at the 7th day were significantly greater in the non-EUGR group than in the EUGR group (*P* = .007). Although the total calorie intake was not significantly different between the 2 groups within the first 14 days (all $P > .05$), a significantly greater total calorie intake was observed on the 28th day in the non-EUGR group compared with the EUGR group (*P* = .049). For the changes in body weight, infants in the non-EUGR group showed a persistently greater body weight compared with those in the EUGR group (all $P < .05$) (Tables 2 and 3).

3.4. Independent risk factors for EUGR

All parameters were included in the multivariate logistic analysis to evaluate the risk factors for EUGR. The analysis demonstrated that 4 factors: gestational age (OR = 0.573, *P* = .001), SGA

Table 2

Nutritional status during the hospital stay between the groups.

Variable	3rd day			7th day		
	EUGR group	non-EUGR group	*P* value	EUGR group	non-EUGR group	*P* value
Total fluid (ml/kg/d)	121.77 ± 28.15	122.04 ± 23.32	.956	155.23 ± 26.21	158.10 ± 17.08	.505
Calories supplied by intravenous nutritional therapy (kcal/kg/d)	53.83 ± 12.75	54.17 ± 11.75	.883	73.42 ± 16.24	74.40 ± 16.15	.741
Calories supplied by amino acids (kcal/kg/d)	8.30 ± 2.28	8.38 ± 2.91	.861	9.75 ± 3.10	11.23 ± 2.64	.007
Calories supplied by fat emulsion (kcal/kg/d)	7.51 (0.00, 9.58)	8.45 (1.64, 9.85)	.282	15.83 (4.52, 19.03)	12.00 (10.19, 12.91)	.995

Data are presented as No. (%), mean ± standard deviation, or median (interquartile range).

(OR = 3.887, *P* = .022), feeding intolerance (OR = 4.632, *P* = .002), and calories supplied by amino acids at the 7th day (OR = 0.786, *P* = .006) were associated with EUGR (Table 4).

4. Discussion

The current study investigated the nutritional status and risk factors for EUGR in VLBWIs. Our findings revealed that gestational age, birth weight, the proportion of SGA infants, length of hospital stay, feeding intolerance percentage, initiation time of lactation, duration of intravenous nutrition, calories supplied by amino acids at the 3rd day, total calorie intake at the 28th day, and body weight at the 3rd, 7th, 28th day, and the day at discharge were significantly different between the EUGR and non-EUGR groups. More importantly, gestational age, SGA, feeding intolerance, and calories supplied by amino acids at the 7th day were high-risk factors for EUGR. Indeed, feeding intolerance could impact the time to achieve full enteral nutrition. However, our study did not report such a result, which might be attributed to the small sample size. As the data of the full enteral nutrition achievement time did not comply with the normal distribution, the MU analysis was adopted for statistical analysis. Therefore, the statistical power was weaker than that of the parametric test. However, the median time of the feeding intolerance was longer in the EUGR group than in the non-EUGR group. We are convinced that if we expand the sample size in future studies, the difference could be significant.

EUGR is a serious clinical problem that occurs frequently in VLBWIs.[3] Although only 27.5% of VLBWIs included in the present study were SGA at birth, 67.2% eventually developed EUGR. The incidence of EUGR in the current study was in line with previous studies.[6,15] Growth failure in VLBWIs may result from multiple factors such as difficulties in digestion, endocrine abnormalities, central nervous system impairment, and morbidities affecting nutrient requirements.[16] Insufficient nutrition, especially within the first postnatal weeks, is largely responsible for the occurrence of EUGR.[17]

Our findings confirmed the fact that gestational age is a risk factor for EUGR.[7] It is reasonable that organ function will develop better and the possibility of feeding intolerance and underlying diseases will decrease as infants mature. EUGR can be assessed by the body weight, head circumference, and body length of the infant. A limitation of this study is that the bodyweight was the only criterion used for EUGR.

Early feeding and nutritional support are strategies for the prevention of EUGR.[4,12,18] Early enteral feeding improves the gastrointestinal tolerance and boosts the growth of the digestive tract.[12] In addition to enteral feeding, parenteral feeding is necessary for VLBWIs to achieve the required amounts of nutrition.[8] In this study, the infants in both the EUGR and non-EUGR group received intravenous nutritional support before the start of enteral nutrition. For the start time of enteral feeding, an early initiation within the first 3 days after birth is suggested.[19] The time of initiation of oral feeding was later in the EUGR group compared with that in the non-EUGR group. Besides, feeding intolerance due to a delayed enteral feeding hurt the body weight gain. Not surprisingly, our results revealed that feeding intolerance was a risk factor for EUGR.

Early enteral feeding decreases the risk of NEC. However, the incidence of complications including NEC did not differ between the groups in the current study, which was inconsistent with findings from previous studies.[18] The limited sample size and observation period in our study may partly explain this discrepancy.

A prompt provision of amino acids induces body weight gain and prevents the occurrence of EUGR in VLBWIs.[20] We found that calories supplied by intravenous amino acids on the 7th day had a positive effect on body weight gain. The body weight in the non-EUGR group was greater than that in the EUGR group, along with higher calories provided by intravenous amino acids.

Table 3

Comparisons of total calorie intake and body weight changes between the groups.

Variable	EUGR group	non-EUGR group	*P* value
Total calorie intake (kcal/kg/d)			
3rd day	57.18 ± 13.49	58.04 ± 13.68	.726
7th day	84.24 ± 19.58	85.34 ± 17.01	.750
14th day	96.14 ± 26.03	98.53 ± 21.98	.597
28th day	108.58 ± 26.74	117.94 ± 24.08	.049
Body weight (g)			
3rd day	1157.07 ± 173.87	1274.00 ± 185.26	.000
7th day	1184.10 ± 162.10	1275.60 ± 193.63	.004
14th day	1307.00 ± 183.05	1372.90 ± 218.50	.066
28th day	1583.26 ± 264.35	1750.44 ± 259.30	.001
at discharge	2206.41 ± 290.30	2376.22 ± 345.05	.003

Data are presented as No. (%), mean ± standard deviation, or median (interquartile range).

Table 4

Independent risk factors for EUGR by multivariate logistic regression analysis.

Risk factor	Odds ratio	95% CI	*P* value
Gestational age	0.573	0.414–0.794	.001
SGA	3.887	1.222–12.368	.022
Feeding intolerance	4.632	1.758–12.203	.002
Calories supplied by amino acids at the 7th day	0.786	0.661–0.934	.006

SGA = small for gestational age.

A local multicenter study pointed out that aggressive nutritional management decreased the incidence of EUGR in VLBWIs.[7] The updated 2013 version of the Chinese guidelines for nutrition support in neonates recommends a daily calorie intake of 120 kcal/kg/d. Specifically, the total calorie intake is recommended to be 105 to 130 kcal/kg/d for neonates, 110 to 135 kcal/kg/d for premature infants, and up to 150 kcal/kg/d for VLBWIs. Within the first postnatal week, remarkably lower body weight was noticed in the EUGR group. However, this difference between the EUGR and non-EUGR groups disappeared on the 14th day, indicating a positive effect of early nutrition support on body weight. With the increase in calorie requirements due to metabolic abnormalities or disease, the total calorie intake in the EUGR group decreased, which resulted in lower body weight compared to the non-EUGR group.

5. Conclusions

Gestational age, the incidence of SGA, feeding intolerance, and calories supplied by amino acids at the 7th day are high-risk factors for EUGR in VLBWIs. The nutrition support guidelines currently implemented are based on the intrauterine growth indicators of normal fetuses. They do not accurately reflect the pathophysiological status of premature infants. Clinically, individualized nutrition support strategies such as reducing feeding intolerance and amino acid nutrition support should be applied for VLBWIs to reduce the incidence of EUGR and to improve the long-term prognosis.

Author contributions

XLZ participated in study design and protocol development. LD carried out the data analysis and interpretation of data. XQC participated in clinical data collection. JW participated in the design of the study and coordination. XPZ made study design, participated in data analysis, interpretation of data and writing of the manuscript. All authors read and approved the final Manuscript.

References

[1] Fanaroff AA, Hack M, Walsh MC. The NICHD neonatal research network: changes in practice and outcomes during the first 15 years. Semin Perinatol 2003;27:281–7.
[2] Patel RM, Kandefer S, Walsh MC, et al. Causes and timing of death in extremely premature infants from 2000 through 2011. N Engl J Med 2015;372:331–40.
[3] Clark RH, Thomas P, Peabody J. Extrauterine growth restriction remains a serious problem in prematurely born neonates. Pediatrics 2003;111:986–90.
[4] Su BH. Optimizing nutrition in preterm infants. Pediatr Neonatol 2014;55:5–13.
[5] Chien-Chou H, Ming-Luen T, Chih-Chen C, et al. Early optimal nutrition improves neurodevelopmental outcomes for very preterm infants. Nutr Rev 2014;72:532–40.
[6] Griffin I, Tancredi DJ, Bertino E, et al. Postnatal growth failure in very low birthweight infants born between 2005 and 2012. Arch Dis Child Fetal Neonatal Ed 2016;101:F50–5.
[7] Shan HM, Cai W, Cao Y, et al. Extrauterine growth retardation in premature infants in Shanghai: a multicenter retrospective review. Eur J Pediatr 2009;168:1055–9.
[8] Hu F, Tang Q, Wang Y, et al. Analysis of nutrition support in very low-birth-weight infants with extrauterine growth restriction. Nutr Clin Pract 2018;34:436–43.
[9] Hiltunen H, Lyttyniemi E, Isolauri E, et al. Early nutrition and growth until the corrected age of 2 years in extremely preterm infants. Neonatol 2018;113:100–7.
[10] Avila-Alvarez A, Boga AS, Bermúdez-Hormigo C, et al. Extrauterine growth restriction among neonates with a birthweight less than 1,500grams. An Pediatr (Barc) 2018;89:325–32.
[11] Pampanini V, Boiani A, Marchis CD, et al. Preterm infants with severe extrauterine growth retardation (EUGR) are at high risk of growth impairment during childhood. Eur J Pediatr 2015;174:33–41.
[12] Kumar RK, Singhal A, Vaidya U, et al. Optimizing nutrition in preterm low birth weight infants-consensus summary. Front Nutr 2017;4:20–9.
[13] Dinerstein A, Nieto RM, Solana CL, et al. Early and aggressive nutritional strategy (parenteral and enteral) decreases postnatal growth failure in very low birth weight infants. J Perinatol 2006;26:436–42.
[14] Moore TA, Wilson ME. Feeding intolerance: a concept analysis. Adv Neonatal Care 2011;11:149–54.
[15] Shlomai NO, Reichman B, Lerner-Geva L, et al. Population-based study shows improved postnatal growth in preterm very-low-birthweight infants between 1995 and 2010. Acta Paediatr 2014;103:498–503.
[16] Curtis MD, Rigo J. Extrauterine growth restriction in very-low-birthweight infants. Acta Paediatr 2004;93:1563–8.
[17] Embleton NE, Pang N, Cooke RJ. Postnatal malnutrition and growth retardation: an inevitable consequence of current recommendations in preterm infants? Pediatrics 2001;107:270–3.
[18] Hamilton E, Massey C, Ross J, et al. Early enteral feeding in very low birth weight infants. Early Hum Dev 2014;90:227–30.
[19] Boo NY, Soon CC, Lye MS. Risk factors associated with feed intolerance in very low birthweight infants following initiation of enteral feeds during the first 72 hours of life. J Trop Pediatr 2000;46:272–7.
[20] Valentine CJ, Fernandez S, Rogers LK, et al. Early amino-acid administration improves preterm infant weight. J Perinatol 2009;29:428–32.