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Parenteral nutrition on growth of low birth weight infants.

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Abstract

Objective: The aim of this study is to evaluate the incidence and risk factors for Intrauterine Growth Retardation (IUGR) and Extra Uterine Growth Retardation (EUGR) and provide more approaches for appropriate nutritional support for preterm infants.

Methods: A total of 144 preterm infants (75 male and 69 female) were involved in this study. According to the relationship between gestational age and birth weight, all the preterm infants were divided into two groups of Appropriate-for-Gestational-Age infants (AGA) and Small-for-Gestational-Age infants (SGA); meanwhile, based on the different nutritional strategy, the infants were classified into group of aggressive nutritional and non- aggressive nutritional strategy. Finally, laboratory examination and the growth parameters in preterm infants were analysed.

Results: The incidence of IUGR in birth weight, length and head circumference was 61.11%, 20.83% and 25.69%, respectively. According to the measurement of birth weight and length, there was significant difference in the incidence of IUGR amongst the three groups based on body weight<1500 g, 1500-2000 g and 2000-2500 g (all p<0.05). Compared between IUGR and AGA group, there was significant difference in birth weight, length, and head circumference at discharge (all p<0.05). Maternal preeclampsia, rather than any other parameters of maternal or neonatal complications, had a significant effect on the occurrence of both IUGR and EUGR. There were significant differences in the weight growth rate, head circumference growth rate, intravenous nutrition application time, height at discharge and head circumference at discharge in infants with aggressive nutritional support (all p<0.05).

Conclusion: Aggressive parenteral nutrition can promote physical development and decrease the incidence of EUGR in low birth weight infants.

Keywords: Parenteral nutrition, Preterm, Low birth weight infants, Intrauterine growth retardation, Extrauterine growth retardation.

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Introduction

In recent years, the survival rate of Very Low-Birth-Weight Infant (VLBWI) and Extremely Low-Birth-Weight Infant (ELBWI) was significantly increased, along with the rapid development of Neonatal Intensive Care Unit (NICU) [1,2]. However, preterm neonates are easily to have intrauterine nutritional deprivation and susceptibility of various complications, which may lead to growth stunting and even Extrauterine Growth Retardation/Restriction (EUGR), especially in VLBWI and ELBWI [3]. The concept of EUGR, firstly proposed by Clark in 2003, was defined as the severe nutritional deficits with the growth indicators (weight, length, and head circumference) less than 10^{th} percentile of average growth parameters in children at the same gestational age [4].

Dusik et al. [5] showed that 16% of VLBWI was small-for-gestational-age infants (SGA); whereas 89% of infants had growth retardation at 36 weeks of corrected gestational age. Shan et al. [6] demonstrated that the incidence of EUGR and severe EUGR in body mass was 49.7% and 21.7% respectively, while the incidence of EUGR and severe EUGR in head circumference was 23.1% and 6.2%, respectively. Previous studies have shown that EUGR may have a serious and long-term influence on the growth and neurodevelopment of neonates after birth or even health in adulthood [7-9]. Therefore, more attention should be given to developing strategies for decreasing the incidence of EUGR.

In this retrospective study, we aim to evaluate the incidence and risk factors of Intrauterine Growth Retardation (IUGR) and EUGR in preterm infants, and to assess the effectiveness, feasibility and safety of aggressive nutritional strategy. The effects of aggressive nutritional and non-aggressive nutritional strategy on the incidence of IUGR and EUGR, indicators of physical growth, and serum biochemical parameters were compared. We believe that our study will provide further understanding for reducing the incidence of EUGR and choosing appropriate nutritional support strategies for preterm children.

Materials and Methods

Patient recruitment

The preterm infants (gestational age<37 weeks, birth weight<2,500 g, admission age<24 hours, and length of stay ≥ 14 days) who were hospitalized in the neonatal unit of our hospital from April 2015 to March 2016 were enrolled in the study. The mean time of hospitalization was 30 days. The infants were discharged when meeting the criteria as follows: the body weight ≥ 2000 g, stable body temperature, normal breastfeeding, no occurrence of apnea or bradycardia, and withdrawal of the oxygen uptake and medication for a period.

The infants were excluded if they died during hospitalization, or suffered from congenital metabolic diseases, chromosomal abnormalities, congenital infections, severe congenital malformations, or their mothers had endocrine and metabolic diseases. Finally, we collected the clinical information including history, measurement of physical development (weight, growth, head circumference), and laboratory indicators (routine detection of blood, urine, and stool; blood glucose monitoring; liver and kidney function evaluation; and blood biochemical examination). Prior written and informed consent were obtained from the patients' families and the study was approved by the ethics review board of Jinan Maternity and Child Care Hospital.

Patient grouping

Based on the relationship between gestational age and birth weight, all the preterm infants were divided into two groups of Appropriate-for-Gestational-Age infants (AGA) (n=105) and Small-for-Gestational-Age infants (SGA) or IUGR (n=39). AGA was defined as that the birth weight was between 10% and 90% of average body weight in infants at the same gestational age; while SGA or IUGR was defined as that the birth weight was less than 10% of average body weight in infants at the same gestational age [8]. Based on the birth weight, all preterm infants were divided into three groups including group with birth weight<1500 g (n=37), group with birth weight 1500-2000 g (n=60), and group with birth weight 2000-2500 g) (n=47). In group with birth weight<1500 g (n=37), infants were further divided into VLBWI group (birth weight 1000 g-1500 g) (n=33) and ELBWI group (birth weight<1000 g) (n=4). According to the different nutritional strategy, the infants were classified into aggressive nutritional strategy group (n=89) and non-aggressive nutritional strategy group (n=55).

Nutritional strategy

There were 89 cases of infants (46 males, 43 females) managed with aggressive nutritional strategy and 55 cases of infants (29 males, 26 females) managed with non-aggressive nutritional strategy. There were no significant differences in the duration of mechanical ventilation, the incidence of PDA, NEC, IVH, PVL, and BPD, and the incidence of breastfeeding, between these two groups, and there were no differences in the formula milk feeding and nutritional enhancement within each group. For aggressive nutritional strategy, infants were given amino acid with the dosage from 1.5-2 g/kg/d at 12-24 hours after birth and, by an increment of 0.5-1.0 g/kg/d, to the maximum dosage of 3.5 g/kg/d. Lipid emulsion was administrated at 24 hours after birth at dosage from 1 g/kg/d, with an increment of 0.5 g/kg/d, to maximum dosage of 3 g/kg/d. For non-aggressive nutritional strategy, infants received amino acid (0.5g/kg/d) and lipid emulsion (0.5 g/kg/d) at 12-24 hours after birth and, with an incremental dose of 0.5 g/kg/d for both nutrients, the maximum dosage of 3.5 g/kg/d and 3.0 g/kg/d, respectively. All infants were given the same dosage of water-/ fat- soluble vitamins and fed with the same method. The nutritional support lasted for 1-2 weeks.

Definition criteria for EUGR and other parameters

EUGR was defined as that the growth indicators (body weight, height, and head circumference) at discharge were no more than 10^{th} percentile of average growth parameters in the growth curvature in infants at the same gestational age [8].

Intrauterine growth curve was created using values of birth weight and head circumference in different gestational age in 15 cities of China (1986-1987) [8], while the infant growth curve was generated using the values of percentile graphs of body weight, length, and head circumference in children (aged 0-3 year-old) in 9 cities of China (1995) [7]. Other parameters were calculated as follows: discharge gestational age (week)=admission gestational age+hospitalization week (hospital days/7); weight decrease after birth (%)=(birth weight-the lowest weight)/birth weight × 100%; weight growth rate (g/kg/d)=(discharge weight-birth weight)/(number of hospitalization days × birth weight).

Statistical analysis

All data were analysed using SPSS 13.0 (IBM, Armonk, NY, USA). The measurement data were expressed as means ± Standard Deviation (SD). Comparison of continuous data between groups was performed with independent-samples t test, and comparison of categorical data was made by chi-square test. Disease risk factors were analysed by Logistic regression analysis. P<0.05 was considered statistically significant.

Results

Clinical profile of IUGR, EUGR and AGA group

A total of 144 preterm infants (75 male and 69 female) were involved in this study. The clinical profile of growth was analysed. The results demonstrated that the incidence of IUGR in birth weight, length and head circumference was 61.11%, 20.83% and 25.69%, respectively. Furthermore, between IUGR and AGA group, there were significant differences in parameters at birth (gestational age and birth weight), parameters at discharge (body weight, body length, head circumference), and recovery time from the status of IUGR to AGA (all p<0.05). However, there were no significant differences in duration of intravenous nutrition, length of hospital stay, and the increase rate of body weight, body length, and head circumference between the two groups (all p>0.05) (Table 1).

Table 1. *Comparison of clinical profile of preterm infants between IUGR and AGA group.*

	IUGR (n=39)	AGA (n=105)	Statistic	P value
Gestational age (w)	33.87 ± 2.24	32.37 ± 2.54	t=3.451	0.001
Birth weight (g)	1557.44 ± 407.60	1813.33 ± 394.87	t=-3.426	0.001
Birth length (cm)	42.69 ± 4.34	44.30 ± 3.50	t=2.286	0.24
Head circumference (cm)	28.95 ± 2.43	29.63 ± 2.06	z=-1.34	0.18
Weight growth rate (g/kg/d)	14.43 ± 4.78	16.23 ± 6.14	t=1.849	0.972
Length growth rate (cm/w)	0.66 ± 0.51	0.69 ± 0.41	z=-1.216	0.224
Head circumference growth rate (cm/w)	0.55 ± 0.26	0.56 ± 0.27	z=-0.014	0.989
Recovery time to birth weight (d)	9.16 ± 4.02	6.97 ± 3.67	z=-3.652	0
Duration of intravenous nutrition (d)	14.24 ± 10.10	13.72 ± 10.83	z=-0.432	0.666
Length of hospital stay (d)	25.59 ± 12.15	24.33 ± 12.69	z=-0.335	0.737
Weight at discharge (g)	1984 ± 244.34	2193.24 ± 298.69	t=-4.286	0
Length at discharge (cm)	45.17 ± 3.10	51.28 ± 4.52	z=-2.943	0.003
Head circumference at discharge (cm)	30.96 ± 1.51	31.67 ± 1.58	z=-2.343	0.019

Incidence of IUGR and EUGR in infants with different birth weight

Based on the birth weight, all preterm infants were divided into three groups including group with birth weight<1500 g, group with birth weight 1500-2000 g, and group with birth weight 2000-2500 g. According to the measurement of birth weight and birth length, there was significant difference in the incidence of IUGR amongst the three groups (all p<0.05). Furthermore, there was highest IUGR incidence in group with body weight<1500 g and lowest IUGR incidence in the group of 1500-2000 body weight (p<0.05). However, in infants with different head circumferences, there was no significant difference in the incidence of IUGR among the three groups (p>0.05) (Table 2). In other hand, in infants with different birth weight, birth length and head circumference, there was significant difference in the incidence of EUGR amongst the three groups (all p<0.05). Additionally, the incidence of EUGR was highest in ELBWI group and lowest in infants group III (Table 2).

Table 2. *Incidence of IUGR and EUGR in infants with different birth weight, length, head circumference and the combination of these parameters.*

Groups		Birth weight	Birth length	Head circumference	Two terms at birth	Three terms at birth
Group with body weight<1500 g (n=37)	IUGR	16 (43.24%)	12 (32.43%)	9 (24.32%)	3 (8.11%)	9 (24.32%)
	EUGR	31 (83.78%)	19 (51.35%)	18 (48.65%)	8 (21.61%)	12 (32.43)
Group with body weight 1500-2000 g (n=60)	IUGR	7 (11.67%)	3 (5.00%)	7 (11.67%)	4 (4.67%)	2 (3.33%)
	EUGR	35 (58.33%)	8 (13.33%)	11 (18.33%)	8 (13.33%)	2 (4.26%)
Group with body weight 2000-2500 g (n=47)	IUGR	16 (34.04%)	3 (6.38%)	10 (21.28%)	4 (8.51%)	1 (2.13%)
	EUGR	23 (48.94%)	4 (8.51%)	8 (17.02%)	10 (21.28%)	2 (4.26%)
Statistic (IUGR)		13.2665	18.1338	2.9676	0.1426	16.7188
Statistic (EUGR)		11.175	26.58	13.7656	1.5519	20.3619
P value (IUGR)		0.0013	0.0001	0.2268	0.9312	0.0002

P value (EUGR)	0.0037	0	0.001	0.4603	0

Two terms at birth: the combination of body weight and body length at birth; Three terms at birth: the combination of body weight, body length, and head circumference at birth.

Incidence of EUGR in IUGR and AGA group at discharge

Next, we analysed the incidence of EUGR in IUGR and AGA infants at discharge. Our results showed that, compared between IUGR and AGA group, there was significant difference in birth weight, length, and head circumference at hospital discharge (all p<0.05). These findings suggest that preterm children with IUGR are more vulnerable to EUGR (Table 3).

Table 3. *The incidence of EUGR in IUGR and AGA infants at discharge.*

	IUGR		AGA		χ^2	P
	N	EUGR	N	EUGR		
Weight at discharge (g)	39	38 (97.44%)	105	50 (47.62%)	29.696	0
Length at discharge (cm)	39	18 (46.15%)	105	12 (11.43%)	20.7913	0
Head circumference at discharge (cm)	39	17 (43.59%)	105	20 (19.05%)	8.9713	0.0027

Incidence of IUGR in VLBWI and ELBWI group

Infants with birth weight<1500 g (n=37) were further divided into VLBWI group (birth weight 1000 g-1500 g) (n=33) and ELBWI group (birth weight<1000 g) (n=4). The incidence of IUGR in VLBWI and ELBWI groups was also analysed. Our results demonstrated that, there were 12 (30.77%) cases of IUGR and 21 (63.64%) cases of AGA in VLBWI group. In other hand, there were 4 (100%) cases of IUGR and 0 (0.00%) case of AGA in ELBWI. There were significant differences in the incidence of IUGR between the two groups, indicating a higher incidence of IUGR in ELBWI (Table 4).

Table 4. *The incidence of IUGR in VLBWI and ELBWI infants.*

	N	IUGR	AGA	χ^2	P
VLBWI (birth weight 1000 g-1500 g)	33	12 (30.77%)	21 (63.64%)		
ELBWI (birth weight<1000 g)	4	4 (100%)	0 (0.00%)	11.0769	0.0009
Total	37	16 (43.24%)	21 (53.85%)		

Table 5. *Comparison of clinical profile of preterm infants in aggressive and non-aggressive nutritional strategy.*

	Non-aggressive nutrition (n=89)	Aggressive nutrition (n=55)	Statistic	P value
Gestational age (w)	32.95 ± 2.61	32.50 ± 2.37	t=1.032	0.304
Birth weight (g)	1761.69 ± 432.81	1715.45 ± 380.89	t=0.651	0.516
Birth length (cm)	43.60 ± 3.93	44.29 ± 3.57	t=-1.071	0.286
Head circumference (cm)	29.20 ± 2.34	29.85 ± 1.83	z=-1.917	0.055
Weight growth rate (g/kg/d)	13.87 ± 5.69	16.42 ± 4.93	t=-2.746	0.007
Length growth rate (cm/w)	0.67 ± 0.33	0.69 ± 0.49	z=-1.417	0.157
Head circumference growth rate (cm/w)	0.50 ± 0.23	0.59 ± 0.27	z=-2.384	0.017
Recovery time to birth weight (d)	8.98 ± 4.30	7.91 ± 3.49	z=-1.432	0.152
Duration of intravenous nutrition (d)	21.43 ± 11.31	14.27 ± 9.92	z=-3.996	0
Length of hospital stay (d)	26.16 ± 12.81	24.67 ± 11.97	z=-0.704	0.481

Weight at discharge (g)	2119.55 ± 302.82	2164.18 ± 293.56	t=-0.869	0.386
Length at discharge (cm)	46.85 ± 2.86	50.81 ± 4.96	z=-2.943	0.003
Head circumference at discharge (cm)	30.94 ± 3.97	31.79 ± 1.26	z=-2.384	0.017
All data were represented as means ± standard deviation (SD).				

The association of pregnancy complications with IUGR and EUGR

In our study, there were variable pregnancy complications including 33 (22.92%) cases of multiple pregnancies, 30 (20.83%) cases of pre-eclampsia (severe), 11 (7.64%) cases of fetal distress, 10 (6.94%) cases of placental abruption, and 8 (5.56%) cases of gestational diabetes. Besides, the neonatal complications after birth included 59 (40.97%) cases of neonatal pneumonia, 25 (17.36%) cases of hyaline membrane disease, and 20 (13.98%) cases of digestive disorders including feeding intolerance, Necrotizing Enterocolitis (NEC), and gastrointestinal bleeding. Multivariate regression analysis demonstrated that maternal preeclampsia, rather than any other parameters of maternal or neonatal complications, had a significant effect on the occurrence of both IUGR and EUGR.

Effects of different intravenous nutritional support on preterm infant growth

In our study, there was 89 cases of infants (46 males, 43 females) managed with aggressive nutritional strategy and 55 cases of infants (29 males, 26 females) managed with non-aggressive nutritional strategy. The results suggested that, between aggressive and non-aggressive nutritional group, there were no significant differences in gender, gestational age, birth weight, birth length, head circumference, growth rate of height, recovery time to birth weight, hospitalization time, and body weight at discharge (all $p>0.05$). However, there were significant differences in the weight growth rate, head circumference growth rate, intravenous nutrition application time, height at discharge and head circumference at discharge in infants with aggressive nutritional support (all $p<0.05$) (Table 5). Our data reveals that aggressive nutrition can promote the growth of body weight, length and head circumference.

Effects of different intravenous nutritional support on preterm infant biochemical parameters

The serum biochemical parameters of preterm infant after two types of intravenous nutritional supports were analysed. The results demonstrated that there was a significant decrease in serum level of Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT), rather than any other indicators, in aggressive nutritional supports group compared with non-aggressive nutritional supports group. The results suggest that no more cholestasis is observed in infants managed with aggressive nutritional supports (Table 6).

Table 6. *Biochemical parameters in aggressive and non-aggressive nutritional strategy group.*

	Non-aggressive nutrition		Aggressive nutrition		Statistic	P value
	N	X ± SD	N	X ± SD		
Calcium	48	2.14 ± 0.19	68	2.17 ± 0.23	-0.605	0.581
Phosphorus	48	1.53 ± 0.50	68	1.82 ± 2.36	-0.838	0.344
Creatinine	48	54.96 ± 17.09	68	56.90 ± 18.21	-0.579	0.357
BUN	48	6.29 ± 5.82	68	3.88 ± 2.20	1.242	0.108
AST	47	39.96 ± 27.31	68	55.97 ± 44.53	-2.198	0.037
ALT	47	8.12 ± 7.28	68	13.31 ± 12.93	-2.49	0.014
Bile acid	47	15.55 ± 12.13	68	18.66 ± 13.40	-1.271	0.206
Triglycerides	31	0.94 ± 0.44	30	0.82 ± 0.29	1.253	0.215
Total cholesterol	31	3.39 ± 1.67	30	2.92 ± 0.51	-1.476	0.145
LDL	31	2.04 ± 1.10	30	1.84 ± 0.48	0.915	0.364
HDL	31	1.00 ± 0.36	30	0.86 ± 0.31	1.623	0.109
Total protein	31	44.58 ± 6.00	40	45.89 ± 22.62	-0.315	0.208
Albumin	31	31.93 ± 3.30	39	31.40 ± 3.78	0.611	0.468
Globulin	31	12.65 ± 4.10	39	13.84 ± 4.17	-1.124	0.266
NBAP	47	220.89 ± 99.35	66	196.98 ± 78.18	1.431	0.272

BUN: Blood Urea Nitrogen; AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase; HDL: High-Density Lipoprotein-Cholesterol; LDL: Low-Density Lipoprotein-Cholesterol; NBAP: Neonate Bone Alkaline Phosphatase. X ± SD: means ± Standard Deviation (SD).

The incidence of EUGR in infants with aggressive and non-aggressive nutritional supports

Finally, we evaluate the EUGR incidence in body weight, length and head circumference at discharge. Our results demonstrated that, compared with infants in non-aggressive nutritional supports group, there was a decrease of EUGR incidence in body weight, length and head circumference at discharge in infants with aggressive nutritional supports. However, only the difference of EUGR incidence in head circumference had statistically significant difference between the two groups (Table 7).

Table 7. *Comparison of incidence of EUGR in aggressive and non-aggressive nutritional strategy group.*

	Non-aggressive nutrition		Aggressive nutrition		Statistic	P value
	N	X ± SD	N	X ± SD		
Weight at discharge (g)	89	56 ± 62.92%	55	32 ± 58.18%	0.3213	0.5708
Length at discharge (cm)	89	22 ± 24.72%	55	8 ± 14.55%	2.1333	0.1441
Head circumference at discharge (cm)	89	29 ± 32.58%	55	8 ± 14.55%	5.7936	0.0161

X ± SD: means ± Standard Deviation (SD).

Discussion

Clark et al. [4] retrospectively analysed the data on 24371 neonates (gestational age<34 weeks) discharged from 124 NICU and demonstrated that, according to the evaluation of weight, length, and head circumference, the incidence of EUGR at discharge was 28%, 34% and 16%, respectively. Meanwhile, their results also revealed that the incidence of EUGR gradually increased along with the increase of gestational age and body weight. In China, incidence of EUGR for body weight and head circumference ranged from 39.22%-80.5% and 23.1%-33.3%, respectively [9]. In addition, based on the calculation of percentage for gestational age at discharge, the percentage of body weight, height and head circumference less than 10% of average value was 60.0%, 58.9%, and 29.5%, respectively, in preterm infants [10]. Our data showed that, the incidence of IUGR for weight, length, and head circumference in preterm infants at discharge was 61.11%, 20.83% and 25.69%, respectively. Lower birth weight led to higher incidence of EUGR. VLBW infants are associated with the highest EUGR incidence at discharge, followed by the babies with BW between 1500 and 2000 grams, and the lowest EUGR incidence is observed for the infants with BW of 2000-2500 grams. The higher incidence of EUGR in our study may be resulted from the involved subjects, who were mostly at higher risk caused by pregnancy and neonatal complications. Besides, the metabolites of fat emulsion, which had a high content in the parenteral nutrition in our study, competitively bound to albumin and subsequently affected the metabolism of unconjugated bilirubin, may also result in the difference of incidence mentioned above. Thus, aggressive nutritional support is necessary and pivotal in preterm infants especially ELBWI with smaller gestational age.

For the preterm and critically ill infants, EUGR had many hazards, including the increased metabolic burden, risk of parenteral nutrition-related complications, and the occurrence of intestinal injury and NEC. These complications ultimately result in enteral nutritional deficiency, growth retardation and decreased potential of growth and development at later stages [11]. Nutrition plays a pivotal role in cell signal transduction pathway in gastrointestinal system, nervous system, and immune system; while the deficiency of nutritional and trace elements may change the infant growth at cell and tissue levels [12]. In the brain, adequate nutrition is necessary in the neuronal activities including cell division and growth, substance transport between neurogliocytes, and myelination [13]. Body mass at birth and body growth after birth can affect the later cognitive function and intelligence development [14]. Postnatal growth retardation has close correlation with nerve disorders, sensory disturbances and poor environmental adaptability in school [15]. It can be predicted that infants with lower head circumference at 8 months of age have poorer language skills and mental development scores, poorer language, speech, reading, spelling and computing capacity and higher the risk of Attention Deficit Hyperactivity Disorder (ADHD) than normal children at 8 years old [16]. Therefore, particular attention should be given to EUGR.

There are several risk factors for the occurrence of EUGR. This study showed that, EUGR incidence in infants after birth was significantly higher in infants with IUGR than that with AGA, no matter which evaluation parameter (weight, length or head circumference) was used. Previous study has also shown that IUGR is closely related to metabolic and cardiovascular complications in infants after birth [17,18], and even neurological and physical development in adulthood [19]. Therefore, positive intervention (prenatal care, early detection of IUGR and reasonable prenatal treatment) is an important solution to avoid IUGR and EUGR; while the infants with IUGR should be managed with adequate nutritional support. Next, we conducted the correlation analysis between the EUGR and maternal high-risk factors including multiple pregnancy, preeclampsia, gestational diabetes, fetal distress, and placental abruption. The results demonstrated that there was close association between severe preeclampsia and IUGR or EUGR after birth. Several diseases in parent can significantly affect fetal health and growth in the respects of fetal nutrient intake, blood supply, and even organ dysfunction. These risk factors also contribute to the susceptibility of IUGR and subsequent EUGR in preterm infants.

Finally, the inherent property (insufficiency of intrauterine nutritional reserves, immature organs, feeding difficulties and high demand for energy) is predisposing factor for the slow body growth and occurrence of complications [20]. However, one of the most prominent side effects of parenteral nutrition is glucose intolerance or hyperglycaemia, which significantly limits its usage. On the other hand, the recent study suggested that the amino acids and fat emulsion can be well tolerated in preterm infants, even in critically ill ELBWI at the first day after birth [21]. In order to avoid the disorders (metabolic acidosis, high ammonia hypertriglyceridemia, azotemia, liver and kidney dysfunction) caused by excessive amount of amino acids, the traditional intravenous nutrition regimen for neonates initiates carefully from amino acids 0.5 g/kg/d from the third day, followed by gradual increase of dosage. But parenteral administration of amino acids within 24 hours after birth in preterm children is well tolerated with no significant side effects. In our study, two different types of parenteral nutrition strategies were designed and applied to preterm infants with IUGR or EUGR. Our results suggested that aggressive nutritional management had the potential to promote the growth in body weight, length, and head circumference. And most importantly, aggressive nutritional management did not increase the incidence of complications such as cholestasis or liver and kidney dysfunction. Moreover, AST and ALT levels were decreased in aggressive nutritional support group. Regarding the increase of AST and ALT in non-aggressive nutritional supports group, we speculate that the limitation of relative small sample size may lead to the bias of statistical analysis. Therefore, further studies with larger sample size are necessary to be carried out.

In summary, EUGR remains a serious problem in preterm infants especially for neonates who are small, immature, and critically ill. Increased attention should be brought to EUGR in China. Our findings suggest that, the incidence of EUGR in the preterm infants in our hospital was significantly higher than that in foreign publications, and lower birth weight was associated with higher EUGR incidence. The physical development indicators of IUGR infants at discharge were significantly inferior to AGA, and it took longer time for the IUGR infants to recover to birth weight. IUGR always indicates high risk of EUGR, which need more aggressive nutritional support to achieve the intrauterine growth rate, and the nutritional deficiencies should be avoided. Enhanced parenteral nutrition in combined with trace amounts of enteral nutrition would dramatically promote the physical development of low birth weight infants during hospitalization, which could decrease the EUGR incidence. The head circumference EUGR incidence was significantly lower than the non-aggressive nutritional strategy group, and there were no serious side effects, suggesting an effective nutrition supporting method. In the enhanced nutrition intervention group, significant differences were observed in the weight gaining rate, head circumference growth rate, duration of parenteral nutrition application, and length and head circumference after discharging, which indicated that enhanced nutrition could promote the growth of body weight, head circumference, and body length. Moreover, the enhanced nutrition intervention showed no limited influence on the renal function, and the levels of serum lipid, plasma protein, bile acid, alkaline phosphatase, calcium, and phosphorus. However, there were significant differences in the liver transaminase, AST, and ALT between these two groups. The AST and ALT levels in the non-aggressive nutritional strategy group were higher than the enhanced nutrition intervention group. However, considering that the limitation of observational period, sample size, and incomplete biochemical data, the baby has complete biochemical parameter data, further in-depth studies (e.g., concerning the cumulative doses of amino acids and lipids in the infants during hospitalization and the statistical analysis of EUGA at discharge) are still needed in the future.

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Disclosures

All authors declare no financial competing interests.

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