Early aggressive nutrition at 22–23 weeks gestational age improves weight gain and does not worsen neurological prognosis

Mayumi Tsukayama
University of the Ryukyu
Tomohide Yoshida (h034910@med.u-ryukyu.ac.jp)
University of the Ryukyus https://orcid.org/0000-0003-0110-3397
Hideki Goya
University of the ryukyudai
kouichi Nakanishi
university of the ryukyus

Research Article

Keywords: EAN, ELBW infants, GA22–23 weeks, Weight gain

Posted Date: September 3rd, 2021

DOI: https://doi.org/10.21203/rs.3.rs-853297/v1

Abstract

The effect of early aggressive nutrition (EAN) on extremely low birth weight (ELBW) infants is unknown. The purpose of this study was to investigate the effect of EAN on ELBW infants, especially premature neonates of 22–23 weeks gestational age (GA22–23-week). Twenty-eight preterm infants of less than 26 weeks were divided into two groups (GA22–23-week group, 10 infants; GA24–25-week group, 18 infants) and compared. Each preterm infant received more than 3.0 g/kg/day of amino acids in the first day after birth and 1.0 g/kg/day of lipid emulsion from the next day. The GA22–23-week group had significantly smaller head circumference (20.4 ± 1.0 cm vs. 22.2 ± 1.4 cm, P = 0.002) and body weight at birth (539 ± 68 g vs. 697 ± 155 g, P = 0.003), but there were no differences in early postnatal weight loss (10.4% ± 6.3% vs. 8.1% ± 6.3%, P = 0.37), and body weight at 37 weeks postmenstrual age (1906 ± 321 g vs. 2081 ± 379 g, P = 0.17). Blood urea nitrogen levels were higher in the GA22–23-week group (59.7 ± 16.6 mg/dl vs. 45.0 ± 10.8 mg/dl, P = 0.004), but there were no differences in direct-bilirubin, bile acids, and ammonia levels. After discharge, there was no significant difference in developmental quotient at 2 years of age (71.3 ± 15.1 vs. 78.1 ± 22.6, P = 0.20) between the two groups.

Conclusion: We suggest that EAN reduces the rate of early postnatal weight loss in ELBW infants and contributes to weight gain until full term age.

Background

What Is Known:

There is limited evidence on the effect of early aggressive nutrition in ELBW infants at GA22–23 weeks.

What Is New:

The GA22–23-week EAN group also had better weight gain and EAN did not worsen neurodevelopmental outcomes.

Introduction

Recently, early aggressive nutrition (EAN) for neonatal care has become standard practice. Preterm infants are suddenly cut off from nutritive supply after birth, mainly protein and glucose from the placenta, causing starvation, endogenous protein loss, and development of hypercatabolism [1]. Protein is used for energy with a constant glucose supply in preterm infants because they do not have enough fat and glycogen. Without exogenous protein, 1–2% of endogenous protein per day is lost due to proteolysis. The purpose of EAN is to prevent protein catabolism by administering amino acids (AAs) after birth, to make the subsequent development as close as possible to fetal development, and to improve developmental prognosis [2, 3]. It has been reported that EAN intake in very low birth weight (VLBW) infants can reduce the rate of weight loss and time to regain birthweight, and provide good subsequent

weight gain [4–6]. It has also been reported that early high protein intake in extremely low birth weight (ELBW) infants improved weight and height growth outcomes [7]. However, there are few reports of EAN targeting ELBW infants between gestational age 22 and 25 (GA22–25) weeks, and the effect is unclear. Furthermore, there are potential complications with EAN, such as long-term growth and neurodevelopment, azotemia, hyperammonemia, and hyper direct bilirubinemia, but studies of these problems are rare in ELBW infants. The purpose of our study was to examine the effects of EAN, including short-term prognosis and complications, and to determine whether beneficial effects could be obtained even for ELBW GA22–25-week infants.

Methods

Subjects

The study design was a retrospective cohort study. All infants admitted to our neonatal intensive care unit (NICU) from January 2015 to December 2019 were included in the analysis. These infants had GA < 26 weeks at birth and reached the postmenstrual age (PMA) of ≥ 37 weeks. Study subjects consisted of 30 preterm infants, and 28 infants were examined. The other two infants died shortly after birth. One of the 28 infants was small for GA (SGA) with a birth weight and height of less than the 10% tile, and was excluded from the analysis of body weight change during hospitalization. The NICU databases were used as information sources: GA, body size (weight, height, head circumference) at birth, presence of SGA, age when the feeding targets (enteral feeds ≥ 100 ml/kg per day, ≥ 160 ml/kg per day) were achieved, body measurements (weight, height, head circumference) at 37 weeks PMA, the ratio of weight less than the 10% tile at 37 weeks PMA, early postnatal weight loss rate, and days to regain birthweight. We also assessed weight change from birth at 41 weeks PMA, short-term prognosis, complications of total parenteral nutrition (TPN), head circumference at 12 and 18 months, developmental quotient (DQ) at 2 years of age, and head circumference and weight at 3 years age. The 2-year-old DQ was assessed using the Enjoji's development scale.

For complications associated with TPN, maximum measurements of blood urea nitrogen (BUN), direct bilirubin (d-bil) and bile acid were recorded from the results of regular blood sampling during hospitalization. Ammonia levels were recorded at 1 week after birth. The endpoint of short-term prognosis was necrotizing enterocolitis (NEC), patent ductus arteriosus (PDA) treated with indomethacin and/or surgery, retinopathy of prematurity (ROP) treated with laser phototherapy, and intraventricular hemorrhage (IVH) grades III–IV. Necrotizing enterocolitis was defined using Bell's classification stage 2 or more. The PDA was diagnosed clinically or with echocardiography and was considered clinically significant when it required medical treatment. The IVH was defined using Papile's classification with ultrasonography. The ROP was treated with laser treatment if it had reached stage III of the international classification as diagnosed by an ophthalmologist. We also investigated the introduction rate of home oxygen therapy, home high-flow nasal canula therapy, home continuous positive airway pressure, tracheostomy, and home tube feeding at discharge.

The protocol for EAN at our facility was as follows: >3.0 g/kg/day amino acid (AA) solution along with a glucose infusion rate of 5.5 mg/kg/min using a 10% glucose solution was started in the first days after birth. At day 2 after birth, lipid emulsion was introduced at 1.0 g/kg/day and was increased every day to a maximum of 3.0 g/kg/day. Fifty mL TPN preparations contained 30 mL of AA (provided as Pleamin-P Injection, Fuso Pharmaceutical Industries, Osaka, Japan), 10 mL of 50% glucose solution, 1 ml of 10% sodium chloride solution, 1 mL dipotassium phosphate solution, and 8 mL distilled water. Additionally, a vitamin preparation (provided as MULTAMIN® FOR INJECTION, AY PHARMACEUTICALS, Tokyo, Japan), and a trace element preparation (provided as Elemenmic Injection, AY PHARMACEUTICALS. Tokyo, Japan) were added. The lipid emulsion (provided as Intralipos Injection 10%, Otsuka Pharmaceutical Factory, Tokyo, Japan) was administered in parallel from the side tube of the central catheter. Fluids were started at a rate of 80–100 ml/kg/day and increased to 150–160 ml/kg/day. For enteral nutrition, breast milk was used at first, and artificial milk was avoided as much as possible until day 5 after birth. The dose of TPN preparations were increased while replacing enteral nutrition with intravenous nutrition, and used in combination until full feeding was reached. Data analysis was divided into two groups, GA22–23 weeks and GA24–25 weeks. The Z score was calculated using the standard physique at birth by gestational age of Japanese. Additionally, body weight was measured daily until 41 weeks PMA, the Z score was calculated, the average value of each body weight was calculated, and the transition of body weight change was shown as data. The data of SGA was excluded.

Head circumference and height could not be calculated because weekly measurements were not taken. The data analysis was performed using the JMP software program, version 14 (SAS Institute, Cary, NC, USA). Data for two groups were compared using the Mann-Whitney U test and chi-square test. The level of significance was set at $P < 0.05$.

Results

Thirty infants were admitted to our NICU during the study period, and 28 infants were included in the analysis: 10 in the GA22–23-week group and 18 in the GA24–25-week group. The remaining two infants had severe respiratory failure, did not respond to resuscitation, and died within 24 h after birth. Table 1 shows the clinical characteristics of the two groups. The GA22–23-week group had a significantly lower weight at birth (GA22–23 vs. GA24–25; 539 ± 68 g vs. 697 ± 155 g; P = 0.003), head circumference at birth (20.4 ± 1.0 cm vs. 22.2 ± 1.1 cm; P = 0.002), and height at birth (29.3 ± 2.0 cm vs. 30.9 ± 4.0 cm, P = 0.027). However, there were no significant differences in the Z score of body weight (0.13 ± 0.7 vs. −0.38 ± 1.1, P = 0.35) and number of SGA infants at birth (0 case vs. 1 case, P = 0.45). Table 2 shows the progress of infants during hospitalization. There was no difference in the days to reach enteral feeds of 100 ml/kg (GA22–23 vs. GA24–25; 13.0 ± 5.0 days vs. 12.7 ± 3.7 days, P = 0.94), but the days to reach enteral feeds of 160 ml/kg was significantly delayed in the GA22–23-week group (45.4 ± 22.5 days vs. 23.7 ± 9.2 days, P = 0.008). The head circumferences (28.8 ± 1.2 cm vs. 30.4 ± 2.1 cm, P = 0.015) and associated Z scores (− 2.6 ± 0.8 SD vs. −1.5 ± 1.4 SD, P = 0.016) at 37 weeks PMA were different between the two groups, as they were at birth, but the body weights (1906 ± 321 g vs. 2081 ± 379 g, P = 0.17) and associated Z scores (− 2.3 ± 1.0 vs. −1.7 ± 1.3, P = 0.16) at 37 weeks PMA were not different between the two groups. There

was only one case of SGA at birth in the GA24–25-week group. However, the number of body weights less than 10% tile at 37 weeks PMA increased in both groups, but the difference was not significant (9 cases vs. 11 cases, P = 0.10). Additionally, there were no differences in the rate of early postnatal weight loss (10.4% ± 6.3% vs. 8.1% ± 6.3%, P = 0.37) and the days of regain to birthweight (13.2 ± 5.9 days vs. 11.8 ± 4.8 days, P = 0.51) between the two groups.

Table 3 shows the short-term prognosis. The prevalence of IVH III–IV (GA22–23 vs. GA24-25; 3 cases vs. 0 case, P = 0.014) and ROP treated with laser phototherapy (8 cases vs. 7 cases, P = 0.037) in the GA22–23-week group was higher than the GA24–25-week group, but the prevalence of NEC, PDA treated with indomethacin treatment, PDA treated with surgery, home oxygen therapy, home high-flow nasal canula therapy, tracheostomy, and home tube feeding was similar in the two groups.

Table 4 shows the complications associated with TPN. The BUN levels were higher (GA22–23 vs. GA24–25; 59.7 ± 16.6 mg/dl vs. 45.0 ± 10.8 mg/dl, P = 0.004) in the GA22–23-week group, but no differences were observed in levels of d-bil (1.5 ± 0.7 mg/dl vs. 1.6 ± 0.8 mg/dl, P = 0.89), bile acids (40.1 ± 20.2 mg/dl vs. 53.2 ± 23.0 mg/dl, P = 0.11), and ammonia (71.5 ± 7.4 μg/dl vs. 55.8 ± 18.3 μg/dl, P = 0.25). Moreover, there were no cases requiring treatment because of complications.

Table 5 shows the progress of the infants after discharge from the NICU. There were no significant differences between the two groups in all endpoints examined, such as 1-year-old head circumference (GA22–23 vs. GA24–25; 43.0 ± 1.2 cm vs. 43.7 ± 1.4 cm, P = 0.13), 1.5-year-old head circumference (44.5 ± 0.9 cm vs. 45.5 ± 1.7 cm, P = 0.11), 2-year-old DQ (71.3 ± 15.1 vs. 78.1 ± 22.6, P = 0.20), 3-year-old head circumference (48.9 ± 0.4 cm vs. 48.2 ± 1.0 cm, P = 0.12), 3-year-old weight (11.4 ± 0.7 kg vs. 12.6 ± 2.4 kg, P = 0.26) and 3-year-old weight Z score (− 1.4 ± 0.5 vs. −0.4 ± 1.6, P = 0.18). No difference in body weight was observed between the two groups at 37 weeks PMA. Figure 1 shows the changes in Z scores during the course of hospitalization and the changes in body weight catch-up. The GA22–23-week group at showed the lowest Z score at 29 to 35 weeks PMA, but then the Z score gradually increased to − 1.0 ± 1.2 SD at 41 weeks PMA. In the GA24–25-week group, the lowest Z score was at 30 weeks PMA, then at 41 weeks PMA the score recovered to − 0.7 ± 1.2 SD (equivalent to the Z score of body weight at birth).

Discussion

We found that the body weight of the GA22–23-week group was approaching that of the GA24–25-week group after 37 weeks of PMA, even though sufficient enteral nutrition was delayed in the GA22–23-week group than in the GA24–25-week group. Thureen et al. showed that there are at least three phases of faltering growth commonly seen in ELBW infants, as follows: (1) several weeks immediately after birth when neonates are the most fragile, (2) intermediate time period when infants are commonly and slowly advanced to full enteral nutrition (catch-up period), and (3) the post-discharge phase [8]. Also, preterm infants develop a growth deficit during the first few weeks of life, and this deficit may persist and worsen during hospitalization, causing extrauterine growth restriction (EUGR) [9]. Furthermore, the longer the period before complete enteral feeding was achieved, the greater the risk of EUGR [10–12]. Although

ELBW infants are often discharged with undergrowth, catch-up growth is likely to occur during the follow-up period after discharge [13, 14]. It has been established that EUGR leads to a decrease in head circumference and body weight Z score, which affects neurodevelopment. Although EUGR is an unavoidable challenge in ELBW infants, improving growth during hospitalization in the NICU may improve psychomotor development. Our data showed that early postnatal weight loss was not significantly different between the two groups, with a marked improvement in weight gain from 38 to 41 weeks PMA in the GA22–23-week group, and from 37 to 41 weeks PMA in the GA24–25-week group.

Moyses et al. reported in both observational studies and randomized controlled trials that early parenteral nutrition significantly shortened the number of days required to regain birth weight without increasing mortality, chronic lung disease, NEC, or IVH [15]. Radmacher et al. reported that early AA administration shortened the number of days to regain birth weight, increased head circumference and weight at discharge, and reduced the risk of EUGR [16]. In a study comparing high-dose and low-dose intake of AAs, high-dose AA intake was similar to the second and third trimesters of pregnancy. [17]. Here, we propose that the AA dose in the current protocol for ELBW infants at GA22–25 weeks reduced the gradient of weight loss during the weight loss period after birth, then led to weight gain during the subsequent catch-up period. In the catch-up period, the body weight Z scores fell again at 33 and 34 weeks of PMA in the GA22–23-week and GA24–25-week groups, respectively. But in both groups, body weight Z scores then increased or stabilized at 37 weeks PMA, and caught up at 41 weeks PMA. The cause of the decrease in Z scores after 33–34 weeks PMA may reflect the adaptation to a changing extrauterine environment, such as transfer from the incubator to the cot and the change from premature formula milk to formula milk. In this study, there was a marked catch-up of weight gain after 37 weeks PMA, and there was almost no difference in weights between the GA22–23-week and GA24–25-week groups at 41 weeks PMA. Therefore, EAN had a certain effect on weight gain from postnatal to modified maturity in ELBW and GA22–23-week infants. Regarding short-term prognosis, compared with the 2003–2017 perinatal maternal and child medical center network database analysis report, the incidence of ROP requiring treatment was higher, and that of IVH III–IV was lower, in the GA22–23-week group versus the national data. The possibility of EAN as a cause of the high incidence of ROP cannot be denied, but in our hospital, factors other than EAN, such as prematurity of the preterm infant and systemic management, are considered to be strong factors and require further investigation. Additionally, BUN levels were higher in the GA22–23-week group than those in the GA24–25-week group, and levels in both groups were higher than the normal range, but no treatment was needed in all cases. Balakrishnan et al. showed that there was a positive association between protein loading and BUN levels, and BUN levels improved over time [18]. It was concluded that concerns about metabolic disorders due to early protein administration in ELBW were not justified. However, further research is needed to determine if AA intake is safe and effective. One limitation of this study is that a multivariate analysis was not performed because of the small sample sizes. Regarding the medium- to long-term prognosis, no significant differences in head circumference, body weight, and 2-year-old DQ were observed, but ongoing detailed examinations are still required.

In conclusion, EAN reduced the rate of early postnatal weight loss in very preterm infants, did not cause serious complications, and appeared to contribute to weight gain similar to the fetal period until the time of modified maturity.

Abbreviations

AAs, Amino acids; CPAP, Continuous positive airway pressure; DQ, Developmental Quotient; EAN, Early aggressive nutrition; ELBW, Extremely low birth weight, GA; Gestational age; IVH, Intraventricular hemorrhage; NEC, Necrotizing enterocolitis; NICU, Neonatal intensive care unit; PDA, Patent ductus arteriosus; PMA, Postmenstrual age; ROP, Retinopathy of prematurity; SGA, Small for gestational age; TPN, Total parenteral nutrition; VLBW, Very low birth weight

Declarations

Acknowledgments

We thank the support from faculties and staff in the Maternal and Child Care Hospital of University of Ryukyus and all participants in this study.

Funding

Not applicable

Availability of data and material

Not applicable

Code availability

Not applicable

Authors' contributions

MT: data collection, data analysis, manuscript writing. TY: data analysis, data management, manuscript editing, project development. HG: data collection. KN: project development, manuscript editing.

Ethics approval

The study was conducted with approval of the Medical Research Ethics Review for people at the University of Ryukyus hospital (No. 1725).

Consent to participate

For parental informed consent, an opt-out procedure was followed.

Consent for publication

Not applicable.

Conflict of interest

The authors declare no competing interests.

References

1. Whitfield JM, Hendrikson H (2006) Prevention of protein deprivation in the extremely low birth weight infant: a nutritional emergency. Proc (Bayl Univ Med Cent) 19:229–231. https://doi.org/10.1080/08998280.2006.11928169
2. Thureen PJ, Hay WW Jr (2001) Early aggressive nutrition in preterm infants. Semin Neonatol 6:403–415. https://doi.org/10.1053/siny.2001.0061
3. Su BH (2014) Optimizing nutrition in preterm infants. Pediatr Neonatol 55:5–13. https://doi.org/10.1016/j.pedneo.2013.07.003
4. Wilson DC, Cairns P, Halliday HL, Reid M, McClure G, Dodge JA (1997) Randomised controlled trial of an aggressive nutritional regimen in sick very low birthweight infants. Arch Dis Child Fetal Neonatal Ed 77:F4–F11. https://doi.org/10.1136/fn.77.1.f4
5. Yu VYH, James B, Hendry P, Macmahon R.A. (1979) Total parenteral nutrition in very low birthweight infants. Arch Dis Child 54:653–661. https://dx.doi.org/10.1136/adc.54.9.653
6. Dinerstein A, Nieto RM, Solana CL, Perez GP, Otheguy LE, Larguia AM (2006) Early and aggressive nutritional strategy (parenteral and enteral) decreases postnatal growth failure in very low birth weight infants. J Perinatol 26:436–442. https://doi.org/10.1038/sj.jp.7211539
7. Maggio L, Cota F, Gallini F, Lauriola V, Zecca C, Romagnoli C (2007) Effects of high versus standard early protein intake on growth of extremely low birth weight infants. J Pediatr Gastroenterol Nutr 44:124–129. https://doi.org/10.1097/01.mpg.0000237927.00105.f7
8. Thureen PJ (2007) Early aggressive nutrition in very preterm infants. Nestle Nutr Workshop Ser Pediatr Program 59:193–208. https://doi.org/10.1159/000098536
9. Clark RH, Thomas P, Peabody J (2003) Extrauterine growth restriction remains a serious problem in prematurely born neonates. Pediatrics 111(5 Pt 1):986–990. https://doi.org/10.1542/peds.111.5.986
10. Steward DK, Pridham KF (2002) Growth patterns of extremely low-birth-weight hospitalized preterm infants. J Obstet Gynecol Neonatal Nurs 31:57–65. https://doi.org/10.1111/j.1552-6909.2002.tb00023.x
11. Sakurai M, Itabashi K, Sato Y, Hibino S, Mizuno K (2008) Extrauterine growth restriction in preterm infants of gestational age < or = 32 weeks. Pediatr Int 50:70–75. https://doi.org/10.1111/j.1442-200X.2007.02530.x

12. Radmacher PG, Looney SW, Rafail ST, Adamkin DH (2003) Prediction of extrauterine growth retardation (EUGR) in VVLBW infants. J Perinatol 23:392–395. https://doi.org/10.1038/sj.jp.7210947
13. Ernst KD, Radmacher PG, Rafail ST, Adamkin DH (2003) Postnatal malnutrition of extremely low birth-weight infants with catch-up growth postdischarge. J Perinatol 23:477–482. https://doi.org/10.1038/sj.jp.7210974
14. Embleton NE, Pang N, Cooke RJ (2001) Postnatal malnutrition and growth retardation: an inevitable consequence of current recommendations in preterm infants? Pediatrics 107:270–273. https://doi.org/10.1542/peds.107.2.270
15. Moyses HE, Johnson MJ, Leaf AA, Cornelius VR (2013) Early parenteral nutrition and growth outcomes in preterm infants: a systematic review and meta-analysis. Am J Clin Nutr 97:816–826. https://doi.org/10.3945/ajcn.112.042028
16. Radmacher PG, Lewis SL, Adamkin DH (2009) Early amino acids and the metabolic response of ELBW infants (< or = 1000 g) in three time periods. J Perinatol 29:433–437. https://doi.org/10.1038/jp.2009.36
17. Thureen PJ, Melara D, Fennessey PV, Hay WW Jr (2003) Effect of low versus high intravenous amino acid intake on very low birth weight infants in the early neonatal period. Pediatr Res 53:24–32. https://doi.org/10.1203/00006450-200301000-00008
18. Balakrishnan M, Tucker R, Stephens BE, Bliss JM (2011) Blood urea nitrogen and serum bicarbonate in extremely low birth weight infants receiving higher protein intake in the first week after birth. J Perinatol 31:535–539. https://doi.org/10.1038/jp.2010.204

Tables

Table 1
Patient characteristics at birth.

	GA22–23-weeks (n = 10)	GA24–25-weeks (n = 18)	P-value
Birth-weight (g)	539 ± 68	697 ± 155	0.003
Birth-weight (Z score)	0.13 ± 0.7	−0.38 ± 1.1	0.35
Head circumference at birth (cm)	20.4 ± 1.0	22.2 ± 1.4	0.002
Height at birth (cm)	29.3 ± 2.0	30.9 ± 4.0	0.027
SGA at birth No (%)	0 (0)	1 (5.6)	0.45[a]

GA22–23-weeks, 22–23 weeks gestational age; GA24–25-weeks, 24–25 weeks gestational age; SGA, small for gestational age.

[a] Chi-square test

Table 2
The progress of nutrition-related factors during hospitalization.

	GA22–23 weeks (n = 10)	GA24–25-weeks (n = 18)	P-value
Days to achieved enteral feeds 100 ml/kg/day	13.0 ± 5.0	12.7 ± 3.7	0.94
Days to achieved enteral feeds 160 ml/kg/day	45.4 ± 22.5	23.7 ± 9.2	0.008
Head circumference at 37 weeks PMA (cm)	28.8 ± 1.2	30.4 ± 2.1	0.015
Head circumference at 37 weeks PMA (Z-score)	−2.6 ± 0.8	−1.5 ± 1.4	0.016
Body weight at 37 weeks PMA (g)	1906 ± 321	2081 ± 379	0.17
Body weight at 37 weeks PMA (Z-score)	−2.3 ± 1.0	−1.7 ± 1.3	0.16
No. of body weights less than 10% tile at 37 weeks PMA	9	11	0.10[a]
Early postnatal weight loss (%)	10.4 ± 6.3	8.1 ± 6.3	0.37
The age of regain to birthweight	13.2 ± 5.9	11.8 ± 4.8	0.51
GA22–23-weeks, 22–23 weeks gestational age; GA24–25-weeks, 24–25 weeks gestational age; PMA postmenstrual age.			
Values shown are mean ± SD.			
[a] Chi-square test			

Table 3
The short-term prognosis.

	GA22–23-weeks (n = 10)	GA24–25-weeks (n = 18)	P-value[a]
NEC No. (%)	1 (10)	0 (0)	0.17
PDA (indomethacin) No. (%)	8 (80)	9 (50)	0.13
PDA (surgery) No. (%)	3 (30)	3 (16.7)	0.41
ROP No. (%)	8 (80)	7 (38.9)	0.037
IVH grade □–□ No. (%)	3 (30)	0 (0)	0.014
Home oxygen therapy No. (%)	3 (30)	10 (55.6)	0.40
Home HFNC No. (%)	1 (10)	1 (5.6)	0.28
Home CPAP No. (%)	0 (0)	0 (0)	
Tracheostomy No. (%)	0 (0)	2 (11.1)	0.27
Home feeding No. (%)	1 (10)	1 (5.6)	0.66

GA22–23-weeks, 22–23 weeks gestational age; GA24–25-weeks, 24–25 weeks gestational age; NEC, necrotizing enterocolitis; PDA, patent ductus arteriosus; ROP, retinopathy of prematurity; IVH intraventricular hemorrhage; HFNC, high flow nasal canula; CPAP, continuous positive airway pressure.

[a] Chi-square test

Table 4
Complications associated with total parenteral nutrition.

	GA22–23-weeks	GA24–25-weeks	P-value[a]
Max BUN (mg/dl)	59.7 ± 16.6 (n = 10)	45.0 ± 10.8 (n = 18)	0.004
Max d-bil (mg/dl)	1.5 ± 0.7 (n = 10)	1.6 ± 0.8 (n = 18)	0.89
Max bile acid (μmol/L)	40.1 ± 20.2 (n = 10)	53.2 ± 23.0 (n = 18)	0.11
NH_3 (μg/dl)	71.5 ± 7.4 (n = 4)	55.8 ± 18.3 (n = 4)	0.25

GA22–23-weeks, 22–23 weeks gestational age; GA24–25-weeks, 24–25 weeks gestational age; BUN, blood urea nitrogen; d-bil, direct bilirubin.

[a] Mann-Whitney U test

Table 5
The anthropometrics and developmental evaluations after discharge from the Neonatal Intensive Care Unit.

	GA22–23-weeks	GA24–25-weeks	P-value
1-year-old head circumference (cm)	43.0 ± 1.2 (n = 8)	43.7 ± 1.4 (n = 14)	0.13
1.5-year-old circumference (cm)	44.5 ± 0.9 (n = 6)	45.5 ± 1.7 (n = 10)	0.11
2-year-old DQ	71.3 ± 15.1 (n = 6)	78.1 ± 22.6 (n = 7)	0.20
3-year-old head circumference (cm)	48.9 ± 0.4 (n = 3)	48.2 ± 1.0 (n = 6)	0.12
3-year-old weight (kg)	11.4 ± 0.7 (n = 5)	12.6 ± 2.4 (n = 9)	0.26
3-year-old weight (Z score)	−1.4 ± 0.5 (n = 5)	−0.4 ± 1.6 (n = 9)	0.18

GA22–23-weeks, 22–23 weeks gestational age; GA24–25-weeks, 24–25 weeks gestational age; DQ, developmental quotient.

Figures

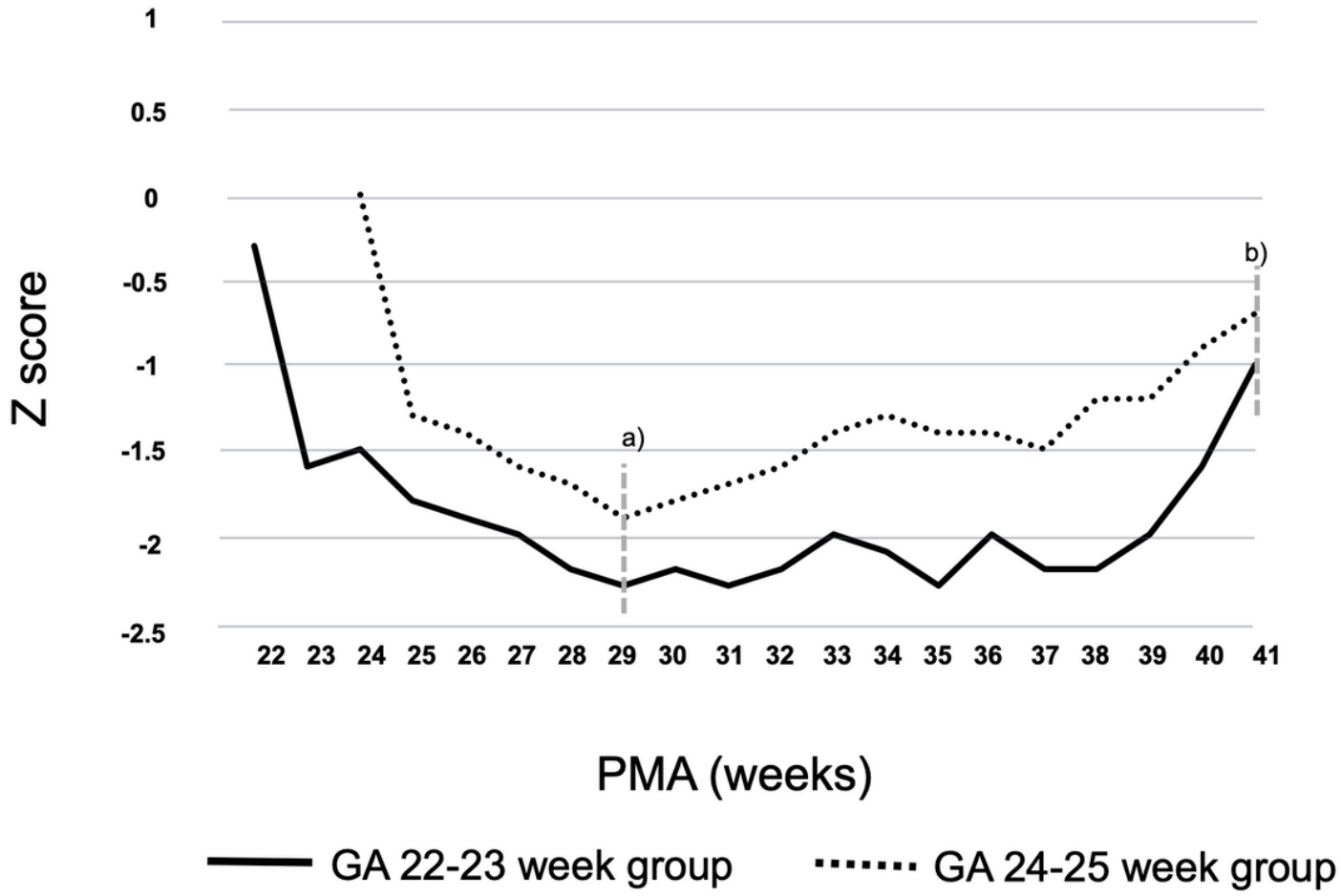

Figure 1

Changes in the Z score of body weight during the course of hospitalization a) Mean Z score of body weight at 29 weeks PMA in the GA22–23-group: −2.3 ± 0.8 (n=10) Mean Z score of body weight at 29 weeks PMA in the GA24–25-group: −1.9 ± 0.6 (n=17) b) Mean Z score of body weight at 41 weeks PMA in the GA22–23-group: −1.0 ± 1.2 (n=8) Mean Z score of body weight at 41 weeks PMA in the GA24–25-group: −0.7 ± 1.2 (n=8) GA22–23-group, 22–23 weeks gestational age; GA24–25-group, 24–25 weeks gestational age; PMA, postmenstrual age.