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Weight growth velocity in low birth weight neonates receiving parenteral nutrition in the Neonatal Intensive Care Unit, Kandou General Hospital, Manado 2022: a retrospective observational study

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ABSTRACT

Neonates with low birth weight (LBW) have a higher risk of growth failure. To optimize their growth to target of 15-20 g/kg/d, neonates must receive adequate nutrition. Parenteral nutrition implementation is one of the approaches to provide adequate energy and nutrition to LBW neonates who can not tolerate enteral feeding. This study aims to investigate growth velocity in LBW neonates receiving parenteral nutrition in hospital settings and observe if the target growth velocity was achieved, also describes current parenteral nutrition practices in tertiary hospital settings. A retrospective observational study was conducted in the Neonatal Intensive Care Unit (NICU), Kandou General Hospital, Manado. Sample in this study were neonates with birth weight <2500 g and received only parenteral nutrition for minimum 7 d. Daily weight measurement data was collected through medical records and parenteral nutrition regimens was collected through electronic prescriptions in the Pharmacy Department. Growth velocity was assessed using two parameters, gain weight velocity and change in weight for age Z-scores (WAZ). A total of 73 neonates were used as samples. The results demonstrated that only the extremely low birth weight (ELBW) group achieved the growth velocity recommendation during parenteral nutrition, 16.17 g/kg/d. All the neonates had a negative change of weight Z-scores indicated a declining growth rate during parenteral nutrition administration. We also found lipid emulsion initiation time was later and relatively low energy intake in parenteral nutrition compared to the recommendation. Vitamin as micronutrient was not yet added in parenteral nutrition regimens. Therefore, we suggest starting lipid emulsion from the first day of parenteral nutrition and add vitamin to parenteral nutrition regimen to optimize nutrient intake in order to improve growth velocity in LBW neonates during NICU stay.

ABSTRAK

Bayi berat lahir rendah (BBLR) memiliki risiko tinggi mengalami kegagalan pertumbuhan. Target kecepatan pertumbuhan 15-20 g/kg/hari untuk mencegah kegagalan pertumbuhan dapat dicapai melalui pemberian nutrisi yang adekuat. Implementasi nutrisi parenteral merupakan salah satu pendekatan untuk menyediakan energi dan nutrisi yang cukup bagi neonatus dengan berat lahir rendah yang belum dapat diberikan nutrisi enteral. Penelitian ini bertujuan untuk mengetahui kecepatan pertumbuhan pada BBLR yang mendapatkan nutrisi parenteral di rumah sakit. Tujuan lain dari penelitian ini adalah mengkaji praktik pemberian nutrisi parenteral di rumah sakit. Penelitian dilakukan dengan metode observasional retrospektif di ruang rawat NICU RSUP Prof. dr. R. D. Kandou Manado. Sampel pada penelitian adalah bayi berat lahir <2500 g dan mendapatkan nutrisi parenteral minimal selama 7 hari. Data berat badan diperoleh dari rekam medis pasien dan resep elektronik untuk regimen nutrisi parenteral. Kecepatan pertumbuhan diukur dengan dua parameter yaitu kecepatan pertambahan berat badan dan perubahan skor-z berat badan. Sampel yang digunakan sebanyak 73 neonatus. Hasil penelitian menunjukkan hanya kelompok bayi berat lahir amat sangat rendah (BBLASR) yang mencapai target

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kecepatan pertumbuhan yaitu 16,17 g/kg/hari. Perhitungan perubahan skor-z berat badan setelah pemberian nutrisi parenteral menunjukkan hasil negatif, mengindikasikan terjadi penurunan berat badan selama pemberian nutrisi parenteral. Hasil penelitian juga menunjukkan bahwa waktu inisiasi emulsi lipid di nutrisi parenteral lebih lama dibandingkan dengan rekomendasi serta asupan energi cenderung lebih rendah dibandingkan kebutuhan energi harian. Vitamin sebagai komponen dari mikronutrisi belum ditambahkan ke dalam regimen nutrisi parenteral. Peneliti menyarankan untuk memberikan emulsi lipid sejak hari pertama pemberian dan menambahkan vitamin ke dalam regimen nutrisi parenteral untuk mengoptimalkan asupan nutrisi sehingga dapat memperbaiki kecepatan pertumbuhan BBLR selama perawatan di NICU.

INTRODUCTION

Low birth weight (LBW) neonate is defined by World Health Organization as birth weight less than 2500 gram. Its prevalence was around 15-20% worldwide according to WHO in 2012, and approximately 6.2% in Indonesia.[1,2] Low birth weight prevalence in North Sulawesi was 5.9 % according to the 2018 Indonesian Basic Health Research data.[2] With its high prevalence, LBW is a critical health issue as it is one of the growth failure risk factors. Low birth weight neonates have a higher risk of extrauterine growth failure and stunting, moreover, most of the LBW are preterm (gestational age < 37 wk) making the risk of growth failure higher. Several studies demonstrated a relationship between growth failure in the early postnatal period and poor neurodevelopmental at 2 years of age.[3,4]

Providing optimal nutrition in the early postnatal period to accomplish growth rate of 15-20 g/kg/d and ensure adequate growth is one strategy to prevent growth failure. Neonate lost their nutrition source that is maternal placenta after birth and require nutrition immediately for their extrauterine growth and development. Parenteral nutrition is one of the approaches to ensure optimal nutrition in neonates who can not tolerate enteral feeding because of prematurity and clinical conditions. Parenteral nutrition consists of macronutrients and micronutrients given parenterally through intravenous route.[5]

Macronutrients in parenteral nutrition consisted of carbohydrate, protein and lipid and contribute to provide energy, especially carbohydrate. Proteins are the structural and functional components of all cells in the body, and it is essential to provide adequate protein supply during early postnatal period to ensure proper growth and avoid malnutrition. Lipid is non-carbohydrate energy source, it is dense of energy and source of essential fatty acids that required for brain development.[6,7] Micronutrition in parenteral nutrition consisted of electrolyte, minerals, vitamins and trace elements. Electrolyte and minerals were required for body homeostasis and for bone development. Vitamins, either lipid soluble (vitamin A, D, E and K) or water soluble (vitamin B, C, folic acid) are needed for metabolic function, growth, and body immune system. Trace elements such as zinc, selenium, iodine and fluoride are needed for metabolic function eventhough not needed in the early postnatal period.[7–10] Macronutrient and micronutrient components in parenteral nutrition can provide optimal nutrition for neonates, especially preterm and LBW neonates, to ensure proper growth and development, therefore avoid malnutrition and growth failure. A study from Roggero *et al.*[11] demonstrated implementation of optimal parenteral nutrition improved growth velocity in NICU, clinical outcomes and neurodevelopmental in 18 mo.

Neonate growth during

hospitalization in the NICU can be assessed and monitored using growth velocity parameters such as gain weight velocity and change in weight Z-score. Both methods more accurately represent growth than daily body weight measurement and can be used by clinicians to determine nutrition strategies.[12,13]

Implementation of parenteral nutrition in LBW neonates is a widespread practice in NICU but there are still limited studies about its effect on neonate growth. Parenteral nutrition is a part of pharmaceutical care in hospital settings and the role of the pharmacist is not only to dispense but also to ensure safety and efficacy during its administration. This study aimed to describe growth velocity in LBW neonates receiving parenteral nutrition in NICU and observe if the target growth velocity was achieved, also describes current parenteral nutrition practices in tertiary hospital settings.

MATERIAL AND METHODS

Study design

A retrospective observational study of growth velocity in LBW neonates receiving parenteral nutrition was conducted in the Kandou General Hospital, Manado, North Sulawesi. Inclusion criteria in this study were neonates admitted in NICU with birth weight less than 2,500 g or LBW neonates and given only parenteral nutrition for minimum 7 d. The exclusion criteria were neonates receiving parenteral nutrition less than 7 d, neonates with major congenital abnormalities, neonates whom already received enteral or parenteral nutrition before admission and incomplete data in medical record (no data of daily weight measurement, diagnosis and nutrition). This study was approved by the Institutional Ethics Committee of Kandou General Hospital, Manado, Indonesia (IRB approval document no.127/EC/KEPK-KANDOU/VIII/2023).

Data collection

Data was collected on neonates born in or admitted to the NICU and starting parenteral nutrition in December 2021 to December 2022 period. Data for each eligible neonate was retrospectively collected from patient medical records. Data regarding gestational age, gender, birth weight, daily weight measurement, the length of hospital stay, comorbidities, and laboratory examinations were recorded. Comorbidities of each neonate were classified using Pediatric Comorbidity Index according to Tai *et al.*[14] and further classified criteria were based on total score of the neonates: 0-2 points (absent), 3-5 points (low), scores ≥ 6 (high).[15]

The body weight of each neonate was recorded every day from birth until discharge. Daily parenteral nutrition regimens were collected from the electronic prescriptions in the pharmacy.

Parenteral nutrition practice

The parenteral nutrition regimen was daily prescripted by NICU clinicians to the pharmacy. The parenteral nutrition solution consisted of glucose 10% and 40% solution, amino acid solutions 6%, and electrolytes (sodium chloride 3%, potassium chloride 7.46%, calcium gluconate 10%, magnesium sulfate, and sodium glycerophosphate). Lipid 20% emulsion was not added to the parenteral nutrition bag but delivered by other intravenous routes.

Growth outcome

Growth velocity was assessed using two parameters: gain weight velocity and change weight for age Z-score at two intervals, from birth until the parenteral nutrition was discontinued and upon discharge. Gain weight velocity was calculated using the exponential (2-point) method by Patel *et al.*,[16]: GWV = 1000 x ln $(W_2/W_1)/D_2$-D_1 where the W_1 is the birth weight, W_2 is the weights (g) measured on evaluated days, D_1 is date of birth and

D_2 is the evaluation date.[13]

Weight for age Z-scores (WAZ) obtained by converted weight on birth and weight on the evaluation date using the 2013 Fenton dataset for preterm neonates and WHO 2006 growth chart for term neonates (17.18). Change in weight for age Z-scores calculated using the following equation[19]:

Change in WAZ = WAZ score in the day measurement – WAZ at birth.

Data analysis

Data were analyzed using Microsoft Excel and SPSS software (version 27.0). Neonates were stratified by birth weight then characteristics between groups, gain weight velocity, change in weight for age Z-scores, parenteral nutrition duration, and length of stay were presented as percentages and mean ± standard of deviation (SD). Daily energy, carbohydrates, proteins, and lipids intake (g/kg/d) were presented as mean ± SD.

RESULTS

From period December 2021 to December 2022, 73 neonates met the inclusion criteria and were included in this study and majority of the sample is male. More than half of neonates categorized as LBW (54.8%), 38.4% were categorized as very low birth weight (VLBW), and 6.8% were categorized as extremely low birth weight (ELBW). Most of the neonates were preterm (gestational age < 37 wk), and only 9.6 % of the sample was term neonates which explained the use of parenteral nutrition. Of the 73 neonates more than half were born by cesarean delivery (64.4%). Majority of the neonates (83.56 %) in this study sample had sepsis and 67.12% had respiratory distress as a comorbid. Detailed demography and clinical characteristics of the sample are shown in TABLE 1.

The neonates were further stratified according to their birth weight, due to the heterogeneity of pathophysiology and maturity. Clinical characteristics based on birthweight are shown in TABLE 2. The LBW group had an average birth weight of 1957.1 ± 310.13 g, VLBW group had an average birth weight of 1247.5 ± 164.18 g, and the EVLBW group had an average birth weight of 860.0 ± 54.77 g. Low birth weight and VLBW groups had similar birth weight Z-scores, -0.88 ±1.37 and -0.89 ± 1.09, respectively. The EVLBW group had the lowest mean birthweight Z-scores, -1.22 ± 0.54. The VLBW group had average length of stay, 25.10 d, it is higher when compared with other groups.

Parenteral nutrition support was summarized in TABLE 3. Each group had similar parenteral nutrition duration around 8 d. All neonates received “2 in 1” parenteral nutrition and contained of glucose solution, amino acids solution, and micronutrients from day 1. Most neonates received lipid emulsion on day 3 or even later. Lipid emulsion initiation was delayed or interrupted when the patient had respiratory distress, thrombocytopenia, or cholestasis.

The average glucose intake in the LBW group was 13.75 g/kg/d, VLBW group was 12.91 g/kg/d and in the EVLBW group was 13,13 g/kg/d. Maximum glucose intake in each group was 19.77 g/kg/d, 25.21 g/kg/d and 18.7 g/kg/d, consecutively.

Average amino acid intake during parenteral nutrition in LBW, VLBW and EVLBW group were 2.83 g/kg/d, 3.73 g/kg/d, and 3.97 g/kg/d, consecutively. Maximum amino acid intake was highest in the LBW group, 6.03 g/kg/d while in VLBW and EVLBW group were 4.67 g/kg/d and 5.33 g/kg/d, respectively.

TABLE 1. Characteristics of the study sample (n=73)

Characteristic	n (%)
Gender	
• Male	42 (57.5)
• Female	31 (42.5)
Birthweight (g)	
• ELBW (< 1000)	5 (6.8)
• VLBW (1000 – 1499)	28 (38.4)
• LBW (1500 – 2499)	40 (54.8)
Gestational age (wk)	
• < 28	3 (4.1)
• 28 – 31 6/7	31 (42.5)
• 32 – 36 6/7	32 (43.8)
• ≥ 37	7 (9.6)
Birth delivery	
• Normal delivery	26 (35.6)
• Cesarean	47 (64.4)
Diagnosis	
• Sepsis	61 (83.6)
• Small for gestational age	6 (8.2)
• Necrotizing enterocolitis	7 (9.6)
• Atresia ani	1 (1.4)
• Patent ductus arteriosus	16 (21.9)
• Respiratory distress	49 (67.1)
Comorbid category by PCI	
• Absent (0-2)	16 (21.9)
• Low (3-5)	35 (47.9
• High (≥ 6)	22 (30.1)
Length of stay (d)	
• < 14	21 (28.8)
• 14 – 28	29 (39.7)
• >28	23 (31.5)
Discharge status	
• Live	29 (39.7)
• Death	44 (60.3)

*ELBW: extremely low birth weight; VLBW; very low birth weight; LBW: low birth weight; PCI: pediatric comorbidity index.

TABLE 2. Clinical characteristics of the sample study based on birth weight.

Characteristic (mean ± SD)	LBW (n=40)	VLBW (n = 28)	ELBW (n=5)
Birth weight (g)	1957.12±310.13	1247.5±164.18	860.00±54.77
Birth Z-score (SD)	-0.88±1.37	-0.89±1.09	-1.22±0.54
Length of stay (d)	22.25±12.33	25.10±12.58	19.2±15.08

*LBW; low birth weight; VLBW: very low birth weight; ELBW: extremely low birth weight.

TABLE 3. Characteristics of parenteral nutrition support

Characteristic	LBW (mean ± SD)	VLBW (mean ± SD)	ELBW (mean ± SD)
Duration of PN (d)	8.95 (± 2.73)	8.92 (± 1.99)	8.8 (±1.92)
Mean glucose during PN (g/kg/d)	13.75 (±1.59)	12.91 (±1.79)	13.13 (±0.90)
Mean amino acid during PN (g/kg/d)	2.83 (±0.24)	3.73 (± 0.27)	3.97 (±0.14)
Average lipid during PN (g/kg/d)	1.67 (±1.15)	2.36 (±0.77)	0.87 (±0.44)
Mean PN energy (kcal/kg/d)	127.46 (±26.58)	87.12 (±14.82)	67.32 (±4.36)
Maximum PN glucose (g/kg/d)	19.77	25.21	18.77
Maximum PN amino acid (g/kg/d)	6.03	4.67	5.33
Maximum PN lipid (g/kg/d)	3.01	3.06	3.09

*PN: parenteral nutrition; LBW: low birth weight; VLBW:very low birth weight; ELBW: extremely low birth weight

Lipid emulsion was not given to all the neonates during parenteral nutrition period, only 24 neonates from total 73 neonates (38.2%) in this study. Clinical conditions such as sepsis, cholestasis and thrombocytopenia were the reason to delay or stop lipid emulsion administration. Lipid emulsion was given on day 3 or later when clinical conditions more stable and usually in the period when neonates not only given parenteral nutrition support but also enteral nutrition support. On average, low birth group received lipid on dose 1.67 g/kg/d, VLBW group received 2.36 LBW and EVLBW group received 0.87 g/kg/d. The maximum lipid dose in every group were similar, around 3 g/kg/d.

Neonates need adequate energy to optimize their growth. Energy in parenteral nutrition is obtained from macronutrients: carbohydrate, protein and lipid. The LBW group had the highest average parenteral nutrition energy among the groups, 127.46 kkal/kg/day. The VLBW group had average energy intake of 87.12 kcal/kg/day, and the EVLBW group had average parenteral nutrition energy of 67.32 kcal/kg/day.

The weight growth velocity calculation in this study used two parameters, gain weight velocity and change in weight Z-scores. Weight growth velocity was calculated when parenteral nutrition was discontinued, and when the patient discharged. Gain weight velocity in each group was demonstrated in TABLE 4.

TABLE 4. Growth velocity during parenteral nutrition and discharge

Group	GWV (mean ± SD)		Weight Z-score (mean ± SD)		Δ weight Z-score (mean ± SD)	
	After PN	Discharge	After PN	Discharge	After PN	Discharge
ELBW	16.17±10.30	11.67± 13.6	-1.26±0.65	-1.59±0.64	-0.04 ±0.38	-0.37 ±0.71
VLBW	6.11±9.89	5.15±7.60	-1.45 ±1.08	-2.03±1.22	-0.56 ±0.31	-1.14 ±0.62
LBW	0.87±7.3	2.32±5.86	-1.64±1.07	-2.25±1.21	-0.78 ±0.74	-1.36 ±0.96

*GWV: Gain weight velocity; ELBW: extremely low birth weight; VLBW: very low birth weight; LBW: low birth weight

Extremely low birth weight group had gain weight velocity 16.17 LBW during parenteral nutrition administration then decreased to 11.67 LBW at discharge time. The VLBW group had gain weight velocity 6.11 LBW during parenteral nutrition then decreased to 5.15 LBW when discharge from hospital. The LBW group had the lowest growth velocity among the group, 0.87 LBW throughout parenteral nutrition administration then increased to 2.32 LBW at discharge time. The gain weight velocity target for neonates to optimize their growth is 15-20 LBW, throughout parenteral nutrition only EVLBW group achieved this target.

The weight Z-scores change of neonates were demonstrated in Table 4. Weight Z-score (WAZ) after parenteral nutrition for each group was similar, EVLBW group had WAZ -1.26, VLBW -2.03, and LBW group had the lowest WAZ -1.64. Our results showna negative change in weight for age Z-score in every group after parenteral nutrition and when the patient discharge from hospital. A negative change in weight for age Z-score indicated declining neonate growth despite receiving nutrition support during hospitalization.

Low birth weight group had the lowest gain weight velocity even though they had higher birthweight. Most of the neonates in this group not received lipid emulsion as a part of parenteral nutrition regimen. Lipid emulsion was one of energy sources in parenteral nutrition and enabled neonate to achieve the energy requirement faster. This could explain the low gain weight velocity in this group. We further classified this group based on their gestational age and comorbidity category to observe their growth velocity. Of a total of 40 LBW neonates, 33 neonates had gestational age < 37 weeks or preterm and 7 neonates had gestational age > 37 weeks or categorized as term neonates. We then observed growth velocity in preterm LBW subgroup. Growth velocity data on this subgroup was demonstrated in table 5.

Neonates with absent comorbid category had gain weight velocity of 2.64 LBW. It is higher when compared with neonates in low and high comorbid category which had gain weight velocity of -0.41 and -7.7 LBW, respectively. A similar result was seen in change of weight Z-score parameter, neonates with absent comorbid category had higher change weight Z-score compared with the other groups.

TABLE 5. Growth velocity in preterm LBW neonate

Comorbidity category	n	Gain weight velocity, g/kg/d (mean± SD)	Birth Z-score (mean ± SD)	Weight Z-score post PN (mean ± SD)	Δ weight Z-score (mean ± SD)
Absent	10	2.64±12.16	-0.80±0.82	-1.49±0.89	-0.69±0.22
Low	13	-0.41±8.62	-0.92±1.23	-1.86± 1.21	-0.93±0.51
High	10	-7.73±6.28	-0.22±0.87	-1.04±0.97	-0.82±0.42

DISCUSSION

Parenteral nutrition implementation in LBW neonates is an approach to prevent growth failure by providing adequate energy and also optimal nutrients daily. This nutrition strategy was aimed to achieve the target of gain weight velocity 15-20 g/kg/d. In this present study despite parenteral nutrition administration in NICU, most of the neonates did not achieve the growth velocity target. Change of weight Z-scores shown negative change indicated decline in growth. Poor growth outcome during parenteral nutrition in preterm and VLBW neonates also reported in study by Wang *et al.*[20] In this previous study, 62% of neonates had poor growth outcome or body weight below 10th centile in growth curves after parenteral nutrition. It was also observed that poor weight gain was associated with insufficient parenteral macronutrients and energy intakes.[20]

Further observation in preterm neonates of LBW group demonstrated neonates with higher comorbid index scores had lower gain weight velocity and change in weight Z-score. This result complied with study reported by Mlay *et al.*[21] that neonates with comorbid such as sepsis and respiratory distress had lower growth weight velocity. A study of preterm infants by Flannery *et al.*[5,6] reported that very preterm infants with sepsis had significant weight deficit.

In this present study, the initiation time of lipid emulsions to neonates was later than the recommendation from Indonesian Pediatric's Society (IDAI) consensus and ESPGHAN guidelines. Lipid emulsions were recommended to give in 24 hr postnatal in pretem and term neonates. Lipid emulsions are part of parenteral nutrition as one of energy sources because it has high energy density. Lipid also have critical role in brain development because containing essential fatty acid (EFA) which is essential for central nervous system development. Minimum dose of lipid emulsions is 0.5-1.0 g/kg/d, then increases gradually to maximum 3.0 – 3.5 g/kg/d within the first week of life.[5,6,22] Average lipid intake in this study complied with recommendation from Indonesian Pediatric Society consensus and ESPGHAN. The maximum dose in each group were similar around 3 g/kg/d, which is also complied with recommended dose from IDAI and ESPGHAN.[22,23] Despite adequate lipid intake in parenteral nutrition, only 38.3% neonates were given lipid emulsion and initiation time of lipid emulsion was later than 3 d. This can be a factor associated with slow growth velocity in this study.

Glucose is the main source of energy also a widely used carbohydrate in parenteral nutrition. The glucose intake recommendation by ESPGHAN was 5.8-11.5 g/kg/d in preterm neonates on first day and increased gradually to target 11.5-14.4 g/kg/d. Glucose requirements in term neonates are lower than in preterm neonates, starting from 3.6-7.2 g/kg/d on the first day and increasing gradually to 7.2-14.4 g/kg/d.[24] This present study demonstrated that glucose intake in each group complied with ESPGHAN recommendation.

During parenteral nutrition, close monitoring of glucose concentration is essential because in the first week of life

of preterm neonates, glucose homeostasis is still immature. Preterm neonates are prone to hyperglycemia as well as hypoglycemia. Glucose blood levels must be maintained within > 40-45 mg/dL on the first day of life and thereafter <150-180 mg/dL. Glucose infusion rates 4-7 mg/kg/min are appropriate for most neonates. We found glucose provision in parenteral nutrition in this study complied with recommendation from IDAI and ESPGHAN, as well.

Amino acids in parenteral nutrition are not only used as source of energy, but mainly used for structural and functional components of body and growth. To achieve anabolic state, amino acid provision in the preterm neonates should begin early, on the first day with minimal intake 1.5 g/kg/d. ESPGHAN recommended amino acid intake 2.5-3.5 g/kg/d for preterm neonates. The study demonstrated that only LBW group complied with the recent recommendation from ESPGHAN. VLBW and ELBW groups had amino acid intake exceeding the recent ESPGHAN recommendation. Previous ESPGHAN guidelines in 2005 recommended amino acid intake of 3.5-4g/kg/d for VLBW neonates, and for EVLBW maximum dose was 4-4.5 g/kg/d.[25] Clinicians in the NICU still use the previous ESPGHAN guidelines. There is also evidence from previous study that amino acid intake up to 3.3-3.9 g/kg/d is well tolerated even though study from Uthaya *et al.* demonstrated there is no short or long benefit of high amino acid intake administration in VLBW neonates.[26]

The daily energy requirement for preterm neonates is 90-100 kcal/kg/d if given parenterally, and the minimum must meet the basal metabolic rate (BMR) needs, 50 kcal/kg/d.[23] ESPGHAN's recommendation for energy in term neonates was 75-85 kcal/kg/d and 90-120 kcal/kg/d for preterm neonates, especially for VLBW neonates.[27] This present study demonstrated LBW group received energy slightly higher than ESPGHAN recommendation. The VLBW and EVLBW groups had lower energy intake than requirements from ESPGHAN, but all the groups received daily energy supply more than BMR needs.

Neonates, especially those with LBW and born preterm need adequate energy to optimize their growth and prevent growth failure. Inadequate energy intake not only risks growth failure, but also may result in impaired cognitive and immunity development, and increased risks of morbidity and mortality. Excess energy may lead to complications such as hyperglycemia and increased risks of infection.[5]

Parenteral nutrition was consisted not only macronutrients but also micronutrients such as electrolyte, vitamins and trace elements. We found that vitamins not yet added in the parenteral nutrition regimens. ESPGHAN were strongly recommended that neonates and children receiving parenteral nutrition should receive parenteral vitamins. Vitamins in parenteral nutrition should be given in sufficient amount, it is essential for growth and development.[8] Vitamin A plays essential role in vision, growth and maintenance of epithelial cells, and immune system. Vitamin D functions mainly in regulation calcium and phosphate that is essential for bone development. Vitamin E and C were potent antioxidant and previous study demonstrated that vitamin E plays hepatoprotective role in preventing parenteral nutrition associated liver disease (PNALD). Thiamine, riboflavin, pyridoxine, folic acid, biotin, panthotenic acid and cyanocobalamin were essential in energy, glucose and lipid metabolism.[6,7]

The shortcomings in parenteral nutrition practice in this study were later initiation of lipid emulsion, relatively low energy intake and vitamins not yet added in parenteral nutrition regimen. Lipid emulsions should be given earlier to improve energy supply. A retrospective study by Fischer *et al.*[28] on EVLBW neonates reported a negative correlation

between the later initiation time of lipid emulsions and growth outcome in the first month in preterm neonates who received parenteral nutrition.

We also observed that neonates in this study had average length of stay more than 14 d and VLBW neonates had the highest average length of stay compared to other groups. A systematic review by Fu *et al.*[29] identified several risk factors affecting length of stay in NICU included LBW, gestational age less than 37 wk, and comorbidities such as sepsis, necrotizing enterocolitis (NEC), bronchopulmonary dysplasia (BPD) and retinopathy of prematurity (ROP). Neonates included in this study had LBW and majority of them were preterm neonates. More than 80% neonates in this study had sepsis, previous study from Rozanska *et al.*[30] shown that infection associated with prolonged hospital stay in VLBW neonates. A cohort study from Verstraete *et al.*[31] shown that prolonged hospital stay not only increase risk of hospital acquired infection in neonates but also mortality rate in this population. Poor weight growth velocity in this study was observed in neonates with high comorbidity index scores. Clinical conditions such as sepsis and respiratory failure combined with prolonged length of stay in NICU can affect growth in LBW neonates.

This study has the following limitations. First of all, growth velocity measurement using body weight was not comprehensive enough to describe neonate growth during parenteral nutrition administration and NICU stay. Another anthropometric data such as body length and BMI also body composition was needed to make more comprehensive and rigorous study. In addition, this study was conducted retrospectively with limited data in medical records and researchers did not know clinicians consideration in parenteral nutrition regimens. Future research using more comprehensive anthropometric data and body composition were needed and conduct in prospective method for better understanding parenteral nutrition effect in neonatal growth.

CONCLUSION

In conclusion, LBW neonates in NICU whom received parenteral nutrition does not achieve target growth velocity as recommended. Parenteral nutrition implementation in LBW neonates in NICU should be applied according to the evidence-based recommendation. We suggest that lipid emulsion and vitamins should be given from the first day of parenteral nutrition in LBW neonates to improve their growth velocity.

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