Curr Pediatr Res 2016; 20 (1&2): 237-241 *ISSN 0971-9032*
www.currentpediatrics.com

Comparative of early parenteral nutrition and late parenteral nutrition in preterm neonates.

Tzu-Rong Peng[1], Fang-Pei Tsai[1], Ta-Wei Wu[1,2]

[1]Department of Pharmacy, Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, New Taipei City, Taiwan.
[2]School of Pharmacy, College of Pharmacy, Taipei Medical University, Taipei City, Taiwan.

Abstract

Objective: To evaluate the differences and influences of early and late Parenteral Nutrition (PN) on preterm neonates.

Methods: Retrospective study, which includes preterm neonates who were born and admitted to Neonatal Intensive Care Units (NICU), weighing under 2000 g and having received PN for more than 7 days. According to the timing of protein provision, divided into two groups-Early Parenteral Nutrition (EPN) and late parenteral nutrition (LPN). EPN is defined with a protein provision within 24 h of birth while LPN with a protein provision after 24 h of birth. The facts to examined include the day of weight gain (times to regain over birth weight), total days of PN, weight gain per day in grams (g), weights at discharge and days of hospitalization.

Results: Among a 25 preterm neonates, 10 neonates received EPN while 15 received LPN. No statistical significance is found between the basic data of EPN and LPN. After the multiple regression analysis and correction of basic data's between EPN and LPN, this study finds that the day of weight gain of EPN is earlier than that of LPN by about 0.41 day, weight gain per day in grams (g) and the weight at discharge of EPN are more than those of LPN by about 0.25 g and 0.27 g, respectively, and the total days of PN and the days of hospitalization in the NICU of EPN are more than those of LPN by about 0.15 day and 0.11 day respectively, however, none of the above is statistically significant.

Conclusion: The results of this study show that early PN may provide the benefits to preterm neonates. No evidence is noted in blood urea blood urea nitrogen and creatinine level.

Keywords: Early parenteral nutrition, Late parenteral nutrition.

Accepted September 26, 2016

Introduction

Baby born before 37 completed weeks of gestation (Preterm neonates) can hardly get the nutrition required for their growth due to the incompetence of sucking and gastrointestinal functions. Their chances of better growth and neural development may be increased though earlier nutrition support right after birth, which also makes the issue of preterm neonates' nutritional needs more crucial, and parenteral administration is often used [1]. Martin et al. [2] shows that early nutrition support is crucial to the growth of preterm neonates. Parenteral amino acid is an part of early neutrition supplementation in preterm neonates. Although safety and efficacy of early nutrition have been demonstrated, benefits for the early administration of high dose amino acid in Very Low Birth Weight (VLBW) neonates are still scarce [3]. For quick nutritional support, evidence from several studies suggest that intravenous nutrition (parenteral nutrition, PN) be given right after birth with protein intake ≥ 2.0 g/kg/day, which is to be raised up to 3.5 g/kg/day in the next two to four days [4,5]. In addition, researchers such as Ziegler suggests that lipid be given to preterm neonates by 1.0 g/kg/day and be slowly raised up to 3.0 g/kg/day in days while Embeleton and Simmer suggest the intravenous fat emulsions be given on the day of birth by ≥ 2.0 g/kg/day and be raised up to 3.0-4.0 g/kg/day in the next two to four days [5,6]. To achieve ideal growth, a total of 90-100 kcal/kg/day is also suggested by Ziegler to be given to preterm neonates in the next few days to a week right after their birth [4,6].

The evidence has demonstrated the benefits of administering protein at least 1.5 g/kg/day within the first 24 h of birth are limited [7]. Early and aggressive nutrition administration for preterm infants has been given attention and has been an interesting issue. However, specific treatment strategies are still needed so that preterm infants may acquire adequate nutrition and improve their growth and development [8].

Although the available evidence suggest the nutrition support be given to preterm neonates as soon as possible, this study, based on the data of a teaching hospital, is going to evaluate the differences and influences of early and late PN on preterm neonates and make a comparison with the references to find out whether early PN is clinically required and make a suggestion on the future use of PN.

Methods

This study is a retrospective study, which includes preterm neonates who, from December of 2013 to December of 2015, were born and admitted to Neonatal Intensive Care Units (NICU), weighing under 2000 g and below 32 weeks of gestation and having received PN for more than 7 days and excludes the ones died in the period of PN and the ones with chromosome anomalies. According to the timing of protein provision, Preterm neonates were divided into two groups-Early Parenteral Nutrition (EPN) and Late Parenteral Nutrition (LPN). EPN is defined with a protein provision within 24 h of birth while LPN with a protein provision after 24 h of birth. The information collected include gestation periods, genders, birth weights, Apgar score (appearance, pulse, grimace, activity, respiration) and calculations of the average calories, glucose, protein and lipid given to each preterm neonates in the first seven days of their birth, serum urea nitrogen (BUN), serum creatinine, bicarbonate during the initial 14 days of life and the basic data are shown with percentages, medians, maximums and minimums.

Data Analysis

For the analysis, Mann-Whitney U test was adopted to examine two groups of continuous variables and Chi-square test for the testing of categorical variables, in which P value was statistically significant when less than 0.05. The basic data, timing of PN and the seven-day average of given nutrition given are all included in the multiple regression analysis. The facts to examine included the day of weight gain (times to regain over birth weight), total days of PN, weight gain per day in grams (g), weights at discharge and days of hospitalization in the NICU.

Results

Of the 29 preterm neonates who met eligibility, which decreased to 25 after excluding the ones that died in the period of PN. These preterm neonates were divided into EPN (10) and LPN (15) groups according to the timing of protein provision after their birth. No statistical significance is found between the basic data of EPN and LPN through Mann-Whitney U test (Table 1). After the multiple regression analysis and correction of days of gestation, genders, birth weights, Apgar scores, average seven-day calories (kcal/kg), glucose (g/kg), protein (g/kg) and lipid (g/kg) between EPN and LPN groups, this study finds that the day of weight gain of EPN is earlier than that of LPN by about 0.41 day, weight gain per day in grams (g) and the weight at discharge of EPN are more than those of LPN by about 0.25 g and 0.27 g, respectively and the total days of PN and the days of hospitalization in the NICU of EPN are more than those of LPN by about 0.15 day and 0.11 day, respectively, however, none of the above is statistically significant (Table 2). The mean and peak serum urea nitrogen (BUN), serum creatinine and bicarbonate during the initial 14 days of life did not differ between EPN and LPN group (Table 3).

Through further analysis of factors that might influence the day of weight gain, weight gain per day in grams (g), weight at discharge, the total days of PN and days of hospitalization in the NICU, possible correlations are found between total days of PN and Apgar score at birth, between days of hospitalization and days of gestation, among weight at discharge, days of gestation, Apgar score at birth and the glucose and protein given in the first seven days (Table 4). Further analysis also finds that among the averages of first-seven-day nutrition given to the preterm neonates in this study, which include 65.9 ± 17.9 kcal/kg of calories, 3.0 ± 0.7 g/kg of glucose and 2 ± 0.8 g/kg of protein and lipid, when compared to the calorie intake standard (90-100 kcal/kg/day) set by the expert opinion and that suggested by American Academy of Pediatrics Committee, the calories and lipids given to the preterm neonates are both lower, the beginning day of fat provision after birth is 2.4 ± 1.1, ten of the preterm neonates (40%) are not given fat within 48 hours, one is not given lipid at all (4%), and only fourteen are given lipid within 48 hours (56%) (Table 5) [9].

Discussion

PN plays an important part in nutrition support of preterm neonates. The research by Amitha shows the long-term growth of preterm neonates may be related to early protein provision, the research by Ibrahim shows that aggressive protein and fat provision is tolerable and Braake has proved that early protein provision is safe and may help preterm neonates achieve positive nitrogen balance [10-13]. For most preterm neonates, to give PN, within 24 h after birth and increasing gradually during the first week of life, including suggested quantities of 3.5-4 g/kg/day of protein, 3-4 g/kg/day of lipid and 90-110 kcal/kg/day of calories, may slow down the weight loss after birth and lift the limits to growth [1,14,15]. Early PN may not only provide the accumulative needs caused by the diseases after birth but also improve the long-term growth and neural development. In our research, the EPN group has an earlier weight gain (by about 0.41 day), a higher weight gain per day (by about 0.25 g), a higher weight at discharge (by about 0.27 g) and a longer PN period (by about 0.15 day) than the LPN group, yet none of the above results is statistically significant. Calories given to preterm neonates, in both EPN and LPN groups, average 65.9 ± 17.9 kcal/kg on the seventh day after birth while only two of these preterm neonates are given ≥ 90 kcal/kg. Fat and calories of the EPN group were lower than the suggested dosage in references from born to 7 days. This could be the

Table 1. Demographics and weight data analyzed by EPN vs LPN

	EPN	LPN
Male sex (n, %) Female sex (n, %) Gestational age*, (days)	7 (70%) 3 (30%) 212 (195-223)	12 (80%) 3 (20%) 208 (180-241)
Birth weight*, (g)	1425 (910-1940)	1225 (830-1785)
Apgar score* at birth	6.5 (2.0-7.0)	5.0(2.0-9.0)
Apgar score* at 5 min	8.0 (6.0-9.0)	8.0 (5.0-9.0)
Nutrient intake during the first weeks		
Calories*, (Kcal/kg)	50.8 (38.4-62.8)	53.2 (33.5-73.9)
Glucose*, (gl/kg)	7.9 (6.1-11.7)	8.8 (6.6-13.0)
Protein*, (g/kg)	2.5 (2.2-3.2)	2.6 (1.9-3.2)
Fat*, (g/kg)	1.3 (0.9-1.7)	1.4 (0.0-2.1)

*Data show with median (Minimum-Maximum)

Table 2. Major outcomes in EPN and LPN

Major outcomes		Standardized Coefficients (β)	P-value
DOL regained BW	EPN	-0.410	0.513
	LPN	Ref.	
Weight gain	EPN	0.252	0.333
	LPN	Ref.	
Discharge weight	EPN	0.274	0.154
	LPN	Ref.	
Days of PN	EPN	0.155	0.401
	LPN	Ref.	
Length of NICU stay	EPN	0.105	0.404
	LPN	Ref.	

DOL: Days of Life, BW: Birth Weight

Table 3. Laboratory data during the initial 14 days of life

	EPN	LPN	P-value
Serum urea nitrogen*, (mg/dL)	20.7 (13.5-63.7)	22.0 (9.0-96.0)	0.637
Peak serum urea nitrogen*, (mg/dL)	22.0 (17.0-82.0)	22.9 (9.0-108.0)	0.560
Serum creatinine*, (mg/dL)	1.0 (0.7-1.2)	1.0 (0.6-2.4)	0.196
Bicarbonate*, (mEq/dL)	21.7 (17.9-25.9)	22.1 (17.2-28.0)	0.578

*Data show with median (Minimum-Maximum)

Table 4. Factors that may affect the growth of the preterm

Secondary outcomes	Factors	Standardized Coefficients (β)	P-value
Discharge weight	Gestational age	-0.841	0.004
	Apgar score at birth	-0.735	0.035
	Glucose	-17.478	0.050
	Protein	-4.374	0.040
Days of PN	Apgar score at birth	-0.873	0.020
	Apgar score*at 5 min	0.699	0.028
Length of NICU stay	Gestational age	-0.586	0.003

Table 5. Daily intakes and nutrients recommendations [9]

	Our study 7th day (SD)	Expert opinion	American Academy of pediatrics Committee Recommendations [9].
Glucose (g/kg/day)	10.0 ± 2.9	13-17	4-16
Proteins (g/kg/day)	3.0 ± 0.7	3 -3.5	2-4
Lipids (g/kg/day)	2.0 ± 0.8	3	3-4
Energy (Kcal/kg/day)	65.9 ± 17.9	90-100	90-100

reason that cased the growth of our EPN preterm neonate slower than other studies. However, EPN group increase days of PN therapy and hospitalization than LPN group. Because after multiple regression analysis by correction the basic data. We found increase days of PN therapy and hospitalization may relate to Apgar score at birth and 5 minutes after birth and gestational age of preterm neonate.

The meta-analysis of 2013 shows that preterm neonates receiving EPN, in 13 observational studies, gain weight earlier than those receiving LPN by about 3.2 days (95% Cl 2.0 to 4.4) while in 8 randomized trials, preterm neonates receiving EPN gain weight earlier than those receiving LPN by 2.2 days (95% Cl 1.1 to 3.2) [16]. As for the cases of weight loss after birth, preterm neonates receiving EPN, in the 13 observational studies, lose less weight than those receiving LPN by about 3.5% (95% Cl 2.6 to 4.3) while in the 8 randomized trials, preterm neonates receiving EPN lose about 3.1% less weight (95% Cl 1.7 to 4.5). The results of the meta-analysis show that EPN may improve the weight at discharge of preterm neonates, but no significant improvement is found in their body lengths and head circumferences and there is no proof that EPN has influences on mortality risk, necrotizing enterocolitis, sepsis, chronic pulmonary disease, internal hemorrhage or cholestasis [16]. Martin et al. [2] shows that early nutrition support is crucial to the growth of preterm neonates. A prospective study conducted by Valentine et al. [14] that show EPN correlates with the weight gain of preterm neonates. This study included 308 preterm neonates; the EPN group received 3 g/kg of protein with 24 h after birth and was also given glucose and lipid to raise the supply of calories to 90 kcal/kg per day. The result of the prospective study proves that the EPN group has better weight gain and requires fewer days of PN, which was believed to be correlated with protein provision within 24 h after birth. Even among preterm neonates with lower birth weights or shorter gestation period, protein provision within 24 h after birth may significantly improve weight gain and shorten the period of PN [14].

Amitha's research, however, shows that there is no difference between EPN and LPN in weight gain per day, weight after 34 weeks of gestation, and the time of food intake by gastrointestinal system [10]. A multi-center randomized trial conducted by Clarke and other researchers show that giving a high dose of protein (3.5 g/kg/day) does not improve the growth of preterm neonates but raise BUN instead [17]. According to the evidence from several studies, the calories given on the first day after birth should be 40 kcal/kg/day, and then be slowly raised to 60-80 kcal/kg/day, and on the seventh day, 90-100 kcal/kg/day [18,19]. The calories given to preterm neonates in this study, compared with those recommendations by the available evidences, are significantly fewer [15,18]. Due to the prematurity of organs, weak gastrointestinal function and a higher Basal Energy Expenditure (BEE) than full-term ones, preterm neonates need more energy to meet daily needs and to maintain a positive energy balance for growth, which consequently leads to more calories required per day. Although references show that early aggressive parenteral nutrition may help preterm neonates achieve better growth, still, the nutritional deficiency often poses a problem in the first week after birth [19-21]. Incomplete glucose metabolism and lipid intolerance often lead to a caloric deficiency. Furthermore, the lack of calories and protein will lengthen the period of PN and delay the timing of nutrition support through the gastrointestinal tract and causes growth retardation. According to the nutrition guidelines of Europe and the US, protein is best given within 24 h after birth and with a dose of at least 1.5-2.0 g/kg/day, which needs to be raised up to a maximum of 4.0 g/kg/day [15,22]. The total of preterm neonates receiving EPN (having protein provision within 24 h) in this study is 10 (41.7%), which falls behind what the references suggest. As for the dosage, the average of protein provision in the beginning is 1.7 ± 0.5 g/kg/day, which is in accordance with the recommended dosage found in the references and is gradually, raised up to 3.0 ± 0.7 g/kg on the seventh day. Preterm neonates receiving PN in this study do not have enough calories within the first seven days. 58.3% of these preterm neonates are not given protein within 24 h after birth, and the dosage of protein is raised up to that recommended by the references. As for lipid, which is recommended to give within one to two days after birth and is proved to be safe and tolerable [23]. Recent meta-analysis have also proved the safety and tolerability of giving fat within two day after birth in very low birth weight (VLBW: birth weight under 1500 g) preterm neonates, while only 56% of preterm neonates in this study are given lipid within two days after birth [19].

Conclusion

There are no statistical significance found among the groups that received EPN and LPN. The lack of statistical significance could be simply related to the small sample size. But, this study shows current nutrition of preterm neonates in this hospital is inadequate. Early aggressive PN, which shortens the period of PN, move the day of weight gain forward, and even raises the weight at discharge and restarts gastrointestinal nutrition support earlier. Medical staff shall be educated to follow the recommended protein and fat intake for premature infants and the need for early initiation of PN for premature neonates.

Study Limitations

This study includes only 25 cases, fewer than those found in the references, and the calories given to preterm neonates within the first seven days are fewer than recommended, which may influence the results of this study. Furthermore, this study, being a retrospective one, needs more support of researches of larger scales and more properly-defined methodologies to examine the effects of EPN and LPN.

Acknowledgement

This work was supported in part by grants from the Taipei Tzu chi Hospital (TCRD-TPE-106–02).

I would like to express my deepest appreciation to all those who provided me the possibility to complete this report. Tzu-Rong Peng: designed research (project conception, development of overall research plan, and study oversight) and wrote paper. Fang-Pei Tsai: data collection and analyzed data. Furthermore I would also like to acknowledge Ta-Wei Wu for his comment and advices. He kindly read my paper and offered invaluable detailed advices on grammar, organization, and the theme of the paper. This work was supported in part by grants from the Taipei Tzu chi Hospital.

References

1. Riskin A, Hartman C, Shamir R. Parenteral nutrition in very low birth weight preterm infants. Isr Med Assoc J 2015; 17: 310-315.
2. Martin CR, Brown YF, Ehrenkranz RA, et al. Extremely low gestational age newborns study investigators. Nutritional practices and growth velocity in the first month of life in extremely premature infants. Pediatrics 2009; 124: 649-657.
3. Yang S, Lee BS, Park HW, et al. Effect of high vs. standard early parenteral amino acid supplementation on the growth outcomes in very low birth weight infants. JPEN J Parenter Enteral Nutr. 2013; 37: 327-334.
4. Ziegler EE. Meeting the nutritional needs of the low-birth-weight infant. Ann Nutr Metab 2011;58:8-18.
5. Embleton ND, Simmer K. Practice of parenteral nutrition in VLBW and ELBW infants. World Rev Nutr Diet 2014; 110: 177-189.
6. Ng DV, Brennan-Donnan J, Unger S, et al. How close are we to achieving energy and nutrient goals for very low birth weight infants in the first week? J Parenter Enteral Nutr 2015.
7. Lapillonne A, Kermorvant-Duchemin E. A systematic review of practice surveys on parenteral nutrition for preterm infants. J Nutr 2013; 143: 2061S-2065S.
8. Ehrenkranz RA. Early, aggressive nutritional management for very low birth weight infants: What is the evidence? Semin Perinatol 2007; 31: 48-55.
9. Ribed Sánchez A, Romero Jiménez RM. Aggressive parenteral nutrition and growth velocity in preterm infants. Nutr Hosp 2013; 28: 2128-2134.
10. Amitha RA, Lalitha Krishnan, Zenaida Reyes. Early versus late parenteral nutrition in very low birth weight neonates. SQU MED J 2012.
11. Ibrahim HM, Jeroudi MA, Baier RJ. Aggressive early total parental nutrition in low-birth-weight infants. J Paerinatol 2004; 24: 482-486.
12. Braake FW, van den Akker CH, Wattimena DJ, et al. Amino acid administration to premature infants directly after birth. J Pediatr 2005; 147: 457-461.
13. Radmacher PG, Lewis SL, Adamkin DH. Early amino acids and the metabolic response of ELBW infants (≦ 1000 g) in three time periods. J Perinatol 2009; 29: 433-437.
14. Valentine CJ, Fernandez S, Rogers LK, et al. Early amino-acid administration improves preterm infants weight. J Perinatol 2009; 29: 428-432.
15. Koletzko B, Goulet O, Hunt J, et al. Guidelines on paediatric parenteral nutrition of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN), Supported by the European Society of Paediatric Research (ESPR). J Pediatr Gastroenterol Nutr 2005; 41: S1-87.
16. Moyses HE, Johnson MJ, Leaf AA, et al. Early parenteral nutrition and growth outcomes in preterm infants: A systematic review and meta-analysis. Am J Clin Nutr 2013; 97: 816-826.
17. Balasubramanian H, Nanavati RN, Kabra NS. Effect of two different doses of parenteral amino acid supplementation on postnatal growth of very low birth weight neonates, a randomized controlled trial. Indian Pediatr 2013; 50: 1131-1136.
18. Riskin A, Hartman C, Shamir R. Parenteral nutrition in very low birth weight preterm infants. Isr Med Assoc J 2015; 17: 310-315.
19. Stephens BE, Walden RV, Gatgus RA. First-week protein and energy intakes are associated with 18 month developmental outcomes in extremely low birth weight infants. Pediatrics 2009; 123: 1337-1343.
20. dit Trolli SE, Kermorvant-Duchemin E, Huon C, et al. Early lipid supply and neurological development at one year in very low birth weight (VLBW) preterm infants. Early Hum Dev 2012; 88: S25–9.
21. Corpeleijn WE, van den Akker CH, Roelants JA, et al. How proteins improve the development of preterm infants. Nestle Nutr Workshop Ser Pediatr Program 2011; 68: 33-45.
22. Kleinmann RE, editor. Pediatric nutrition handbook. 6th ed. Elk Grove Village (IL): American Academy of Pediatrics 2009; 519-540.
23. Vlaardingerbroek H, Veldhorst MA, Spronk S, et al. Parenteral lipid administration to very-low-birth-weight infants-early introduction of lipids and use of new lipid emulsion: A systematic review and meta-analysis. Am J Clin Nutr 2012; 96: 255-268.

Crrespondence to:

Ta-Wei Wu,
289, Jianguo Road,
Xindian City,
New Taipei City 23142,
Taiwan,
Republic of China.
Tel: +886-2-6628-9779-8900
Fax: +886-2-6628-5288
E-mail: tawei@tzuchi.com.tw