PARENTERAL NUTRITION IN VERY LOW BIRTH WEIGHT INFANTS. WHEN TO START?

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Abstract

Objective: To assess the effects of parenteral nutrition (PN) initiation time in very low birth weight neonates on: the birth weight recovery time, enteral nutrition (EN) initiation time, duration of hospitalization, and incidence of death. **Methods:** This retrospective case-control study was performed in the neonatal intensive care unit (NICU) of a tertiary center: Santo Amaro Hospital, Salvador, Brazil. All infants with birth weights ≤ 1500 g who were treated in the NICU during the study period (*n*= 114) were included. The sample was divided in two groups: early (≤ 48 h after birth) and late (> 48 h after birth) onset of PN. We also analyzed a subgroup of neonates with birth weights ≤ 750g, as well as a group for whom PN was initiated very early (≤ 24 h after birth). **Results:** A total of 114 neonates (*n*=48 / 39.8% in early PN group),were included in the study. Birth weight recovery time (9.9 ± 4.0 vs 12.8 ± 6.1, p = 0.007), lenght of hospitalization (43.2 ± 4.0 vs 71.8 ± 41.7, p = 0.007), and time of EN onset (2.2 ± 1.2 vs 7.9 ± 5.8, p <0.001) , were significantly lower in the early PN onset group than in the late onset group. Lenght of hospitalization was positively correlated with the timing of EN onset (r= 0,37, p = 0,001). No significant difference in adverse outcomes: death (18.6% vs 13.6%, p = 0.6), intracranial hemorrhage (ICH) (8.3% vs 12.1%, p = 0.9) and patent ductus arteriosus (PDA) (8.3% vs 31.8%, p = 0.1) was obbserved between groups. **Conclusion:** In this study, the early initiation of nutritional support in very low birth weight neonates can reduce the length of hospitalization thereby reducing costs, without increasing the incidence of adverse effects.

Keywords: Very low birth weight; Premature infant; Parenteral nutrition; Enteral nutrition.

INTRODUCTION

Prematurity is the leading cause of neonatal morbidity and mortality,[1] and premature neonates, have greater nutrient and energy requirements than infants born at term. Neonatal nutrition remains a critical issue for neonatologists, as many high-risk premature infants

receive insufficient amounts of enteral nutrition (EN) or receive only parenteral nutrition (PN), which frequently leads to growth restriction.[2]

Nutritional support is provided to preterm infants with the aims of: reducing mortality, length of hospitalization and infectious processes, as well as maintaining gastrointestinal function and modulating the inflammatory response.[3,4] Deferring nutritional therapy, with the expectation of neonatal stability, ignores the consequences of failure to begin nutritional support immediately after birth; the newborn enters a state of catabolism that does not contribute to clinical stability, development or growth.[3-5] Therefore, the medical team must recognize that premature birth is a nutritional emergency and every effort should be made to reduce nutritional deficits.[5,6]

The objective of this study was to assess the effects of PN initiation time in very low birth weight neonates on: the birth weight recovery time, EN initiation time, duration of hospitalization, and incidence of death.

MATERIAL AND METHODS

This retrospective case-control study was performed in the neonatal intensive care unit (NICU) of a tertiary Center: Santo Amaro Hospital, Salvador, Brazil.

Data were obtained from the medical records of all preterm infants born between January and December 2007. All infants with birth weights ≤ 1500 g who were treated in the NICU during that period (n= 114) were included in the study. Neonates with congenital anomalies or birth asphyxia, and those who were transferred to another hospital or for whom data were missing, were excluded.

The sample was divided in two groups: early (≤ 48 h after birth) and late (> 48 h after birth) onset of PN. We also analyzed a subgroup of neonates with birth weights ≤ 750g, as well as a group for whom PN was initiated very early (≤ 24 h after birth).

The following demographic variables were obtained: birth weight, gestational age, mode of delivery, and APGAR score.[7] Weight was recorded daily and the percentage of weigth loss was determined.

We analyzed the following respiratory outcomes: duration of intermittent mandatory ventilation (IMV), continuous positive airway pressure (CPAP) and duration of oxygen therapy.

Nutritional outcomes included in the analysis were PN and EN initiation times, birth weight recovery time, enteral and parenteral fluid and calorie rates on 10th day of life. Enteral and parenteral fluid and calorie rates were recorded daily for the duration of the study protocol.

The following adverse outcomes were considered: death, intracranial hemorrhage (ICH), patent ductus arteriosus (PDA) and length of hospitalization.

PDA was diagnosed by a pediatric cardiologist using two-dimensional echo imaging. Cranial ultrasound examinations were conducted by an experienced neonatologist.

Statistical analysis: Variables were characterized using means and standard deviations. Before the analysis, symmetry and kurtosis testing were performed to identify the normality of the data and the assumptions of the analysis. Means were compared by Student's t test for independent samples. All analyses were performed using SPSS software (Statistical Package for Social Sciences) version 13.0; (SPSS Inc., Chicago, IL USA.) with a significance level of 5%.

Ethical aspects: This study was performed according to the guidelines on human research of the Declaration of Helsinki and Resolution 196/96 of the National Health Council. All study protocols were approved by the Institutional Ethics Committee.

RESULTS

A total of 114 neonates (*n*=48 / 39.8% in early PN group), were included in the study. Mean birth weight was 1103.8 ± 246.8g and mean gestational age was 29 ± 1 weeks. The groups did not differ in term of birth weight (1185,8 ± 227,4 *vs* 1081,8 ± 253,4g; p=0,16), Apgar score (8,1±1,*2 vs* 8,1 ± 1,2; *p*=0,95). Birth weight recovery time (9.9 ± 4.0 vs 12.8 ± 6.1, p = 0.007), lenght of hospitalization (43.2 ± 4.0 vs 71.8 ± 41.7, p = 0.007), and time of EN onset (2.2 ± 1.2 vs 7.9 ± 5.8, p <0.001), were significantly lower in the early PN onset group than in the late onset group. Lenght of hospitalization was positively correlated with the

timing of EN onset (r= 0,37, p = 0,001). The early PN onset group had a significantly greater enteral fluid intake on the 10th day of life (91.5 ± 61.1 vs 31.0 ± 39.6, p <0.001; Table 1).

Table 1 - Comparison between early and late onset of parenteral nutrition in neonates with birth weight ≤ 1500g

	EARLY PARENTERAL NUTRITION 48(39,8%)	LATE PARENTERAL NUTRITION 66(60,6%)	p
NUTRITIONAL OUTCOMES			
Initiation of parenteral nutrition (days)	2,0 ± 0,6	2,6 ± 1,1	0,010
Initiation of enteral nutrition(days)	2,2 ± 1,2	7,9 ± 5,8	0,000
Total fluid rate 1ºd (ml/kg)	60,0 ± 28,6	61,6 ± 36,0	0,796
Total Calorie rate 1ºd (cal/kg)	6,4 ± 14,8	3,2 ± 11,2	0,204
Enteral fluid rate 10ºd (ml/kg)	91,5 ± 61,1	31,0 ± 39,6	0,000
Enteral calorie rate 10ºd (cal/kg)	64,1 ± 42,8	27,5 ± 45,6	0,000
Parenteral fluid rate 10ºd (ml/kg)	69,9 ± 61,4	116,8 ± 44,2	0,000
Parenteral calorie rate 10ºd (cal/kg)	32,4 ± 37,1	64,8 ± 32,6	0,000
Total fluid rate 10ºd (ml/kg)	159,5 ± 29,0	168,6 ± 157,1	0,707
Total calorie rate 10ºd (cal/kg)	97,6 ± 25,8	64,8 ± 32,6	0,050
Birth weight recovery time (days)	9,9 ± 4,0	12,8 ± 6,1	0,007
Hospitalization time (days)	43,2 ± 4,0	71,8 ± 41,7	0,007
VENTILATORY OUTCOMES			
IMV time (days)	6,9±12,2	8,9±16,8	0,492
CPAP time (days)	4,6±6,9	5,2±7,6	0,688
O_2 time (days)	13,0±15,6	15,5±21,3	0,487

Parenteral nutrition (PN); Intermitent Mandatory Ventilation (IMV); continuous positive airway pressure (CPAP).

No significant difference in adverse outcomes: death (18.6% vs 13.6%, p = 0.6), intracranial hemorrhage (ICH) (8.3% vs 12.1%, p = 0.9) and patent ductus arteriosus (PDA) (8.3% vs 31.8%, p = 0.1) was obbserved between groups (Table 2).

Table 2 - Adverse outcomes

	EARLY PARENTERAL NUTRITION 48(39,8%)	LATE PARENTERAL NUTRITION 66(60,6%)	p
Death	8 (18,6 %)	9 (13,6%)	0,59
Intracranial hemorrhage	4 (8,3 %)	8 (12,1 %)	0,90
Patent ductus arteriosus	4 (8,3 %)	21 (31,8 %)	0,10

In the subgroup analysis of neonates with birth weights ≤ 750 g, no significant difference was found between the early and late onset groups (Table 3).

Table 3 - Comparison between early and late onset of parenteral nutrition in neonates with birth weight ≤ 750g

	EARLY PARENTERAL NUTRITION	LATE PARENTERAL NUTRITION	p
Birth weight (g)	657,1±77,0	649,0±78,3	0,861
IMV time (days)	16,7 ± 13,5	28,2 ± 19,1	0,247
CPAP time (days)	11,3±13,6	8,0±6,2	0,587
0_2 time (days)	28,1±14,7	43,0±29,5	0,343
Hospitalization time (days)	54,9±33,1	104,6±89,0	0,199
Birth Weigth recovery time (days)	11,1±3,8	8,0±7,0	0,335
Start enteral (days)	4,0±4,2	8,0±5,1	0,165

Intermitent Mandatory Ventilation (IMV); continuous positive airway pressure (CPAP).

PN initiation in the first 24 h of life, significantly reduced the duration of IMV (3.7 ± 5.4 *vs* 15.6 ± 8.6, $p = 0.033$), a variable that showed no difference between groups in which PN was initiated ≤ 48 h or > 48 h after birth (6,9 ± 12,2 *vs* 8,9 ± 16,8, p=0,49).

Birth weight recovery time (12,6 *vs* 10,5; p=0,05) and the time of EN onset (7,2 *vs* 4,4; p=0,01) were significantly longer in preterm infants of preeclamptic mothers.

DISCUSSION

In this sample of preterm infants PN onset in the first 48 h of life, reduced the timing of EN initiation, and progression to full EN, birth weight recovery time, and lenght of hospitalization. No increase in adverse outcomes such as death, ICH and PDA was observed. We found no difference between early and late PN onset in premature infants with birth weights ≤ 750 g, but this group is at high risk.

Garcia et al.[8] obtained similar results in a sample of 58 premature infants weighing <1500 g; the early PN onset group regained birth weight sooner and had shorter hospital stays, and showed no increase in cases of PDA, death or IMV duration. These findings are particularly important in very low birth weight premature neonates, who are expected to undergo greater weight loss and require a longer time to recover birth weight than are full-term infants.[5] In premature infants, the combination of reduced nutrient supply with high demands and losses, leads to a catabolic state.[3,4] The early initiation of nutritional support reverses the catabolic state and helps to achieve clinical stability.[3-6,10] In our early PN onset group, EN onset and full EN occurred sooner and calorice intake on the 10th day of life was greater than in late onset group. The early initiation of EN, in the first week of life, is important in maintaining the intestinal barrier and preventing bacterial

translocation; it has a trophic effect on the maintenance of the intestinal mucosa and leads to an attenuation of the metabolic response.[2,3,6,9,10] The reduction in time to reach total EN reduces the risk of infection by venous colonization and decreases the time needed to achieve total EN independent of PN.[6,9] Although the early and late PN onset groups showed no difference in the duration of ventilatory suport, IMV was reduced in the subgroup that began nutritional support in the first 24 h after birth. This finding was in accordance with Wenhomer et al.[11] who showed that very low birth weight premature infants who developed bronchopulmonary dysplasia (BPD) had lower EN intake. BPD is an important cause of long-term ventilatory support.

Especially in very low birth weight neonates PDA and ICH are related to the rate of fluids and also can lead to increased mortality.[12] In this sample, we found no increase in adverse events in the early PN onset group.

The early PN onset group showed reductions in birth weight recovery time and lenght of hospitalization, two important clinical and economic outcomes. The reduction in the lenght of hospitalization, has a strong psychological impact on the family and on public health spending. A recent study performed in Brazil showed that the average cost of a premature infant's stay in the intensive care unit for a day was USD 96 per day.[13] Premature infants with the lowest birth weights incurred the highest daily costs,[13] thus, the reduction of hospital stays is economically important.

The findings of this study indicate that the early initiation of nutritional support in very low birth weight neonates can reduce the length of hospitalization thereby reducing costs, without increasing the incidence of adverse effects.

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