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Weight gain and metabolic complications in preterm infants with nutritional support

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ABSTRACT

Objective. To analyze the weight gain and to describe the metabolic complications in preterm newborns with nutritional support (NS) and to describe nutritional practices in the first month of hospitalization for 52 preterm newborns. **Material and methods.** Descriptive and prospective study of preterm infants (30-36 gestational weeks), with birth weight > 1 kg, hospital stay >12 days, without respiratory support or complications, conducted at a public hospital in Leon, Guanajuato, Mexico from January to November 2006. Weight, serum glucose, insulin, cholesterol, triglycerides, gamma-glutamyl-transferase, creatinine, urea nitrogen, type of NS (parenteral PN, enteral EN, mixed MN), energy content, and macronutrient intake were measured weekly. To obtain representative data, nutritional practices were not altered by the study protocol. One way ANOVA and Wilcoxon tests were used in data analyses. **Results.** Overall, 52 newborns were included, averaging 33 gestational weeks and 1,590 g of weight. The NS was started by the fourth day on average. Parenteral nutrition was the most frequent NS during the first 2 weeks (75%). Energy and macronutrient supply was 50% less than the recommended. Weight gain ranged from -100 to 130 g/week. Parenteral nutrition showed better weekly weight gain, followed by EN. The metabolic complication rate per person-day was greater for MN (0.56), than for EN (0.16) or PN (0.09). Routine surveillance of weight and metabolic complications was deficient. **Conclusions.** Late onset of NS, insufficient energy supply, and deficient surveillance were obstacles to weight gain and to prevent the metabolic complications in these newborns.

Key words. Hospital practices. Hyperglycemia. Weight gain. Preterm infant. Energy intake.

*Ganancia de peso y complicaciones metabólicas en **neonatos pretérmino que reciben soporte nutricio***

RESUMEN

Objetivo. *Analizar la ganancia de peso y las complicaciones metabólicas en neonatos pretérmino que recibieron soporte nutricio (SN) y describir las prácticas nutricionales en 52 neonatos pretérmino durante un mes de hospitalización.* ***Material y métodos.*** *Estudio descriptivo y prospectivo en neonatos pretérmino (30-36 semanas de gestación), peso al nacimiento > 1 kg, estancia hospitalaria > 12 días, sin soporte ventilatorio u otra complicación. El estudio se realizó en un hospital público de León, Guanajuato, México, de enero a noviembre 2006. Se obtuvo el peso, glucosa, insulina, colesterol, triglicéridos, gamma-glutamyl-transferasa, creatinina y nitrógeno ureico por tipo de SN (parenteral NP, enteral NE, mixta NM); la energía y la ingestión de macronutrimentos fueron medidos de forma semanal. Para el análisis estadístico se aplicó ANOVA de una vía y prueba de Wilcoxon. Para obtener datos representativos, las prácticas nutricionales no fueron alteradas en el estudio.* ***Resultados.*** *Se estudiaron 52 neonatos con un promedio de 33 semanas de gestación y 1,590 g de peso. El SN comenzó en promedio al cuarto día. La NP fue el SN más frecuente durante las primeras dos semanas (75%). El aporte de energía y de macronutrimentos estuvo 50% por debajo de las recomendaciones. La ganancia de peso estuvo en un rango de -100 a 130 g/semana. La NP mostró mejor ganancia de peso, seguida de la NE. Las complicaciones metabólicas neonato/día fueron mayores para la NM (0.56) que para la NE (0.16) o NP (0.09). La ganancia de peso esperada fue deficiente.* ***Conclusiones.*** *El inicio tardío del SN, la falta de vigilancia e insuficiente aporte energético y de macronutrimentos fueron obstáculos para la ganancia de peso y la disminución de complicaciones metabólicas para estos neonatos.*

Palabras clave. *Prácticas hospitalarias. Hiperglucemia. Ganancia de peso. Neonatos pretérmino. Ingestión energética.*

BACKGROUND

Nowadays, nutritional support (NS) is part of the integral treatment of any critically ill patient. It is especially important in preterm infants (< 38 gestational weeks) who had feeding problems due to insufficient development of suck and swallow reflexes, digestive immaturity, inadaptation of gastrointestinal hormonal responses, poor absorption capacity, low tolerance to enteral feedings, and risk of developing necrotizing enterocolitis.[1-3] NS avoids malnutrition due to prolonged fasting, decreases morbidity and mortality, reduces costs and length of hospital stays, which improves the prognosis of infants in the short, medium, and long terms.[4,5]

Nutritional support may be provided by parenteral nutrition (PN), enteral nutrition (EN), and trophic or mixed nutrition (MN), transitioning from PN to EN. Parenteral nutrition is the main NS for premature infants, due to their gastrointestinal immaturity, their inability to use the gastrointestinal tract for several days, or because of high metabolic requirements that are impossible to meet with enteral feedings exclusively.[6,7] Parenteral nutrition is costly, requires special equipment and infrastructure, close surveillance, and is the cause of infectious and metabolic complications.[4,6] On the other hand, EN is cheaper and physiologically safer, prevents mucosal atrophy, prevents bacterial translocation, and promotes adequate weight gain.[6,8,9] However, it may also have functional, mechanic, infectious, and metabolic complications. Finally, in MN small volume of trophic feeds (8-20 kcal/kg/day) are provided with simultaneous PN; this method fulfills nutritional needs and stimulates the gastrointestinal system.[10]

Metabolic complications and energetic depletion in premature infants lead to failure in weight gain and produce future abnormalities in metabolism and hormonal function, as well as neurologic abnormalities that result in central obesity, diabetes, cardiovascular diseases, and low school performance at an early age.[9,11,14-16]

At the Regional General Hospital in Leon, state of Guanajuato, 2,605 deliveries were attended during 2006, and 458 newborns (17.6%) required hospitalization in the neonatal unit. Overall, 65% of the newborns admitted to the neonatal unit are premature (11% of all deliveries in the hospital). Being so, more than half of admissions in the neonatal unit are premature infants potentially requiring will some kind of NS.

As the NS has its risks, monitoring of complications is recommended by checking biochemical (serum glucose, cholesterol, triglycerides and liver function tests) and anthropometrical parameters (such as weight gain). This monitoring permits the opportune intervention to avoid the complications of NS. Compliance with this recommendation, however, is not constant.

OBJECTIVE

The goals of this study were to assess the weight gain and metabolic complications in premature infants by type of NS, to evaluate weight and complication surveillance practices to describe nutritional practices in the first month, in order to have information to design standards for prescription and supervision.

MATERIAL AND METHODS

A descriptive and prospective study was designed to evaluate weight gain and metabolic complications in preterm newborns with different types of NS (PN, EN, or MN). The study was conducted from January to November 2006, at the Neonatology Unit of a second-level public teaching hospital (General Regional Hospital in Leon), from the Ministry of Health of the State of Guanajuato, Mexico.

A convenience sample was gathered with consecutive neonates who fulfilled the inclusion criteria entering the study. Preterm newborns with 30 to 36 gestational weeks, with birth weight 1 to 2.5 kg, who received NS, without ventilatory support or previous infectious or metabolic complications were included. The weight gain was registered and controlled according to the intake of liquids and to the use of radiating incubator. Newborns with < 12 days of hospital stay, incomplete surveillance of laboratory tests, or with pathologies that affected their digestive system, sepsis, or those who had surgery during their hospital stay were excluded. For their description and to obtain representative data, preterm infants were matched for gestational age, birth weight and postnatal age. Nutritional practices were not altered by the study protocol. Energy intake data were recorded from the clinical records.

To determine sample size for proportion comparisons, we choose a 95% confidence level ($\alpha = 0.05$) and power of 80% ($\beta = 0.20$). Hyperglycemia is the most frequent metabolic complication in newborns with NS and its frequency range goes from 10 to 30%.[17] A sample size of 52 premature infants was calculated, using an estimated 30% frequency of hyperglycemia in newborns with NS.[18]

To standardize procedures and criteria in data collection and weight measurement, we performed a pilot study with eight newborns. During the study, trained personnel collected all required information, and using standardized techniques, the weight was measured every week. Personnel who drew blood from babies were blind to the study's hypothesis. Only the physicians in the neonatal unit decided the prescription, type, start, or changes in the NS. The study personnel collected data about the NS, as well as date of birth, gestational weeks, weight, length, cephalic perimeter, diagnostics, and complications.

Nutritional diagnosis

To get a nutritional diagnosis for each newborn, weight, length, and head circumference values were compared to Lubchenco's charts for preterm newborns.[19,20] For their description, preterm infants were matched for gestation, birth weight and postnatal age (Table 1). Patients were classified as appropriate for gestational age (AGA, weight > 10th and < 90th percentile), small for gestational age (SGA, < 10th percentile) or large for gestational age (LGA, > 90th percentile). To assess intrauterine malnutrition, we calculated the ponderal index (PI), which relates weight for height at birth:[21]

$$PI = \text{Weight at birth (g)} \times 100/\text{height}^3 \text{ (cm)}$$

In chronic intrauterine malnutrition, the newborn will have a PI between the 10th and 90th percentile, is proportionated and symmetric, and may be AGA or SGA. Conversely, in acute intrauterine malnutrition, the PI is in <10th percentile, the baby is asymmetric, disproportionate, and may be AGA or SGA. Finally, every week the weight gained was compared against the expected gain. For the first week, a weight gain of 10-15 g/day or 70 to 105 g/week was considered appropriate; from the 2nd to the 4th week, an increase of 15-40 g/day or 105 to 280 g/week was judged appropriate.[15,22]

Metabolic complications

Every week and 48 hrs after a change in NS, a blood sample (1-3 mL) was obtained from the back of the hand, to evaluate glucose, insulin, urea nitrogen, creatinine, gamma-glutamyl-transferase (GGT) cholesterol, and triglycerides. From the hepatic tests, GGT was considered the surrogate of hepatic damage. Metabolic complication was defined as an abnormal laboratory result, according to the recommended range for age and weight in premature infants.[23] As the pilot study identified poor compliance with laboratory and clinical surveillance, permission was asked to the clinicians to make sure that all the included newborns had at least determinations of serum glucose and cholesterol, as well as the registry of weight gain.

Energy and macronutrient intake

The information about energy and macronutrient intake (proteins, fat and carbohydrates) was obtained from the clinical file, and was compared to the guidelines and recommendations of the American Dietetic Association (ADA), being the most frequently used by the clinicians.[15] We calculated the fitting percentage, for which normal values range from 90 to 110%. This figure allowed us to determine the real intake, contrasted with the 100% daily recommendation. The PN was prepared in the metabolic unit in the hospital. For the EN only commercial formula for premature infants (PRENAN®, Nestlé, Mexico, D.F.) was provided and none of the newborns received breast milk. Finally, we describe the surveillance or monitoring practices during the NS.

Statistical analysis

Changes in weight, energy and macronutrient intake were evaluated using the Wilcoxon signed ranks test. The comparison of laboratory test results by type of NS was performed with one-way-ANOVA test. The frequency of complications per patient by type of NS was calculated dividing the total of complications by the patients who receive the NS. The rate of metabolic complications per person-day (incidence density) by type of NS was calculated dividing the total of complications by the sum of exposure days to the type of NS; 95% confidence intervals were also calculated.[24] The alpha significance level for all the tests was < 0.05. NCSS software (version 2001) was used for all statistical analyses.

The study was approved by the Ethical and Research Committees from the Institute of Medical Research and the institution of study. All the parents of the newborns selected for the study signed an informed consent. The study did not represent a health risk for the newborns, since weekly blood samples were obtained only in the recommended amounts by trained personnel.

Table 1. Weekly weight gain by type of nutritional support.

Follow up	Weekly weight gain (g) by type of nutritional support									Overall weight gain†		
	Parenteral			Enteral			Mixed					
	Median	(Range)	N*	Median	(Range)	N*	Median	(Range)	N*	Median	(Range)	N*
1st week	150	(-100 to 250)	N =39	110	(-200 to 340)	N = 10	-90	(-260 to 180)	N = 3	125	(-100 to 420)	N = 52
2nd week	-60	(-100 to 340)	N = 41	-60	(-340 to 190)	N = 5	200	(20 to 350)	N = 6	-110	(-340 to 190)	N = 52
3rd week	150	(150-150)	N = 4	40	(-60 to 210)	N = 3	-115	(-250 to 60)	N = 3	25	(-250 to 210)	N = 10
4th week	—		N = 0	100	(-60 to 210)	N = 4	185	(-230 to 140)	N = 2	130	(-60 to 230)	N = 6

* Number of premature infants who receive that type of nutritional support. † Overall weight gain from all the types of NS. American Dietetic Association recommendations: For the 1st week the appropriate weight gain is 70-105 g, from the 2nd to the 4th week the weight gain should be 105-280 g per week.[15]

Table 2. General characteristics of preterm infants at the beginning of the study.

Variable	Mean ± ED (range) n = 52	
Gestational weeks	33 ± 2	(30-36)
Weight (g)	1,590 ± 496	(1,000-3,010)
Length (cm)	39.1 ± 2.8	(33-47)
Head circumference (cm)	29 ± 1.4	(27-32)
Days to start the nutritional support	4 ± 1	(2-6)
Hospital stay	17 ± 4	(13-29)
Nutrition diagnosis according to:	N	(%)
• Birth weight n (%)		
- Small for gestational age (SGA)	28	(54)
- Appropriate for gestational age (AGA)	24	(46)
•Head circumference		
- Small for gestational age	8	(15)
- Appropriate for gestational age	44	(85)
Diagnostic according to ponderal index (PI) *		
Proportionate	22	(42)
Disproportionate	30	(58)
• Disproportion by nutritious diagnostic		
- Disproportion among infants SGA	11/28	(39)
- Disproportion among infants AGA	19/24	(79)

* PI: Weight for height at birth: PI = Birth weight (g) x 100/Height at birth^3 (cm).

RESULTS

During the study period 83 premature infants were eligible for the study. However, 18 were excluded due to insufficient blood samples for analysis of metabolic complications, and 10 more were excluded because their hospital stay was ≤ 12 days. In addition, three patients with PN died due to catheter related sepsis, during the 2nd and 3rd week of follow up, and were eliminated from the study. The final sample consisted of 52 premature infants, 34 males (65%), who had an average of 33 gestational weeks (range 30-36), and an average weight of 1,590 g (range 1,000-3,010 g). Twenty-eight premature babies (54%) were SGA, while 30 (58%) were classified as disproportioned according to their ponderal index. The NS was started on average on the fourth day of hospital stay, and the average length of hospitalization was 17 days (Table 2). The majority of the infants started the NS with EN (38, 73%), only 8 (15%) started with PN, and 6 (12%) with MN. However, during the first two weeks of follow up, 75% of the newborns received PN.

Weight gain

Thirty infants (58%) did not show weight gain according to the ADA recommendations.[15] There was no weight recovery after the physiologic loss of the first week. Weekly weight gain in premature infants ranged from -110 to 130 grams (Table 1). There was a significant difference between the overall weekly weight gain and the one recommended by the ADA (Wilcoxon Rank test $p < 0.05$). Weekly weight gain seemed to be more advantageous with PN and EN, whereas MN showed greater weight loss during the 1st and 3rd week of hospitalization. After stratifying by age and weight, no difference was found for prescribed supply (Table 3).

Energy intake

The energy and macronutrient intake provided during the first week was 50% below the ADA re-

Table 3. Anthropometric characteristics of preterm infants: Weekly weight gain in strata defined by gestational age and birth weight.

	Birth weight, g			Gestational age, wk		
	1,000-1,500	1,501-2,000	> 2,500	30-31	32-33	34-36
N (g)	26	17	9	13	18	21
			Median (range)			
1st week	115 (-200-805)	110 (-10-220)	125 (-200-805)	140 (-30-805)	115 (-200-340)	120 (-200-266)
2nd week	-110 (-805-109)	-110 (-210-10)	-115 (-805-150)	-131 (-805-20)	-110 (-340-190)	-120 (-260-180)
3rd week	N* = 8 60 (-60-160)	–	N* = 3 150 (150-210)	N* = 3 50 (-60-160)	N* = 5 25 (-10-60)	N* = 2 180 (150-210)
4th week	N* = 5 130 (-60-230)	–	N* = 1 210	N*=2 175 (140-210)	N*=4 130 (-60-230)	– –

* Number of premature infants who were stratified by gestational age and birth weight.

Table 4. Energy and macronutrient intake per week.

Follow up	N	Energy (Kcal/kg) Median (range)	Carbohydrates (g/kg) Median (range)	Proteins (g/kg) Median (range)	Lipids (g/kg) Median (range)
Start–1st week *	52	40 (15-129)	7 (2-34)	2 (1-6)	2 (1-6)
2nd week	52	94 (20-288)	11 (2-32)	3 (1-8)	5 (1-14)
3rd week	10	93 (34-187)	10 (4-21)	3 (1-5)	4 (2-9)
4th week	6	137 (25-212)	15 (5-24)	4 (1-6)	7 (1-10)
ADA recommendations†	-	143 (88-330)	14 (9-32)	4 (2-8)	7 (2-9)
Fitting percentage for the 1st week‡	52	51 (8-135)	53 (5-153)	48 (3-139)	59 (15-132)

* The energy and macronutrient intake for the first week was significantly different to the ADA recommendations (Wilcoxon Signed Ranks Test, $p < 0.05$). † ADA: American Dietetic Association.[15] ‡ Fitting percentage refers to the percentage in which the amounts of energy and macronutrients supplied to the infants are similar to the recommended values; its normal range is 90-110%.

commendations, with a significant difference according to the Wilcoxon Rank test ($p < 0.05$) (Table 4). There were no significant differences between the energy and macronutrient intake and the recommended amounts during the following weeks of hospitalization. Changes in the infant's energy intake did not follow ADA guidelines. There were no differences when the preterm infants were stratified by gestational age and birth weight (Table 5).

Metabolic complications

Thirty one (60%) premature infants had more than one metabolic complication per week during their hospital stay. During the first week of follow up, the median complications per patient were 2 (range 0-5). Table 6 shows the frequency of each metabolic complication overall and by type of NS. The frequency of complications per patient was greater for MN (3.4), and was practically the same for NE (1.6) and for PN (1.5). The rate per person-day (or incidence density) was significantly greater for MN (0.56), than for EN (0.16) and for PN (0.09). In the comparison of the continuous results for each laboratory test, we found that only the mean level of creatinine was significantly higher in infants with EN (1 ± 0.3 (range 0.3-1.7) than with PN [0.7 ± 0.2 (0.5-1.7)] or with MN [0.7 ± 0.2 (0.3-1.7)] (one-way ANOVA, $p = 0.04$).

Hospital practices for the surveillance of metabolic parameters during the NS

According to the ADA,[15] a set of blood tests must be done at the beginning of the NS and weekly thereafter. We observed that the suggested surveillance with all the laboratory tests was done in 10 infants only at the beginning (19%), and in 11 infants (21%) during the weekly follow up. There was no survei-

Table 5. Energy and macronutrient intake per week (from combination parenteral, enteral and mixed routes) in strata defined by gestational age and birth weight.

	Birth weight, g			Gestational age, wk		
	1,000-1,500 N* = 26	1,501-2,000 N* = 17	> 2,500 N* = 9	30-31 N* = 13	32-33 N* = 18	34-36 N* = 21
	Median (range)					
Energy (Kcal/kg)						
1st week	40 (15-129)	35 (15-83)	40 (16-75)	57 (15-129)	40 (15-110)	40 (15-109)
2nd week	97 (20-288)	94 (23-165)	101 (85-208)	138 (20-288)	94 (20-168)	100 (43-165)
3rd week	N* = 8	–	N* = 3	N* = 3	N* = 5	N* = 2
	100 (34-187)	–	100 (68-152)	55 (34-152)	93 (63-148)	100 (68-187)
4th week	N* = 5		N* = 1	N* = 2	N* = 4	
	137 (25-212)	–	153	159 (153-165)	137 (25-212)	–
Carbohydrates (g/kg)						
1st week	6 (0-34)	5 (1.1-11)	5.6 (0.9-34)	8 (1-14)	7 (0-12)	7 (1-34)
2nd week	11 (2-32)	11 (3-23)	11 (10.5-24)	14 (2-32)	11 (3-23)	11 (5-23)
3rd week	11 (4-21)	–	11 (7.6-17)	8 (4-17)	10 (8-16)	11 (8-21)
4th week	15 (5-24)	–	17	18 (17-18)	15 (5-24)	–
Proteins (g/kg)						
1st week	2 (0-6)	2 (0.3-3)	2 (0.1-2.5)	2 (1-5)	2 (0-6)	2 (0-3)
2nd week	3 (1-8)	3 (1-5)	3 (2-6)	4 (1-8)	3 (1-5)	3 (1-6)
3rd week	3 (1-5)	–	3 (2-4.3)	2 (1-4)	3 (2-4)	3 (2-5)
4th week	4 (1-6)	–	4.3	4 (4-5)	1 (4-6)	–
Lipids (g/kg)						
1st week	2 (0-6)	2 (0.5-4)	2 (0.4-3.5)	3 (1-6)	2 (0-5)	2 (0-5)
2nd week	5 (1-14)	4.5 (1-8)	5 (4-10)	6 (1-14)	5 (1-8)	5 (2-8)
3rd week	5 (2-9)	–	5 (3-7)	3 (2-7)	4 (3-7)	5 (3-9)
4th week	7 (1-10)	–	7	8 (7-8)	7 (1-10)	–

* Number of premature infants who were stratified by gestational age and birth weight.

Table 6. Metabolic complications in 52 premature infants during hospital stay, by type of nutritional support.

Complications or abnormal laboratory test results*	Type of nutritional support			
	Parenteral (N = 41) N (%) †	Enteral (N = 22) N (%) †	Mixed (N = 14) N (%) †	Total N (%) ‡
Hyperglycemia (>150 mg/dL)	4 (10)	4 (18)	1 (7)	9 (17)
Hypoglycemia (< 40 mg/dL)	0 (0)	1 (5)	3 (21)	4 (8)
Hypertriglyceridemia (> 96-150 mg/dL)	2 (5)	2 (9)	3 (21)	7 (13)
Hyperinsulinemia (> 20 μU/L)	5 (29)	5 (23)	14 (100)	24 (46)
High urea nitrogen (mg/dL, according to age)*	3 (7)	4 (18)	6 (43)	13 (25)
Low creatinine (mg/dL, according to age*)	15 (36)	13 (59)	6 (43)	34 (65)
High gamma-glutamyl-transferase (GGT) (> 56-233 U/L)	31 (75)	7 (32)	14 (100)	52 (100)
Total abnormal tests results	60	36	47	143
Frequency of complications per patient	1.5	1.6	3.4	
Complication's rate per person-day of exposure§	60/697 = 0.09	36/220 = 0.16	47/84 = 0.56	
(95% Confidence Interval)	(0.07-0.11)	(0.12 -0.22)	(0.45-0.67)	
Complication's rate per 100 days of NS exposure	8.6	16.4	56.0	

*Reference values for premature infants according to Perlman.[23] †N: Sum of premature infants who receive each type of NS. The percentage represents the cumulative incidence, which is the number of complications divided by the exposed infants to that type of NS. ‡This percentage was obtained with respect to the total number of infants in the study (n = 52). §The complication rate per person-day of exposure represents the incidence density, calculated with the total number of complications divided by the sum of the days of exposure to that type of NS.

llance or monitoring of weight, length, or head circumference registered in the clinical file.

DISCUSSION

This is the first study done in the State of Guanajuato, to analyze the weight gain and the metabolic complications of premature babies receiving NS. The most important findings of our study concern the late starting of the NS, the scarce weight gain, and the deficiencies in both the energy intake and in the compliance with the ADA guidelines.

Several studies recommend the beginning of the NS during the first day of life, with small amounts and gradual increments according to the recommendations.[2,3,6,23,25] Providing MN, Donovan reported a greater increase in weight and less frequency of hyperglycemia when the NS was started during the first 24 hrs.[26] However, in our study the NS was started on average at the fourth day, and perhaps this delay may explain in part the deficit in weight gain. On the other hand, Horbar proposed to start with breast milk,[2] but in our study all the enteral support was done with commercial formula for premature infants. Another probable cause of the deficit in weight gain is the inadequate supervision of weight and complications, since energy and macronutrient intake were not adjusted according to the weight.

Although the EN has been described as the preferred NS practice to favor trophism and immunologic function and to avoid complications,[3,22,27,28] since the last decade the recommendation has been to start the NS with PN.[1,28] Most of the infants in our study received PN during the first two weeks of life; however, switching from PN to EN was done without MN, decreasing roughly the nutrient intake and resulting in less gain or even weight loss, as reported by Ehrenkranz.[5] McClure[9] reported that the weight gain was better with EN, with no differences between MN and PN in this respect. In this study, PN showed the best weight gain, followed by EN.

Some clinical trials have found that premature infants with early MN had better tolerance to milk, normal tests of hepatic function, less metabolic bone disease, less hospital stay, and appropriate weight gain.[22] In contrast, in our study the patients with MN had the greatest frequency of complications and the worst weight gain compared to the other forms of NS. However, there were few patients with MN and EN, and more patients are required to compare rigorously the types of NS. Of significance is that even when the PN showed the most favorable weight increases and the lowest rate of metabolic complications, the risk of fatal infectious complications in a setting like ours is high, and careful supervision must be provided to assure that the benefits of this NS surpass their risks.

The most frequent metabolic complication was the increase in surrogate GGT. Ruy-Díaz-Reynoso,[29] Gura,[30] and Zambrano[31] point out this test as a marker of hepatic metabolic stress and of decreased bone mineral density, which increase the risk of fatty liver or histological hepatic lesions.[32] For this reason, it is necessary to give long-term follow up to patients that have received PN.

Metabolic complications such as hyperglycemia, hyperinsulinemia, and hypertriglyceridemia, have been related to future complications such as diabetes mellitus type 2, cardiovascular diseases, and hepatic pathologies.[26,33] A case-control study found significant abnormalities in the insulin levels of children who were premature.[24] Puntis[1] points out that constant increases of serum glucose lead to increases in insulin levels and later pancreatic damage.[3,6,12-14] In addition, for Hofman[34] hyperglycemias are a prognostic mortality factor in preterm infants and its constant occurrence may have medium- and long-term implications for the development of diabetes mellitus. Another potential explanation for hyperglycemia is a lower protein intake, because proteins stimulate the insulin production.[35] Our study did not have the ability to determine the reasons for suboptimal carbohydrate and total energy delivery, because nutritional practices were not altered by the study protocol. The increased serum urea found in some newborns is a marker of protein loss, which may explain some weight lost.[36]

This study has the typical limitations of observational and cohort studies. As a consequence of our convenience sampling, the generalization of our results is limited. Being an observational study about a dynamic nutrition process, the comparison groups are not necessarily similar. In addition, there is a chance of selection bias, because the physician might have assigned a type of NS based on patient characteristics (weight, severity of illness) that could have influenced the study results. Furthermore, because the exposure status might change over time, there are transitions between the types of NS without a "washout" period, and it is difficult to isolate the benefits and effects of the types of NS during these transitions.[37]

CONCLUSIONS

We found that the weight gain was better with the PN, while the frequency of metabolic complications was greater during transition from PN to NE (this transition constitutes MN). The NS did not lead to proper weight gain because the energy intake was scarce and started late, in the context of a deficient surveillance of weight and metabolic complications. These problems can be associated with a reduced life span by increasing cardiovascular risk, obesity, and noninsulin dependent diabetes. Randomized clinical trials should be performed to evaluate whether different nutritional management practices will permit birth weight to be regained earlier, leading to more rapid growth, more appropriate body composition, and improved short- and long-term outcomes.

Our findings were useful for the local design of programs and NS surveillance policies, to assure that energy and macronutrient intake are appropriate and that changes are implemented in a timely manner by a multidisciplinary team. Our final goal is to offer good medical attention to preterm infants so that they can be well integrated to society and have a better chance of achieving a good quality of life.

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