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Original article

First week weight dip and reaching growth targets in early life in preterm infants

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SUMMARY

Background & aims: Aggressive parenteral nutritional practices were implemented in clinical practice over a decade ago to prevent early growth retardation in preterm infants. We aimed to study adherence to current nutritional recommendations in a population of very preterm infants, and to evaluate growth in early life.

Methods: Preterm infants (gestational age <30 weeks and birth weight <1500 g) were included in a prospective observational cohort study. Data on parenteral and enteral intake were collected on days 1–7, 14, 21 and 28 (d28) of life. Growth data were collected at birth, at moment of maximal weight loss (dip), and either at discharge from the neonatal intensive care unit or at d28, whichever came first. Nutritional intakes were compared to recommendations of current guidelines. The target growth rate was 15–20 g/kg/d.

Results: Fifty-nine infants (63% male) were included. Median gestational age was 27 3/7 (interquartile range 25 6/7;28 4/7), and birth weight was 920 g (720;1200). Median macronutrient intakes were within or above the targets on all study days, but energy targets were not met before day 5. Median growth rates were 9.5 and 18.1 g/kg/d, when calculated from respectively birth and dip to discharge/d28. Eight (14%) versus 46 (78%) infants met the growth targets, when evaluated from respectively birth and dip to discharge/d28.

Conclusions: In this cohort, only energy intake up to day 5 was lower than recommended. Growth targets were achieved in the majority of the infants, but only when evaluated from dip onward, not from birth.

1. Introduction

Early nutrition and growth are pivotal for short- and long-term health of very preterm infants, with growth retardation being associated with mortality and poor neurodevelopmental outcome [1,2]. Adequate energy and protein intakes via the parenteral route can significantly increase postnatal growth in very preterm infants [3–5].

In 1977, the American Academy of Pediatrics stated that postnatal growth of very preterm infants ideally should mimic fetal growth [6]. Despite the implementation of parenteral nutrition in neonatal care in the early 1970s, growth retardation during hospital stay remained very common in the following decades [7–9]. In 2005 and 2002 the latest guidelines for parenteral nutrition in preterm infants were released by respectively the European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the American Society for Parenteral and Enteral Nutrition (ASPEN) [10]. Both guidelines recommended aggressive parenteral nutrition regimes for preterm infants, with the start of

Abbreviations: ESPGHAN, European Society for Pediatric Gastro-enterology, hepatology and nutrition; NICU, neonatal intensive care unit; GA, gestational age; d, day; IQR, interquartile range.

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amino acids and lipids soon after birth. Randomized controlled trials showed that these recommendations were safe and improved growth on the short term [11–13]. However, soon after the release of the guidelines, concerns were expressed about the feasibility of the recommendations in clinical practice, and about the persistent high rates of in-hospital growth retardation [14–16]. This was supported by a survey in 2013 showing that parenteral nutrition practices are frequently not compliant with current recommendations, especially in the first days of life [17].

The aggressive nutritional practices have been introduced in clinical neonatal practice over a decade ago. We presume that general improvements of perinatal and neonatal care over time affect nutritional practices and growth. We therefore aimed to evaluate adherence to current nutritional recommendations in a population of very preterm infants on a tertiary neonatal intensive care unit (NICU). Additionally, we aimed to evaluate their growth in the first month of life.

2. Methods

This prospective observational study was part of an ongoing cohort study at the level IV NICU of the Erasmus MC – Sophia Children's Hospital, Rotterdam, the Netherlands. Infants born before 30 weeks of gestational age (GA) and birth weight below 1500 g were included between September 2014 and December 2015. Exclusion criteria included congenital anomalies (including chromosomal defects), severe brain injury (i.e., intraventricular hemorrhage grade III/IV and post-haemorrhagic ventricular dilatation) and admission to the NICU after 48 h of life [18]. Informed consent was asked shortly before expected discharge (around 30 weeks GA). This study was conducted according to the guidelines laid down in the Declaration of Helsinki, and approved by the local medical ethical review board (MEC-2014-379). Written parental informed consent was obtained prior to enrollment in the study.

2.1. Local nutritional protocol

All infants were treated according to our local nutritional protocol, which is based on the parenteral (2005) and enteral (2009) ESPGHAN guidelines [10,19]. In short, parenteral glucose administration was started directly after birth, with a minimum of 4.0 mg/kg/min and a maximum of 12 mg/kg/min. Amino acid administration (Primene 10%, Baxter, Utrecht, the Netherlands) was also started directly after birth at 2.4 g/kg/d, and increased to 2.9 g/kg/d the next day. The target dose of amino acids was 3.5–4.0 g/kg/d. Lipids were started on the day after birth (Intralipid 20% or SMOFlipid 20%, both Fresenius Kabi, Bad Homburg, Germany) at 1.4 g/kg/d, and increased to 2.8 g/kg/d on the next day. The target dose for lipids was 2.5–3 g/kg/d. Parenteral intake was gradually increased with ~20 ml/kg/d to reach the target of 160–180 ml/kg/d. At an enteral intake of 130 ml/kg/d, parenteral nutrition was ceased.

Triglyceride and urea levels were monitored on regular basis. Parenteral amino acid administration was temporarily lowered if plasma urea concentrations were above 10 mmol/l, and interrupted when above 14 mmol/l. Similarly, lipid administration was temporary lowered when triacylglycerol concentrations were above 3 mmol/l and interrupted when above 5 mmol/l.

Enteral bolus feeding was started on day 1, and increased daily according to our local protocol [20]. Only if expressed breast milk was insufficiently available, preterm formula was supplemented (Neonatal start, Nutricia Advanced Medical Nutrition, Zoetermeer, the Netherlands). Breast milk fortification was started at an enteral intake of 100 ml/kg/d (Neonatal Breast Milk Fortifier, BMF, Nutricia, Zoetermeer, the Netherlands).

2.2. Data collection

Maternal, obstetrical and neonatal data were collected from electronic medical records. Intake data were collected from the bedside Patient Data Monitoring System on 10 study days: day (d) 1–7, day 14, 21, and 28 of life. These intake data included (1) parenteral and enteral nutritional intake of fluids, macronutrients and energy, and (2) fluid, carbohydrate and energy intake via intravenous drug administration if either continuously administered or if intermittent boluses exceeded 2 ml/day. Intakes are expressed in ml/kg/d for fluids, in mg/kg/min for carbohydrates, in g/kg/d for amino acids and lipids, and in kcal/kg/d for energy.

As infants are born around the clock, duration of the "first day of life" ranges form 0–24 h. Locally, daily planned changes in (nutritional) therapy are carried out at 4 pm. Therefore, in infants born *before 4 pm*, day 1 was defined as day of birth. In those born *after 4 pm*, day 1 was defined as the period from birth until 11:59:59 pm of the day after birth. Duration of day 1 thus ranged from 8 to 32 h. To adjust to an intake per 24 h, the following formula was used: cummulative intake day 1/(duration of day 1 (in hours)/24 hours).

Table 1
Summary of recommendations of ESPGHAN guidelines in preterm infants.

		Parenteral nutrition (2005) Day 1–7	Enteral nutrition (2009) Day 14, 21, 28
Fluid (ml/kg/d)	Day 1	80–90	135–200
	Day 2	100–110	
	Day 3	120–130	
	Day 4	130–150	
	Day 5	140–160	
	Day 6	160–180	
	Day 7	140–180	
Energy (kcal/kg/d)	Starting day	Day 1	110–135
	Dose	110–120, no increment scheme provided	
Carbohydrate (mg/kg/min)	Starting day	Day 1	8.05–9.20
	Dose	4–8, no increment scheme provided	
Amino acid (g/kg/d)	Starting day	Day 1	<1 kg: 4–4.5
	Dose	1.5–4, no increment scheme provided	1–1.8 kg: 3.5–4.0
Lipids (g/kg/d)	Starting day	Start supply no later than 3rd day of life, but may start on day 1	4.8–6.6
	Dose	Maximum of 3–4, no starting dose, minimum dose or increment scheme provided	

ESPGHAN, European Society for Pediatric Gastroenterology Hepatology and Nutrition; ml, milliliter; d, day; (k)g, (kilo)gram; kcal, kilocalories; mg, milligram; min, minute.

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