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Original Article

Nutrient-enriched Diet in the Early Neonatal Period Influences the 3-year-old Height in Very Low Birth Weight Infants

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Abstract. Nutrient-enriched milk has been advocated to enhance premature infants' growth and early nutritional intervention is effective for growth failure in very low birth weight infants (VLBWI). We studied the 3-yr-old physical growth of VLBWI who received nutrient enriched diets in the early neonatal period. VLBWI, who were born in 1996, received nutrient enriched milk around 1 mo of age. By contrast, in VLBWI born in 1998, nutrient enriched milk was started at 1–2 wk after birth. The daily calorie intake of VLBWI in 1998 had a tendency to be high compared to that of VLBWI in 1996. Height and body weight SD of 3-yr-old children who were born in 1998 tended to be greater than those of children who were born in 1996 (mean ± SD, –0.27 ± 0.54 vs. –1.01 ± 0.67; p=0.043, –0.47 ± 0.61 vs. –0.97 ± 1.10; p=0.31). Our study suggests that early feeding of nutrient-enriched milk for VLBWI in the neonatal period may affect their growth.

Key words: nutrient-enriched diet, 3-year-old height, dexamethasone, very low birth weight infant

Introduction

Postnatal growth failure is extremely common in very low birth weight infants (VLBWI). Ford *et al.* demonstrate VLBW children were significantly shorter and lighter and had smaller head circumferences than normal birth weight children at ages 2, 5, 8, and 14 yr (1). This growth failure may result from a complex interaction of genetic and environmental factors, including inadequate nutrition, morbidities affecting nutrient requirements, endocrine abnormalities and treatments. Among VLBWI, those small for gestational age (SGA) at birth and those with postnatal growth failure at the time of discharge are at higher risk of later growth failure and long-term consequences. The most critical period for catch-up growth is during the first 3 to 9 mo of life, but it isn't known whether SGA subjects equally grow up during infancy, childhood and puberty. It is controversial whether postnatal catch-up growth is influenced by nutritional status (2).

Nutritional intervention with aggressive nutrition during the first weeks of life may minimize the interruption of nutrients that occurs at birth. Supplementary formula feeding carries with the danger of increased mortality and gastrointestinal infections. Recently, it was

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reported that new human milk fortifier had safety comparable to reference human milk fortifier and promoted faster weight gain and head circumference growth (3). Even in extremely low birth weight infants, very early feeding within 48 h after delivery had a benefit, reducing the incidence of severe infection, necrotizing enterocolitis and cholestasis, and the feeding promoted sufficient growth (4). The aim of this study was to analyze the influence of nutritional supply in the early neonatal period on 3-yr-old height in VLBWI.

Subjects and Methods

The study was conducted on 14 neonates admitted to the Neonatal Intensive Care Unit of the Department of Pediatrics, Kyoto Prefectural University of Medicine. Inclusion criteria were: infants weighing less than 1,500 g at birth with 3-yr-old medical check-up record. Exclusion criteria included the following: any major congenital malformation, chromosomal anomaly and severe mental retardation. Retrospectively, detailed history and clinical examination including the anthropometry record of the baby were evaluated. Gestational age was calculated from the first day of the last menstrual period of the mother, and confirmed by clinical assessment of gestational age using the Dubowitz scoring system.

VLBWI received parenteral nutrition matched to their general condition, such as respiratory distress syndrome, patent ductus arteriosus (PDA), and had enteral intake as soon as possible. Of 14 infants, 4 had bronchopulmonary dysplasia (BPD) and received dexamethasone therapy (0.2 mg per kilogram every 12 h for 2 d, with a tapering of the dose in the next 4 d). Infants who were born in 1996 received nutrient-enriched milk (Neomilk pm, Yukijirushi; nutrient composition per 100 ml: calories 76 kcal, calcium 68 mg, phosphorus 37 mg, vitamin A 960 IU, vitamin D 256 IU, osmotic pressure 378 mOsm/kgH_2O) from around 1 mo of age. On the other hand, infants who were born in 1998 received fortified human milk (HMS-1, Morinaga; nutrient composition per 100 ml: calories 69 kcal, calcium 97 mg, phosphorus 54 mg, vitamin A 170 IU, vitamin D 6 IU, osmotic pressure 330–340 mOsm/kgH_2O) or preterm formula (SMA-LBW, Icreo; nutrient composition per 100 ml: calories 82 kcal, calcium 80 mg, phosphorus 40 mg, vitamin A 240 IU, vitamin D 47 IU, osmotic pressure 268 mOsm/kgH_2O) with vitamin supplement as early as possible, around 1–2 wk old.

Anthropometric measurements consisting of weight, length and occipitofrontal head circumference were obtained. Growth parameters were transformed into standard deviation score (SDS) corrected for gestational age and sex according to the growth standards of Ogawa, as previously reported (5). Volume of enteral feeds and intravenous fluids were recorded daily. Water quotient (WQ) and energy quotient (EQ) were calculated from the values; EQ was calculated as total energy intake in 24 h divided by the body weight. All infants were followed-up longitudinally until 3 yr of age.

The results are given as means and standard deviations (SD). The data were analyzed by the Mann-Whitney U test, and a P value of less than 0.05 was considered statistically significant.

Results

Seven VLBWI were born in 1996, and 7 were born in 1998. Table 1 shows the clinical characteristics of the two groups. They had a gestational age between 25 and 33 wk, a birth weight between 650 and 1,250 g, and a birth length between 30 and 38 cm. Each group included appropriate and small for gestational age (AGA and SGA) infants. The infants born in 1998 were relatively tall at birth, but they were born at a later gestational age than the infants in 1996. There were no other significant differences between the two groups. Asphyxiated infants

Table 1 Clinical characteristics of the two groups at birth

	1996	1998	
Sex			
Male	5	2	
Female	2	5	
Gestational age at birth (wk)	29.1 ± 2.1	29.7 ± 2.7	p=0.56
Birth weight (g)	1,002 ± 223	991 ± 136	p=0.91
SDS	–0.96 ± 0.83	–1.02 ± 0.81	p=0.88
Length (cm)	34.1 ± 2.2	35.6 ± 1.7	p=0.16
SDS	–1.22 ± 0.77	–0.99 ± 0.78	p=0.60
Apgar score			
At 1 min	6.3 ± 2.4	4.9 ± 3.2	p=0.36
At 5 min	8.1 ± 1.3	6.7 ± 2.8	p=0.24
Size for gestational age (no.)			
Appropriate	5	3	
Small	2	4	
Duration of hospitalization (d)	103 ± 25	108 ± 34	p=0.77

Table 2 Clinical characteristics of the two groups at 3 yr old

	1996	1998	
Body weight (kg)	11.8 ± 2.1	12.4 ± 1.6	p=0.51
SDS	–0.97 ± 1.10	–0.47 ± 0.61	p=0.31
Height (cm)	89.9 ± 4.3	92.6 ± 3.6	p=0.23
SDS	–1.01 ± 0.67	–0.27 ± 0.54	p=0.04
Head circumference SDS	–0.49 ± 0.95	0.44 ± 1.43	p=0.17
Developmental quotient	85.8 ± 16.1	79.0 ± 9.2	p=0.37

were resuscitated following the same procedure in each group. Table 2 shows the clinical characteristics of the two groups at the age of 3 yr. There was no statistical difference between any of the parameters. Body weight and height SDS of children born in 1998 tended to be greater than those of the children born in 1996. Figures 1 (A) and (B) show the weekly fluid intake and energy intake, calculated as WQ and EQ, respectively, in the neonatal period. Throughout this period daily calorie intake in the children born in 1998 was slightly higher than that of the children born in 1996. Especially, after 14 wk of birth, daily calorie intake statistically increased in children born in 1998. There was no significant difference in the height SDS during hospitalization (data were not shown), but the 3-yr-old height SDS was significantly improved in the VLBWI who were born in 1998 and received the enriched nutrition from the early neonatal period to discharge (Fig. 2).

Discussion

Studies describing the incidence of short stature in individuals born prematurely, especially VLBWI, are rare because of the possible factors which influence on growth. Study of growth of

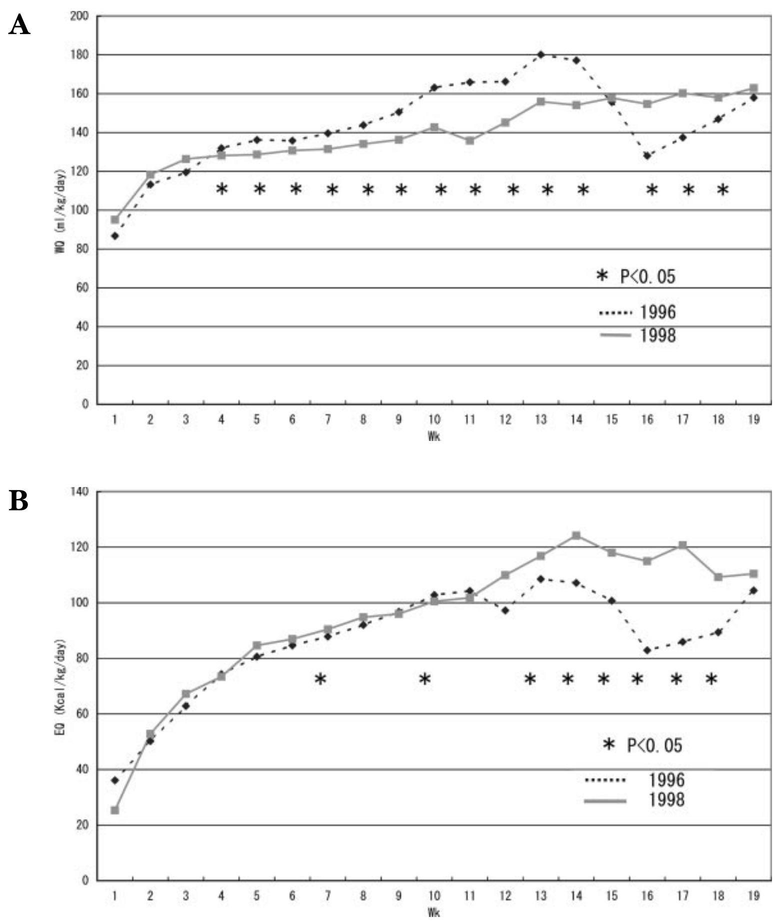

Fig. 1 Change in water (A) and energy (B) intake of the two groups. Data were analyzed using the Mann-Whitney U test. The asterisks indicate significant differences between the two groups. Throughout the period water quotient was controlled to prevent retinopathy of prematurity and daily calorie intake was slightly higher in 1998. Especially, after 14 wk of birth, daily calorie intake had statistically increased.

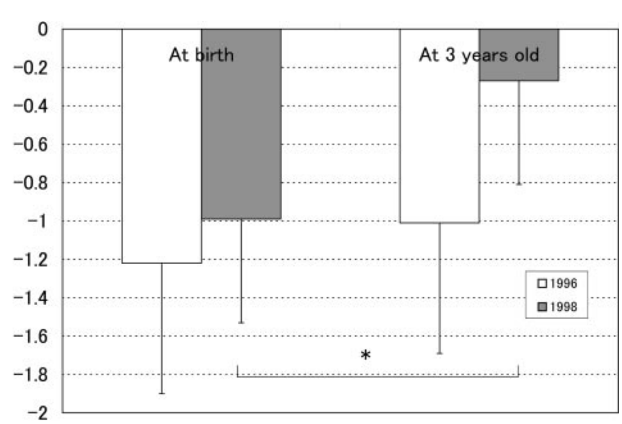

Fig. 2 Comparison of height SDS corrected prematurity, gender and age at follow-up between the VLBWI born in 1996 and 1998. The 3-yr-old height SDS was significantly improved in the VLBWI who were born in 1998, while it was not significant in those born in 1996 (p=0.48).

VLBWI has become of interest recently as increasing numbers of infant survive. The usual recommendation for feeding preterm infants is to provide sufficient nutrients to support rates of growth and nutrient accretion equal to intrauterine rates, but most preterm infants don't tolerate feedings immediately (6). This study was designed to retrospectively describe the growth of VLBWI unselected for degree of medical illness.

The infants given earlier feeding of nutrient-enriched milk with slightly higher daily calorie content demonstrated a tendency of increased weight and height SDS. The nutrient-enriched milk was designed to meet the nutritional needs of VLBWI more effectively (high contents of calcium and phosphorus). For improving the acceptance and tolerance, the osmolality was reduced (3). Several studies have shown that aggressive nutritional support is well tolerated and is effective at improving growth (7). In our study, early initiation of nutrition seemed to be effective for growth at 3 yr of age. Until 19 wk after birth calorie intake of VLBWI born in 1998 who received intravenous hyperalimentation, nutrient-enriched milk and MCT oil was slightly higher than that of VLBWI born in 1996. Recent data indicate that after discharge nutrient-enriched formula is beneficial for growth in addition to continued provision of appropriate nutrition throughout the neonatal intensive care unit stay (8). Thus, higher daily calorie intake may be effective on growth at 3 yr of age. However, our study population was small. To draw any conclusion, we must study a large number of patients.

Caloric intake should be increased during the early days without exceeding metabolic and renal tolerances for fat, glucose, and protein, which are usually decreased during the first 7 to 14 d. Growth acceleration in childhood increases the later risk of insulin resistance and coronary artery disease, whereas catch-up growth in the first 4 mo of life has been linked to later obesity. In preterm infants, any potentially advantageous effect of slower growth on long-term cardiovascular health must be balanced against the adverse effects of undernutrition on the brain (9). It is also reported that early restoration of IGF-1 to levels similar to those present in utero might help prevent retinopathy of prematurity by promoting normal vascular development. This perhaps could be accomplished by assuring sufficient nutrient intake (10).

In our study, both AGA and SGA patients were included. The numbers of both groups were too small to separate AGA and SGA. SGA infants among VLBWI have a higher risk of later growth failure and long-term consequences than AGA. Whether the response to the early initiation of nutrient-enriched milk is different between AGA and SGA infants must be further studied.

Our study suggests early nutrient-enriched milk initiation and subsequent calorie intake may reduce the growth restriction at 3 yr of age. Additional trials are necessary to address the role of nutrition and growth of VLBWI.

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