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Original Article

Effect of a high density formula on growth and safety in congenital heart disease infants☆

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SUMMARY

Background & aims: Infants with congenital heart disease (CHD) have elevated energy expenditure; however, they also have poor sucking and fluid restriction, which act as barriers to the delivery of adequate nutrition. The objective of this study was to investigate the effects of a high density formula (HDF) on safety, weight gain, and nutrient intake in CHD infants

Methods: We conducted a retrospective analysis of 21 CHD infants, comparing between two 4-week periods in which the children were given a standard density formula (SDF; 0.67 kcal/ml) and then a high density formula (HDF; 0.77–1.03 kcal/ml), respectively. In these children, we analyzed both safety parameters (serum creatinine, BUN, AST, ALT, and the frequencies of vomiting and diarrhea) and effective parameters (energy and protein intake, fluid volume, weight gain, and serum albumin).

Results: The mean concentration of formula in the HDF period was 1.21 times greater than that in the SDF period. Energy and protein intake per body weight, weight gain, and serum albumin in the HDF period were significantly higher than in the SDF period. There was no clinical evidence of any adverse effects related to the HDF.

Conclusion: Use of an HDF formulation is able to safely increase nutrient intake and promote weight gain in CHD infants. This nutritional formulation could potentially prevent malnutrition and failure to thrive in CHD infants.

1. Introduction

Infants with congenital heart disease (CHD) have higher energy expenditures than normal infants, as a consequence of congestive cardiac failure and pulmonary hypertension. Although these infants require more nutrition than normal infants, they additionally experience fluid restriction, which acts as an obstacle to the delivery of adequate nutrition.[1] Owing to a combination of these factors, CHD infants often develop malnutrition and failure to thrive.[2–5]

Several methods have been reported that aim to increase the energy intake of infants. One such approach involves concentrating the infant formula.[6] The advantage of this approach is that it is easy to practice, is inexpensive, and is able to increase the intake of protein and micronutrients. However, the efficacy and safety of this formulation method in CHD infants have not been clearly established.

The objectives of this retrospective study were to investigate the feasibility of using a high density formula (HDF) in terms of safety and to assess the effects of this type of formulation on energy and protein intake and on body weight in CHD infants.

2. Subjects and methods

2.1. Subjects

CHD infants admitted to Hyogo Prefectural Kobe Children's Hospital, who received both standard and high density formulas during their stay in the hospital between December 2006 and June 2009, were eligible for the study (Table 1). The applicability of HDF was left to the discretion of the cardiac surgeons or cardiologist caring for the patients. Infants who were fed weaning food were excluded. Ethical approval for this study was obtained from the

Abbreviations: CHD, congenital heart disease; HDF, high density formula; SDF, standard density formula

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Table 1
Subject demographics[a]

n (F/M)	21 (9/12)
Age (months)	2.6 ± 2.5
Weight (kg)	3.6 ± 1.4
Height for age (%)	93.1 ± 4.5
Weight for height (%)	78.8 ± 8.3
Nasogastric tube feeding (n)	16

[a] Data are n or the mean ± SD.

Research Ethics Board at Hyogo Prefectural Kobe Children's Hospital (Kobe, Japan).

2.2. Study design

A retrospective analysis was conducted to compare between two 4-week periods in which the infants were given the standard density formula (SDF) or HDF followed by SDF (Fig. 1). During the two periods, we analyzed the following parameters: the intake of nutrients and fluids; weight gain; serum albumin; and adverse effects on cardiac (heart rate, blood pressure), gastrointestinal (the frequencies of defecation and vomiting), renal (blood urea nitrogen, serum creatinine), and hepatic (serum aspartate aminotransferase, alanine aminotransferase) functions.

2.3. Formulas

The standard infant formula available in Japan was used in the two investigation periods. HDF was prepared from the standard formula by using less water than recommended by the manufacturer, thereby proportionally concentrating all nutrients contained in the feed. Compared with SDF (13% w/v), HDF (15% 20% w/v) was 1.15–1.54 times more concentrated (Table 2). The surgeons or cardiologist determined the density of formula that was adequate for the patients using the estimated energy requirement in healthy infants (90 120 kcal/kg bodyweight^{-1}) as a guide, and tailored the concentration of the formula by monitoring the degree of growth.

2.4. Statistical methods

Statistical analysis was performed using StatView 5.0 (SAS, Cary, NC, USA). A paired *t*-test was used to determine whether statistically significant differences existed between the compared periods. A *P*-value of 0.05 was considered significant. Data are presented as the mean ± SD.

3. Results

The mean concentration of formula used in the HDF period was 15.7% ± 0.22% (80.9 ± 1.13 kcal/100 ml).

There was no clinical evidence of any adverse effects related to the HDF with respect to the indicators of cardiac, renal, and hepatic

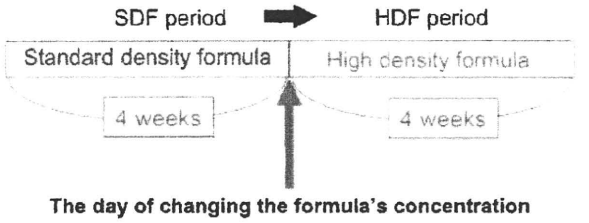

Fig. 1. Study design of retrospective analysis

Table 2
Composition of the two formulas.[a]

		SDF	HDF
		13%[b]	15.7% ± 0.22%[b]
Energy	kcal	67.0	80.9
Protein	g	1.55	1.87
Fat	g	3.60	4.35
Carbohydrate	g	7.23	8.73
Vitamin A	μg	55	66
Vitamin B1	mg	0.052	0.063
Vitamin C	mg	7.8	9.4
Vitamin D	μg	0.9	1.1
Calcium	mg	49	60
Phosphorus	mg	27	33
Iron	mg	0.91	1.1
Zinc	mg	0.39	0.47
Sodium	mg	18	22
Potassium	mg	62	75

[a] per 100 ml.
[b] Percentage indicates weight per volume

functions. However, among the parameters of gastrointestinal function, the frequency of defecations during the HDF period was significantly lower compared with that in the SDF period (Table 3).

The daily intake of energy and protein intake per body weight in the HDF period were significantly higher than those in the SDF period, although no significant difference was observed in the fluid intake during the two periods (Fig. 2).

The amount of daily weight gain during the HDF period was significantly higher than during the SDF period (20.1 ± 14.2 g vs. 10.4 ± 17.0 g). Further, the level of serum albumin in the HDF period was significantly higher than that in the SDF period (Fig. 3).

4. Discussion

A high density formula could be used safely in CHD infants and promoted growth resulting from an increase in nutrient intake. Although the frequency of defecation in the HDF period was less than that in the SDF period, adverse events such as abdominal distension did not occur.

CHD infants often have symptoms—including vomiting, gastroesophageal reflux, dysphagia, and respiratory distress—that reduce nutrient intake. In this study, there was no adverse event that might have warranted the discontinuance of HDF, and no significant difference in the examined parameters of organ function between the two periods. Thus, the safety of this nutritional formulation would appear to have been demonstrated.

It is known that CHD infants have poor weight gain, and, indeed, the daily weight gain (10.4 ± 17.0 g/day) in the SDF period tended to

Table 3
Parameters indicating adverse effects during the two investigation periods[a]

		SDF period	HDF period
Cardiac function			
Heart rate	(/min)	136 ± 10.6	136 ± 13.1
Systolic blood pressure	(mmHg)	94 ± 6.9	94 ± 6.0
Gastrointestinal function			
The frequency of defecation	(/day)	2.9 ± 1.7	2.0 ± 0.9*
The frequency of vomiting	(/day)	0.1 ± 0.2	0.1 ± 0.4
Renal function			
BUN	(mg/dl)	14.3 ± 9.6	12.6 ± 6.8
Creatinine	(mg/dl)	0.28 ± 0.10	0.26 ± 0.08
Hepatic function			
AST	(IU/l)	33 ± 14	39 ± 21
ALT	(IU/l)	22 ± 13	31 ± 28

*$P < 0.05$ vs the SDF period
[a] Data are the mean ± SD

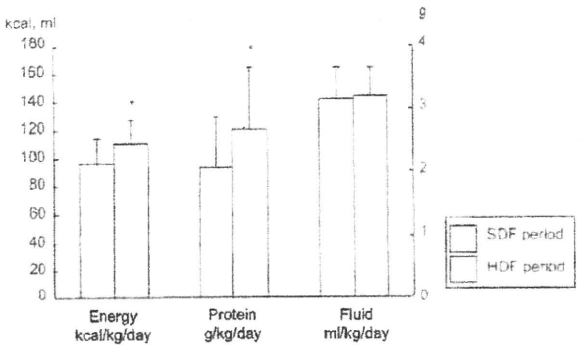

Fig. 2. Nutrient and fluid intake in the two investigation periods $n = 21$ CHD infants. Differences between the periods were determined using Student's *t*-test *Significantly different from the SDF period, $P < 0.05$. SDF: Standard density formula, HDF: High density formula.

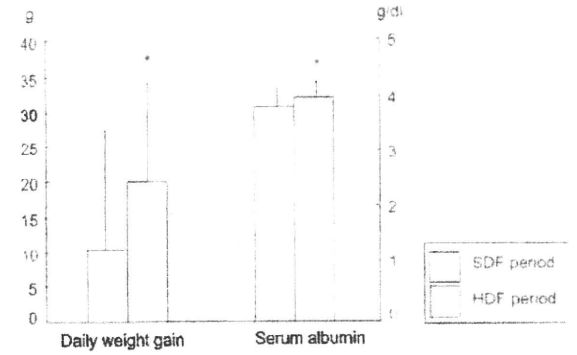

Fig. 3. Weight gain and serum albumin levels in the two investigation periods n 21 CHD infants. Differences between the periods were determined using Student's *t*-test *Significantly different from the SDF period, $P < 0.05$. SDF: Standard density formula, HDF: High density formula

be lower than the ideal level of 20–30 g. However, the daily weight gain (20.1 ± 14.2 g/day) in the HDF period was closer to the ideal status. Leite et al. reported that hypoalbuminemia is common among children who have heart diseases and who are at high surgical risk.[8] In the present study, levels of serum albumin were higher in the HDF period than in the SDF period. There appeared to be no effect of dehydration because the hematocrit value was not significantly different between the HDF and SDF periods (data not shown). Thus, the HDF could be considered to improve the nutritional status of CHD infants from the aspects of increased weight gain and elevated serum albumin levels.

Infants who do not receive a sufficient volume of formula because of fluid restriction and feeding difficulties also have deficiencies in protein, vitamins, and minerals. Clarke et al. suggested that increasing the energy content of normal infant formula without concomitant increments of protein and micronutrients should not be practiced in infants with faltering growth.[9] Although the methods designed to increase energy intake by adding carbohydrate or fat supplements to formulas do not increase protein, vitamins, and minerals,[10] the HDF described in the present study can increase the intake of macro- and micronutrient proportionately. Additionally, the HDF is a practical method that ensures compliance in outpatients undergoing dietary treatment because the formula is inexpensive and easy to prepare.

5. Conclusion

The high density formula described in this study is safely able to increase nutrient intake and to promote weight gain in CHD infants. This nutritional formulation could therefore potentially prevent malnutrition and failure to thrive in CHD infants.

Statement of authorship

AT-F conceived this study, participated in its design and the data analyses, and drafted the manuscript. MM contributed to the acquisition and analysis of data. TA participated in the design of the study and critically reviewed the manuscript. All authors read and approved the final manuscript.

Conflict of interest

The authors declare that they have no conflicts of interest.

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References

1. Rogers EJ, Gilbertson HR, Heine RG, Henning R. Barriers to adequate nutrition in critically ill children. *Nutrition* 2003;**19**:865–8.
2. Vaidyanathan B, Roth SJ, Gauvreau K, Shivaprakasha K, Rao SG, Kumar RK. Somatic growth after ventricular septal defect in malnourished infants. *J Pediatr* 2006;**149**:205–9
3. Vaidyanathan B, Radhakrishnan R, Sarala DA, Sundaram KR, Kumar RK. What determines nutritional recovery in malnourished children after correction of congenital heart defects? *Pediatrics* 2009;**124**:e294–9.
4. Jadcherla SR, Vijayapal AS, Leuthner S Feeding abilities in neonates with congenital heart disease: a retrospective study *J Perinatol* 2009;**29**:112–8.
5. Nydegger A, Bines JE Energy metabolism in infants with congenital heart disease. *Nutrition* 2006;**22**:697–704
6. Pillo Blocka F, Adatia I, Sharieff W, McCrindle BW, Zlotkin S. Rapid advancement to more concentrated formula in infants after surgery for congenital heart disease reduces duration of hospital stay: a randomized clinical trial. *J Pediatr* 2004;**145**:761–6.
7. ASPEN Board of Directors and the Clinical Guidelines Task Force. Guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients. *JPEN J Parenter Enteral Nutr* 2002;**26**(Suppl. 1):1SA–138SA
8. Leite HP, Fisberg M, de Carvalho WB, de Camargo Carvalho AC. Serum albumin and clinical outcome in pediatric cardiac surgery *Nutrition* 2005;**21**:553–8.
9. Clarke SE, Evans S, Macdonald A, Davies P, Booth IW. Randomized comparison of a nutrient-dense formula with an energy-supplemented formula for infants with faltering growth. *J Hum Nutr Diet* 2007;**20**:329–39.
10 Jackson M, Poskitt EM The effects of high-energy feeding on energy balance and growth in infants with congenital heart disease and failure to thrive *Br J Nutr* 1991;**65**:131–43.