

Premature Formula: Update

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Preterm and low birth weight (LBW) infants require more energy and nutrients per kilogram than term infants in order to have growth comparative to fetus with the same post-conceptional age in uterus. These infants are aimed to gain about 15 grams per day and for 1 gram of weight gain, energy of 4-6 kcal would be required. Therefore, they would need extra 75 kcal/kg/day other than basal metabolic rate (approximately 50 kcal/kg/day) to reach the goal. Moreover, the digestive system of the preterm and LBW infants is not completely developed and these infants spend greater energy expenditure due to their comorbid illness. As a result, premature formulas were developed for preterm and LBW infants during hospitalization. Studies showed that preterms who were fed with preterm formulas had better growth and cognitive function compared with those fed with term formulas. Table 1 shows nutrient composition of the preterm formulas available in Thailand. Other than the preterm formulas, human milk is also appropriate for the preterm and LBW infants, but it should be fortified with several nutrients such as protein, calcium, and other micronutrients.

Protein

Protein requirement depends on infant's birth weight. The preterm with birth weight of 1200-1800g would require 2.7-3.5 g/kg/day of protein and those who weighed less than 1200 g would require protein as high as 3.5-4 g/kg/day. Generally, protein intake of 3.5 g/kg/day at 120 kcal/kg/day is appropriate because protein synthesis requires energy. The expert panel recommended that protein to energy ratio for preterm infant formula is 2.5-3.6 g/100 kcal. Type of protein added in preterm formulas is also important to acquire plasma amino acid profiles and metabolic parameters comparable to those of breast-fed infants. Whey protein is a major protein in breast milk (whey: casein ratio of 60:40) and easier to digest and absorb than casein protein. Recently, several conditionally essential nutrients, which are detected in human milk, are added in preterm formulas.

● Taurine

Taurine is synthesized from cysteine. It is an essential amino acid for preterm infants and involves in several metabolic reactions, such as growth and fat absorption, but not incorporated into protein. It is also found mostly in retina and brain of the fetus and taurine deficiency could produce delay of visual and hearing development.

● Carnitine

Carnitine is abundant in human milk. It is synthesized from lysine and methionine. Even though carnitine is not a part of structural protein, it is conditionally essential for preterm and LBW infants. Carnitine has a significant role in transportation of long-chain fatty acids into the matrix of the mitochondria for β -oxidation.

● Choline

Choline is an important component of phospholipids, essential part of cell membranes, and the neurotransmitter acetylcholine. Other than dietary choline, it can be endogenously synthesized from phosphatidylcholine. Animal experiments demonstrate that choline plays an important role in the development of the brain and its function.

● Nucleotides

A nucleotide is composed of one purine or pyrimidine bases added with phosphorylated pentose sugar. Other than dietary sources, nucleotides can be synthesized from amino acids and nucleic acids. Nucleotides participate in nucleic acid synthesis as well as immune function. It also enhances the development of the small intestine and growth of intestinal microflora. However, the evidence is preliminary. The expert panel recommends that adding nucleotides to LBW formulas is optional.

Carbohydrate

Carbohydrates are the main energy source. Preterm and LBW infants need 10-14 g/kg/day of carbohydrates which would be approximately 40-50% of their total energy intake. Lactose is the main source of carbohydrate in human milk and LBW infants tend to tolerate it very well. On the other hand, studies suggest that these infants may not be able to tolerate a large amount of lactose in preterm formulas, because the activity of lactase enzyme is low in preterm infants until about 36 weeks of gestational age. Thus, glucose polymers such as corn syrup solids, which have low osmolarity and are easily digested and absorbed, are added to preterm formulas. The ratio of lactose to glucose polymers in preterm formulas is usually about 40-50:50-60.

● Oligosaccharides

Oligosaccharides are lactose added with monosaccharides and are found in human milk. Human milk oligosaccharides are not digested. They improve the growth of the

TABLE 1. Nutrient Composition of Formulas for Low-Birth-Weight and Preterm Infants (Per 100 ml)

Nutrients		PRENAN (Nestle)	Enfalac Premature (Mead Johnson)	S-26 LBW Gold (Wyeth)	NEOSURE (Abbott)
Energy distribution					
Prot : CHO : Fat		11:43:46	12:44:44	10:42:48	10:41:49
Energy	kcal	80	81	82	74.4
Protein	g	2.3	2.4	2	1.9
whey:casein ratio		78:22	60:40	60:40	NA
Carbohydrate	g	8.6	9	8.6	7.7
Maltodextrin	%	35 (3.0 g)	60 (5.4 g)	79	69
Lactose	%	65 (5.6 g)	40 (3.6 g)	21	31
Fat	g	4.16	4	4.4	4.1
		MCT 30%,	MCT 40%,	MCT 11%,	MCT 25%,
Linoleic acid (LA)	mg	590	731.4	550	558
Linolenic acid (ALA)	mg	64	73	NA	74.4
LA/ALA Ratio		9.3	10	NA	7.5
Vitamin A	IU	280	310	297	342
	mcg	84.1	93	90	103
D	IU	80	81	60	52
E	IU	2	11	1.8	2.7
K ₁	mcg	6.4	6.5	8	8.2
C ₁	mg	13	16	11	11.2
B1	mcg	56	162	120	163.7
B2	mcg	120	243	200	111.6
B6	mcg	60	121.5	72	74.4
B12	mcg	0.24	0.2	0.3	0.3
Niacin	mcg	800	3240	820	1450.8
Folic acid	mcg	56	28	48	18.6
Pantothenic acid	mcg	360	972	450	595.2
Biotin	mcg	1.8	3.2	2.4	6.7
Choline	mg	12	14.6	15	11.9
Inositol	mg	5.2	36.5	3.4	4.5
Taurine	mg	6.4	5.3	6.9	5
Carnitine	mg	1.7	NA	NA	4
Sodium	mg	29	47	35	24.6
Potassium	mg	86	81	85	105.6
Chloride	mg	56	69	60	55.8
Calcium	mg	99	97	80	78.1
Phosphorus	mg	54	53	43	46.1
Ca : P ratio		1.8	1.8	1.8	1.7
Magnesium	mg	8	7.3	8	6.7
Iron	mg	1.2	0.4	0.8	1.3
Iodine	mcg	20	20	10	11.2
Copper	mcg	80	97	83	89.3
Zinc	mg	0.64	0.7	0.8	0.9
Manganese	mcg	6	13.8	10	7.4
Selenium	mcg	1.6	NA	NA	1.8

NA = not available

(Ref: Rerksupphol S. Preterm Infant formula)

intestinal microflora. However, evidence is not strong enough to recommend an addition of oligosaccharides in preterm formulas.

• Inositol

Inositol is a six-carbon, cyclic sugar-related alcohol which is found more in human milk than in cow milk. Inositol assists in the synthesis of phosphatidylglycerol, a component of lung surfactant. Studies showed that inositol supplementation with other therapies improved respiratory distress syndrome and bronchopulmonary dysplasia. Moreover, the incidences of retinopathy and intraventricu-

lar hemorrhage were reduced in preterm infants supplemented with inositol. Thus, it is recommended that preterm formulas should contain at least 4 mg of inositol per 100 kcal.

Fat

Preterm formulas usually supply 5-7 g/kg/day of fat that account for 40-50% of total energy. Other than energy, vegetable oils in preterm formulas also provide an adequate amount of essential fatty acids. It is recommended that preterm formulas should contain 5% of total energy as linoleic acid (LA) and 1% of total energy as

α -linolenic acid (ALA). Preterm formulas also contain medium-chain triglycerides (MCT) as 40-50% of total fat content. Fatty acids in MCT oil have about 6-12 carbons. MCT is easier to be digested and absorbed than LCT. It is also more readily oxidized. However, recent studies indicated that MCT had little benefit on growth and mineral absorption of preterm and LBW infants. Thus, the addition of MCT oil is not recommended and should not exceed 50% of the total fat content.

- **DHA and AA**

Docosahexaenoic acid (DHA) and arachidonic acid (AA) are derivatives of α -linolenic acids and linoleic acids, respectively. DHA and AA are found in human milk but not in cow milk. DHA is essential for retinal and brain development, while AA involves in growth and cognition. Previous studies showed that DHA and AA supplementation improved growth, vision, and cognitive function of preterm and LBW infants, but the effect was transient. Therefore, the supplementation of AA and DHA in preterm formulas is optional.

Calcium and phosphorus

Calcium and phosphorus are the main components of bone mass and are stored mostly after 34 weeks of gestation. Preterm infants are at increased risk for the development of osteopenia and fractures. Human milk contains

about 250 mg/L of calcium and 140 mg/L of phosphorus. Preterm formulas usually have a greater amount of calcium and phosphorus than in human milk, because calcium and phosphorus in the formulas are harder to be absorbed and ionized than in human milk.

Vitamin and minerals

Vitamins and minerals are also important for optimal growth and development of preterm and LBW infants. Preterm formulas contain various amounts of vitamins and minerals, but they are generally adequate as shown in Table 1.

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