ABSTRACT

Breast milk is the gold standard for infant formulae. The closer the essential amino acid pattern of an infant formula matches that of breast milk, the lower the protein content of such a formula can be. This minimizes the risk of renal overload in the infant. The application of whey protein concentrates low in or free from the casein derived glycomacropeptide provides two additional benefits: closer resemblance to plasma amino acid patterns from breast milk fed infants (lower threonine, higher tryptophan and cysteine) and the possibility to lower protein levels in the infant formula towards recommended levels considered to be adequate and safe for infant growth and development.

INTRODUCTION

The composition of infant formulae is under continuous development following the latest scientific insights. Recently, the Codex Committee on Nutrition and Foods for Special Dietary Uses requested and received an opinion of an international expert group, coordinated by ESPGHAN (The European Society for Pediatric Gastroenterology, Hepatology and Nutrition), on recommended levels of nutrients in infant formulae, based on scientific analysis and taking into account existing scientific reports on the subject. The Nov 2005 report (1) of this consultation with experts from Germany, France, US, Canada, Japan, Australia, India, Brazil, Singapore, Thailand, Mexico, Israel and China, proposes compositional requirements for energy, protein, lipid, carbohydrates, vitamins, minerals and trace elements and other substances / optional ingredients. Nutrient contents are generally given per 100 kcal basis for ready to use formulae, as this is considered as physiologically meaningful. Although the acceptable protein content covers the full range between 1.8 and 3.0

Whey protein concentrates from acidic whey: benefits for use in infant formulas

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# Also know as caseinate whey, casein whey, non-rennet whey or GMP-free whey
amount and sources. It is evident that whey proteins are an important protein source, but it is also clear that protein levels are chosen on the high end side of the recommendation. The majority of the whey protein sources are derived from cheese whey. This paper will show that usage of casein derived whey protein concentrations offers two additional benefits: better comparison with breast milk amino acid patterns and potential for a lower, and thus more cost-effective, yet adequate protein level.

Mimicking breast milk amino acid composition

Jost et al (2) have reviewed a number of aspects with regard to whey protein usage in infant nutrition. They calculated the amino acid profiles of infant formulas with the casein to whey protein ratio varying from 100:0 to 1:100; the proteins in non-fat milk solids and rennet (cheese) whey were chosen as source references for the amino acid compositions. Within the class of (semi-) essential amino acids the levels of threonine, cysteine, isoleucine, valine, leucine, lysine and tryptophan increase with higher contributions of whey protein, whereas the levels of methionine, phenylalanine, tyrosine, histidine and arginine decrease. When the casein contribution was set at 40% and the whey protein part at 60%, the ratio found in human breast milk, the levels of threonine, methionine and lysine were in excess of the reported range for breast milk, whereas the levels of tryptophan and histidine were below the minimum reported levels. It was further concluded that with protein densities below 2 gram per 100 kcal, the supply of one or more of the (semi-) essential amino acids would become insufficient (depending on the protein mix). The closer the essential amino acid pattern of a formula matches that of breast milk, the lower the protein content of such a formula can be. This not only minimizes the renal load in the infant, but potentially also has an effect on the cost price of the formula. At present there are two approaches that allow reduction of protein content and provide closer resemblance to plasma amino acid patterns from breast-fed babies. On the one hand one can enrich the formula with the tryptophan-rich protein alpha-lactalbumin. On the other hand, one can modify the whey protein part of the formula, primarily aiming at reduction of protein-bound threonine (3).

The high content of threonine in whey dominant infant formulas using cheese whey derived protein sources is reflected in the plasma pattern. This so-called hyperthreoninemia has been the subject of some debate as there is some concern about a potential risk for neurotoxicity during early development. Rat studies have shown that increased dietary load of threonine results in increased levels in the brain (4, 5), whereby threonine itself or its conversion product glycine might affect neurotransmitter balance. However, Castagné et al (6) did not find indications from neurochemical and behavioural (alimentary, olfaction, locomotion) rat studies that moderate hyperthreoninemia markedly influences the central nervous system.

Table 2 compares the amino acid composition of casein derived whey protein concentrate (Nutri Whey, DMV International) with a typical composition of cheese derived whey protein concentrate (WPC). A clear drop in threonine levels is seen in the casein whey derived WPC. The reason for this decrease of about 30% is that the cheese whey derived WPC contains a fair amount of glycomacropeptide (GMP), the C-terminal peptide sequence of kappa-casein, which is split off during cheese manufacturing. On a total of 64 amino acids, this sequence contains 13 threonine residues, which therefore makes a major contribution to the amino acid composition of cheese whey protein where GMP constitutes 10-15% of the total protein. Furthermore, GMP is devoid of the amino acids cysteine, tyrosine, phenylalanine, histidine, arginine and tryptophan. As a consequence the levels of these important amino acids are enhanced in the casein whey derived WPC. Table 3 shows the comparison with the breast milk reference amino acid
pattern of cow’s milk based infant formulas (1.8 g protein / 100 kcal) where the protein part comprises 40% casein and 60% of either casein or cheese whey derived WPC. The benefit of the casein whey derived WPC is that cysteine and tryptophan have a better match with the breast milk pattern, and that the threonine level decreases with 35% compared to cheese whey derived WPC. These changes are the result of the absence of GMP and the relatively higher levels of β-lactalbumin and β-lactoglobulin. It has been shown in preterm infants that hyperthreoninemia can be decreased by feeding a casein whey based formula without GMP compared to a cheese whey based formula with GMP, as the result of a 20% reduced intake of threonine (7). Räihä et al (8) compared healthy term infants with respect to their growth (weight and length) during 4 months on whey modified infant formulas, with either 2.2 g protein / 100 kcal or 1.8 g protein / 100 kcal. Growth was the same for all 3 formulas. However, in the high protein density formula the whey protein / casein ratio was 60% / 40%, whereas in the low protein density formulas this ratio was 70% / 30%. Furthermore, the latter formulas were free from GMP, achieved by either using casein derived whey protein (+ some non-specified free tryptophan) or a modified sweet whey protein fraction. Turk et al (9) also compared the growth of breast milk fed and formula-fed infants for 4 months to assess whether a low protein formula was adequate and safe for term infants. The low protein formula (1.8 g / 100 kcal) had a casein / whey protein ratio of 30 / 70 compared to 70 / 30 for the high protein formula (2.6 g / 100 kcal). Again a modified whey protein fraction was apparently obtained via ion exchange technology applied on demineralized sweet (cheese) whey. Both formulas were well tolerated and without adverse effects. The conclusion of the study was that the low protein formula ensured normal growth of healthy term infants. The weight gain of the breast-fed infants during the first month of life was similar to that of the formula-fed babies, but appeared slightly slower thereafter. Thus, it can be concluded that application of casein whey free from GMP provides two additional benefits for infant formula manufacturing: substantially lower plasma threonine levels and the possibility to lower protein levels in the infant formula towards recommended levels considered to be adequate and safe for infant growth and development (1).