

Feeding high-risk infants with family history of allergy

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Abstract. – Since the turn of the century, CM (cow's milk) formulas have become progressively more common as breast milk substitutes when mother's milk is unavailable, and CM allergy (CMA) has thus gradually become a more common disorder. Therefore the management of CMA infants confronts pediatricians and allergists with one of the most demanding challenges. In the first year of life of many children, CM provides almost the entire dietary supply of proteins, carbohydrates, and fat; its high nutritional value and low cost should be noted. However, children with CMA can avoid CM without nutritional loss if nutrients are provided by other foods such as meat, fish, vegetables and fruit. Thus the choice of an adequate CM substitute for high-risk infants with family history of allergy is mandatory. The ideal CM substitute should be hypoallergenic; have an adequate nutritional value according to the infant's age; be easily available and inexpensive; and be palatable in order to obtain a good compliance. CM substitutes now available are soy protein formulas (SPF) and hydrolysate formulas (HF). Consequently pediatricians are now overwhelmed with a variety of information on new formulas called hypoallergenic and are faced with a difficult choice among them.

Key Words:

High-risk infants, Family history of allergy, CM substitutes, Unsupervised dietary manipulations, Nutritional adequacy.

Introduction

A recent paper on high-risk infants with family history of allergy exclusively breast-fed or fed partial whey hydrolysate, soy formulas (SPF) and conventional CM formulas¹, offers some pregnant considerations. The author states that DBPCFC (Double-blind,

placebo-controlled food challenges) were done mixing the foods to be tested in elemental formula. Unfortunately these formulas are so unpalatable, that most children observed by us refused or vomited the food so disguised. In addition, results of DBPCFC show that foods highly allergenic, such as egg, peanut, fish, and other unspecified foods were not positive between 1-6 months, and were highly positive only between 13-60 months¹. This contradicts several data showing that food allergy attains a very high prevalence between 6-12 months²⁻⁵.

In addition, this study confirms a data first shown by Høst al, that SPF allergy may be higher in babies and disappears at about 24 months⁴. In the Chandra study soy positivity with DBPCFC was 14% at 1-6 months, 12% at 7-12, and only 3% at 13-60 months.

This is also confirmed by the statistical analyses stemming from data shown by Chandra in Figure 3 and Table V, where there are no statistically significant differences between SPF and GoodStart in the period prevalence of eczema and asthma between ages 18 months and 60 months¹.

Chandra¹ agrees with the conclusions of a recent paper⁶: only a not scientific "consensus of opinion" speaks against the use of SPFs in the atopy prevention, however not the scientific data thoroughly discussed there. As we have demonstrated, only the studies employing SPFs in an atopy prevention program with positive results are supported by statistically significant differences⁶. Obviously SPFs are useful for infants with proven CM allergy⁶.

We do not agree with what Figure 4 suggests, since the CM formula to be provided for the first 6 months of life for all infants with parental history of allergy¹, after only two drops shall trigger an anaphylactic shock

in most of those babies, as demonstrated in a recent work⁷. On the contrary, SPFs have provoked a clinical case of anaphylaxis every 22,3 years⁶.

Feeding High Risk Infants With an Appropriate CM Substitute

SPFs have been used for feeding CMA infants since 1929. They contain purified soy proteins, the fat is a mixture of vegetable oils, and carbohydrates are represented by maltodextrines, starch, or saccharose. SPFs are well accepted by most infants, and their nutritional adequacy is comparable to that of CM formulas. Recent studies in infants fed exclusively SPFs failed to confirm immunologic abnormalities, or increased infection morbidity as formerly reported⁶. The use of SPFs for the prevention of the atopy marsh is rather controversial. Studies have shown that SPFs, or breast-feeding supplemented with SPFs for the first 6 months of life significantly reduced the prevalence of atopic dermatitis (AD)^{8,9}, but others did not confirmed this^{10,11}.

Studies regarding the possibility of AD prevention in high-risk babies have shown that the onset of AD is significantly reduced with the preventive measures previously reported¹². More recently in a multicenter study comprising 2,291 babies with the cooperation of many Italian Maternity Hospitals, the babies fed breast- and/or SPFs and whose parents strictly followed the environmental measures had at one year of age a lower AD prevalence in comparison with CM-fed babies ($p = 0.0001$). Summing up our studies using a SPF when breast-milk was not available, there was no increased prevalence of soy sensitization⁶. However in the last decade soy allergenicity has been amplified in the literature. Only 5% of 204 children with AD showed soy sensitivity, as demonstrated by DBPCFC¹³. Our studies confirmed that only 4% of 143 children with AD had positive DBPCFC to soy¹⁴. Although soy proteins can be sensitizing, they are less allergenic than CM proteins. SPFs are nutritionally adequate and well accepted by many infants. A variety of foods such as cakes, biscuits, ice cream, desserts and drinks can be made with SPFs thus offering CMA children a varied diet. It should be taken into consideration that SPFs are less expensive and have a more pleasant taste than other CM substitutes⁶.

The use of HFs is based on the premise that pre-digested protein, when fed as amino acids and peptides, provides nutrients in a not antigenic form. Thus, HFs have been defined as hypoallergenic. HFs are processed using two main techniques: heat denaturation and enzymatic hydrolysis to reduce the molecular weight (MW) of peptides. Heat treatment eliminates conformational antigenic determinants, while enzymatic hydrolysis affects sequential determinants. These different technical procedures are necessary to obtain an acceptable palatability. The reduction of the antigenicity (peptides with very low MW) is associated with a reduction also of the palatability. The allergenicity of these formulas is dependent on the degree of digestion, post-hydrolysis processing, elimination of the enzymes used for the hydrolysis and protein source. According to the protein source, there are several types of HFs. Moreover a bovine whey partly HF with lactose has been developed. These formulas are integrated with vegetable lipids, and Alfa-Rè, Alimentum and Pregestimil contain also MCT (medium chain triglycerides). All HFs, except Good Start and similar, are lactose free, contain small amounts of carnitine and are rather unpalatable (except for Good Start) and compliance is therefore poor. Albeit HFs are considered nutritionally adequate and infants usually gain weight until they refuse the formula because of its bad taste, it has been recently reported that the total essential amino acid (EAA) concentration and the ratio of E to total AA concentration were higher in term infants fed a whey HF (Good Start) in comparison with breast fed infants, in addition they showed higher threonine and lower proline and tyrosine values¹⁵. Caution should be taken when HFs are given for prolonged periods; no data is available on nutritional assessment of infants exclusively fed with HFs for many months¹⁵.

Extensively HFs are considered the most hypoallergenic, whereas partly HFs are considered less hypoallergenic and even hazardous in children with CMA^{16,17}. MW profiles of HFs are an index of the extent of hydrolysis. Good Start contains a greater percentage of peptides, more than 6,000 D. The analysis of the components of different HFs is very surprising, since casein is present in a larger amount in Good Start HA but it is not pre-

sent in two casein hydrolysates (Alimentum and Nutramigen)

We first reported anaphylactic reactions in 5 infants with IgE-mediated CMA fed a whey HF (Alfa-Rè). All these infants were successfully given a SPF (Isomil). All the infants had positive skin tests and RAST to CM proteins and to Alfa-Rè. This data shows that whey HFs can trigger severe anaphylactic reactions in children with IgE-mediated CMA¹⁸, as confirmed by a recent study which demonstrated residual casein epitopes in all the HFs tested, such as Alfa-Rè, Pregomin, Beba HA¹⁹. We have recently shown that HFs have provoked adverse reactions in 20 children and 180 additional pediatric cases²⁰.

The above data agrees with a study¹⁶ showing that antibodies raised against a CM formula recognized epitopes displayed by peptides of some HFs. In addition the same investigators showed that HF in experimental animals induce cell mediated immunity, and that cross-reactivity exists also between IgE antibodies to CM and peptides of HF in this limb of the immune response. It was confirmed that HFs contain protein fractions which resulted in a specific IgE binding after incubation with serum samples from patients allergic to CM¹⁷. Although the proteins of HFs have been processed by heat and enzymatic hydrolysis and therefore contain peptides of lower MW than the native protein source, the peptides still have allergenic potency and can be recognized by the cell-bound IgE of a child allergic to CM. As shown by an elegant study, 9/15 children sensitive to CM and with a positive histamine release from mixed leukocytes also had a positive histamine release to at least one of five tested HFs²¹. It was also shown that basophils of patients with IgE-mediated CMA incubated with HFs release histamine, thus strongly suggesting that HFs still have epitopes recognized by IgE bound to basophils. It has been shown that CMA children have IgE to CM proteins and to many HFs²². It has been reported²³ that children with IgE mediated CMA had positive skin test responses to both whey and casein hydrolysates, however the wheal diameter to the whey hydrolysate was significantly higher. A recent elegant study²³ showed that DBPCFC with 2 extensively casein HFs (Alimentum and Nutramigen) were negative in children with documented IgE-mediated CMA.

Soy is antigenic, can be perhaps allergenic, but never cross-reacts with IgE antibodies to CM. HFs are both antigenic and allergenic, moreover they do cross-react with IgE antibodies to CM. Therefore SPFs should be used in babies with IgE-mediated CMA whereas whey partly HFs should not^{6,20}.

Conclusion

The management of infants with CMA is a common problem encountered by pediatricians. Dietary treatment is one of the approaches that must be considered, provided that the nutritional adequacy is carefully controlled. However, unsupervised dietary manipulations and unorthodox approaches to allergy treatment are potentially hazardous for children with IgE-mediated CMA. Further studies are needed to evaluate the nutritional adequacy of HFs in babies exclusively fed such formulas for several months.

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