

Nutritive Casein Formula Elicits Pseudoallergic Skin Reactions by Prick Testing

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Key Words

Nutritive formula as histamine releaser · Hydrolyzed casein · Skin prick test · Wheal reactions

Extensive hydrolyzed casein formulas (EHCF) have been used in children with cow's milk allergy and intolerance (CMA/CMI) for more than 50 years. An extensive enzymatic hydrolysis of casein results in peptides ranging from 0.5 to about 20 kD. Although EHCF contains 'nonallergenic', peptides adverse reactions to formulas have been noted. These are IgE-mediated or intolerance reactions to residual epitopes, new epitopes, native milk proteins, or lactose due to inadequate hydrolysis or filtration, immunogenic casein peptides or contamination [1]. Interestingly, some peptides from hydrolyzed casein ranging from 0.5 to 1 kD acquire opioid properties and become histamine releasers [2, 3]. We speculated that EHCF, similar to histamine-releasing drugs (e.g. morphine), and foods (e.g. strawberries, tomatoes), contributes to some of the intolerance reactions. We reported that 1 in 8 samples of hydrolyzed casein contained in commonly prescribed EHCF, exerts as secretory effect on isolated peritoneal rat mast cells and human cutaneous mast cells, similar to synthetic casein exorphins [4]. Although the samples were obtained directly from the producer (POLFA, Kutno-Poland S.A.), the final formulas remained unnamed. Having assumed that Nutramigen, Pregestemil or Terapin (used in Poland) contain this hydrolyzate, we tested 26 children

(ages between 9 and 60 months) with a history of CMA/CMI and 10 healthy controls (ages between 24 and 43 months) using the skin prick test (SPT) technique. Specific IgE in serum for casein (f-78) and milk (f-2) was evaluated by a CAP system (Pharmacia). For SPT, commercial products (Allergopharma), 1% codeine and 2% (g/vol) suspensions of the suspect formulas and hydrolyzate in saline were used. SPT were performed on the volar side of the forearm with standard lancet (pricking through the drop). Wheals were corrected by negative controls and noted for further evaluation of skin reactivity. Only wheals larger than 3 mm were taken as positive SPT results. For statistical evaluation, the t tests for paired or two samples or assumed equal variances, and linear regression analysis were used. Specific IgE findings were positive (>class 1) in 50% children with a story of CMA/CMI only. Skin reactivity to tested products was similarly expressed in the controls. Skin reactions to cow's milk, Nutramigen, Pregestemil, Terapin and the hydrolysate, appeared in 42, 31, 19, 73 and 73% and were positive in 30, 15, 4, 73 and 73% of the children, respectively (n = 26) (table 1). Reactions to Terapin seem to be better expressed than those to cow's milk (p = 0.05). Linear regression was found between skin reactions to Terapin and the hydrolysate (r = 0.872; p < 0.05). Two children reacted to Terapin and the hydrolysate with wheals greater than by SPT with histamine and codeine. It seems possible that individual hypersensitivity towards histamine-releasing peptides plays a role in some intolerances of casein formulas.

Table 1. SPT with Nutramigen, Pregestemil, Terapin, and hydrolyzate

Tested substance	Overall wheals %	Mean wheal $\pm$ SD cm ²	Positive SPT %	Comparison ^a milk/formulas p	Linear regression ^b hydrolysate/Terapin r (p)
Histamine	100	2.5 $\pm$ 1.2	96		
Codeine	100	2.2 $\pm$ 1.4	92		
Cow's milk	42	0.5 $\pm$ 0.8	30		
Nutramigen	31	0.3 $\pm$ 0.8	15	n.s.	
Pregestemil	19	0.3 $\pm$ 0.6	4	p < 0.05	
Terapin	73	0.8 $\pm$ 1.2	73	p = 0.05	
Hydrolysate	73	0.6 $\pm$ 1.0	73	n.s.	r = 0.872 (p < 0.05)

Comparison of skin reactivity to tested substances and those to cow's milk. Linear regression analysis between reactions to tested hydrolyzate and nutritive casein formulas.

^at test: paired two samples for means; ^bregression statistic (Anova test).

References

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