

Key Clinical Research Summaries



Contents

- Allergy to extensively hydrolyzed cow milk proteins in infants: Identification and treatment with an amino acid-based formula.** 1
de Boissieu D, Matarazza P, Dupont C.
Journal of Pediatrics, 1997; 131: 744-747.
- Intolerance to protein hydrolysate infant formulas: An under recognised cause of gastrointestinal symptoms in infants.** 2
Vanderhoof JA, Murray ND, Kaufman SS, et al.
Journal of Pediatrics, 1997; 131: 741-744.
- The natural history of intolerance to soy and extensively hydrolyzed formula in infants with multiple food protein intolerance.** 3
Hill DJ, Heine RG, Cameron DFS, et al.
Journal of Pediatrics, 1999; 135: 118-121.
- Efficacy and safety of hydrolyzed cow milk and amino acid-derived formulas in infants with cow milk allergy.** 4
Isolauri E, Sutas Y, Makinen-Kiljunen S, et al.
Journal of Pediatrics, 1995; 127: 550-557.
- A consistent pattern of minor immunodeficiency and subtle enteropathy in children with multiple food allergy.** 5
Latcham F, Merino F, Lang A, et al.
Journal of Pediatrics, 2003; 143: 39-47.
- 

Allergy to extensively hydrolyzed cow milk proteins in infants: Identification and treatment with an amino acid-based formula.

de Boissieu D, Matarazza P, Dupont C.
Journal of Pediatrics, 1997; 131: 744-747.

Objective

Infants with suspected cow's milk allergy and persistent symptoms on extensively hydrolyzed protein formulas (eHF) were investigated using Neocate, a nutritionally complete, amino acid-based infant formula.

Method

The study included 16 infants presenting with one or more symptoms of persistent vomiting, diarrhoea, feed refusal and irritability while receiving extensively hydrolyzed casein or whey formulas. Growth failure was present in 9 infants, of which 6 infants had a body weight index <90%. SCORAD index was used to assess atopic dermatitis lesions (n=5). All infants had a history of adverse reactions to cow's milk proteins, Infants were started on Neocate. Following stabilisation on Neocate, infants underwent a double blind, placebo-controlled challenge with the eHF used previously. Intestinal permeability (ratio of oral lactitol/mannitol excreted, L/M ratio, %) was assessed in infants prior to commencement of Neocate and approximately 1.5 months later (range 1-3 months), before challenge with the eHF.

Results

In 13 infants, Neocate feeding resulted in the disappearance of non-cutaneous symptoms within 3 days and improved eczema (SCORAD : 16 +/- 12 vs 35 +/- 13, $p<0.05$). All 13 infants gained weight on Neocate and a statistically significant increase in body weight index (97.9 +/- 5.1% vs 90.2 +/- 7.2%, $p<0.001$) was observed. A positive challenge to eHF was reported in these 13 infants. Reintroduction of eHF resulted in immediate recurrence of symptoms (8 infants) or recurrence within 2 days (5 infants). 11 infants with positive reactions to eHF showed increased intestinal permeability which decreased on Neocate (L/M ratio: 3.8% +/- 1.6% vs 6.1% +/- 3.2%, $p<0.05$).

Conclusions

Allergy to eHF should be considered in infants allergic to cow's milk with persistent symptoms on an eHF. Neocate, an amino acid-based formula, proved an effective treatment in allergy to eHF with resulting resolution of symptoms and significant weight gain.

Intolerance to protein hydrolysate infant formulas: An underrecognized cause of gastrointestinal symptoms in infants.

Vanderhoof JA, Murray ND, Kaufman SS, et al.
Journal of Pediatrics, 1997; 131: 741-744.

Objective

To determine the effectiveness of an amino acid-based infant formula in infants with continued symptoms suggestive of formula protein intolerance whilst receiving casein hydrolysate formula (cHF).

Method

28 infants, 22 to 173 days of age were enrolled. Each had received cHF for an average of 40 days (range 10-173 days) and continued to have bloody stools, vomiting, diarrhoea, irritability, failure to gain weight, or a combination of these symptoms. Sigmoidoscopy with rectal biopsy was performed in all infants. The infants then received an amino acid-based infant formula (Neocate) for 2 weeks. Stool frequency, crying time and vomiting episodes were recorded and compared on days 1-2 and 13-14 to assess the effect Neocate had on these symptoms. After treatment, infants demonstrating resolution of symptoms underwent challenge with cHF.

Results

Within 14 days symptoms had resolved in all but 3 infants who had continued presence of occult blood in stools but all other symptoms had resolved. Of the 25 infants who were challenged, 8 tolerated the cHF and the remainder had recurrences of their symptoms. Crying time declined from 2hr/day to 1hr/day by days 13 and 14 ($p=0.003$), as did the number of vomiting episodes (from 0.35 episodes per day to 0.21, $p=0.028$). Stool frequency reduced from an average of 0.73/day to 0.5/day ($p=0.041$).

Conclusions

It was concluded that not all infants with apparent formula protein induced colitis respond to cHF and that these infants may have resolution of their symptoms when fed an amino acid-based infant formula.

The natural history of intolerance to soy and extensively hydrolyzed formula in infants with multiple food protein intolerance.

Hill DJ, Heine RG, Cameron DFS, et al.
Journal of Pediatrics, 1999; 135: 118-121.

Objective

This study followed up a cohort of 18 patients with multiple food intolerance through to the age of three years to monitor the long-term efficacy of Neocate and to assess the duration of their intolerance to eHF and soy.

Method

A total of 18 infants (11 boys, 7 girls) were followed up until their third birthday. All infants had been diagnosed with multiple food allergies including allergies to soy (n=15), cHF (n=18) and eHF (n=13). Following conversion to Neocate, low-allergenic foods including rice, pumpkin, potato and zucchini (courgette) were added sequentially at 2-4 week intervals. Tolerance to eHF, soy and cow's milk were assessed using double-blind, placebo-controlled challenge 2-12 months (mean 4 months) after commencement of Neocate.

Results

In all 18 children, symptoms of food allergy (irritability, vomiting, diarrhoea, growth failure and atopic dermatitis) remitted within 2 weeks of conversion to Neocate. 6 patients developed tolerance to cow's milk (n=1), soy (n=1), cHF (n=2) and eHF (n=2) during their first year. The remaining 12 children were re-challenged in their second and third years, and intolerance was found to persist in 5 of 8 patients challenged with cow's milk, 6 of 7 challenged with soy, and 2 of 6 challenged with eHF. Most patients tolerated cereal, meats, fruits and vegetables by the end of their second year and by 36 months, only 3 required Neocate for ongoing nutritional support. Four patients presented with significant failure to thrive, with a mean Z score for age-for-weight of -2.4. Within 6-12 weeks of commencing Neocate these patients had achieve catch-up-growth, and by 24 months of age their poor weight gain had reversed to a mean Z score of -0.4. This improvement was sustained at 36 months. Similarly, the mean Z score for height-for-age improved from -2.0 at 6 months to -0.4 at 36 months of age.

Conclusions

These children with multiple food protein intolerance and formula intolerance responded well to Neocate indicating that it offers a valuable treatment for children with multiple food allergies who are intolerant to soy and eHF.

Efficacy and safety of hydrolyzed cow milk and amino acid-derived formulas in infants with cow milk allergy.

Isolauri E, Sutas Y, Makinen-Kiljunen S, et al.
Journal of Pediatrics, 1995; 127: 550-557.

Objective

To determine the antigenicity, nutritional adequacy and growth promoting efficacy of protein hydrolysate or amino acid-derived formulas in infants with cow milk allergy.

Method

Several protein hydrolysate or amino acid-derived formulas were graded for B-lactoglobulin content and skin reactivity in 74 atopic children proved by a double blind placebo controlled challenge. A randomized prospective follow up study of 9 months included 22 infants with a mean age of 6 months, who were fed an extensively hydrolysed whey formula and 23 infants (mean age of 7 months) who were given Neocate.

Results

Both formulas were clinically and biochemically tolerated with a significant reduction of symptoms. The relative weight and length increased in both groups. There was a different trend between the groups in weight ($p=0.09$) and length ($p=0.006$). Growth was promoted in the group who received Neocate during the follow up; it was constant during the first months, followed by a gradual decline in rate in the group receiving the whey hydrolysate feed.

Conclusions

Both extensively hydrolyzed cow's milk and amino acid derived formulas proved to be nutritionally efficient and safe for infants with cow milk allergy. Adequate growth was achieved in both groups of allergenic infants but growth was only promoted in the Neocate fed infants. For patients with growth retardation or multiple food allergies requiring a highly restricted dietary regimen, the use of amino acid-derived formula appears to be preferable.

A consistent pattern of minor immunodeficiency and subtle enteropathy in children with multiple food allergy.

Latcham F, Merino F, Lang A, et al.
Journal of Pediatrics, 2003; 143: 39-47.

Objective

To identify a consistent pattern of clinical features for non-immunoglobulin (Ig)E-mediated allergies in children, even in the absence of immediate reactions.

Method

A retrospective analysis of clinical, histologic and immunologic characteristics from a cohort of 121 affected infants and children with multiple food allergy (MFA) assessed during 1997 through 1999 at a tertiary referral centre. Mean age was 17.3 months (range 1-93 months) and inclusion criteria included a secure diagnosis of MFA by currently accepted criteria, i.e. reproducible adverse responses to 2 or more dietary antigens, with clinical response to exclusion diet and recurrence of symptoms on challenge, and the availability of blood test results for circulating immunoglobulin concentrations and/or lymphocyte subsets.

Results

The children were divided into 2 groups: group 1 (n=44) included those showing hypersensitive reactions within 1 hour, of whom 41 also showed additional delayed non-IgE-mediated reactions identical to those in group 2, which included children with delayed reactions only (n=77). Children with immediate responses had higher mean IgE and a higher chance of positive food-specific IgE and skin prick tests. Other findings were common to both groups including increased IgG1, decreased IgG2 and IgG4, and low normal IgA. Lymphocyte subsets were skewed with increased CD4 and CD19, and decreased CD8 and natural killer cell percentages. Supportive clinical findings included gastrointestinal dysmotility with gastro-oesophageal reflux, constipation, or both, together with endoscopic evidence of oesophagitis or subtle enteropathy evident in both groups. Family history is an important risk factor and this study demonstrated a maternal dominance of autoimmunity. Of the 55 exclusively breastfed infants, 44 sensitised before weaning with no difference between groups.

Conclusions

Although excess IgE production is associated with allergy, other mechanisms are important in determining sensitisation. Disturbed gut motility is particularly common, as is a maternal history of autoimmunity. It was concluded that there appears to be a recognisable pattern of immune deviation and subtle enteropathy in children with MFA, irrespective of the speed of reactions.

Norge:
Nutricia Norge AS
Holbergsgate 21
N-0166 Oslo
Tlf: 23 00 21 00
www.nutricia.no

Sverige:
Nutricia Nordica AB
Döbelnsgatan 21,
11183- Stockholm
Tel: 08-241530
www.nutricia.se

Danmark:
Nutricia A/S
Rørmosevej 2A
3450 Allerød
Tlf: 70 21 70 07
www.nutricia.dk