



Case Study: Baby O

1 year old girl with persistent eczema, gastro-oesophageal reflux disease and gastrointestinal symptoms despite trying a couple of amino acid formulas.

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Background

Baby O was born at term via vaginal delivery and formula fed from a few days of age due to apparent difficulties with milk supply. At 2 weeks of age, an allergy focused clinical history^{1,2} was completed by the health visiting team as mum was concerned that Baby O may have Cow's Milk Allergy (CMA), as her 10 year old sister still suffers from CMA and fructose intolerance and is on the autistic spectrum. Her half-brother has just been diagnosed with coeliac disease at the age of 6 years. Dad suffers from eczema and mum had CMA as a baby.

Baby O would scream in discomfort for much of the day, feeding could take up to 1.5 hours, she was passing offensive, mucousy stools x 6-8 daily, was suffering from eczema and using aqueous cream, constantly sneezing and congested, hiccups and had a chesty cough. Multiple symptoms such as these are well recognised in children with food protein induced gastrointestinal allergies³. There were no concerns over weight, being born on the 25th centile which increased gradually to the 50th centile by 1 month of age. As a result, the health visitor coordinated prescription for a 4 week cow's milk exclusion trial using an extensively hydrolysed formula (EHF) in line with the Nottinghamshire Area Prescribing Committee Cow's Milk Allergy Guidelines² which align with national recommendations^{4,5}.

Four days into the trial on an EHF, Baby O's symptoms deteriorated, developing a rash on her face, mucousy frequent stools, nasal congestion, poor sleeping and very distressed. Given the strong family history of CMA and development of new symptoms, the health visitor decided to change her to Neocate LCP, an amino acid formula, at 3 weeks of age^{2,6}. A week later her bowels were more settled but she was showing signs of gastro-oesophageal reflux and was started on Gaviscon Infant, but continued to cry constantly despite using a thickener and following advice on positioning in line with NICE and NASPGHAN/ ESPGHAN gastro-oesophageal reflux guidelines^{7,8}.

Management

Baby O changed to Carobel but developed loose stools and a rash on her face after feeds almost as soon as she started it. At 5 weeks of age, she was referred to our community paediatric dietetic department, saw a hospital paediatrician at 7 weeks of age who prescribed the antacid Ranitidine^{7,8} and I met her for the first time at 2 months of age.

She was taking 4 x 6-7 fl oz bottles Neocate LCP plus

1 double sachet Gaviscon Infant [total of 8 doses (max recommended is 6)]. The Gaviscon was making her prone to constipation and they were giving more water to achieve a daily bowel motion. Although I am not aware of any publications to support introduction of solids as a feed thickener from 17 weeks of age in infants with gastro-oesophageal reflux disease (GORD), given the difficulties associated with available feed thickeners it was recommended, starting with root vegetables. It was advised not to introduce soya milk substitutes until around 8-10 months of age due to the risk of her reacting to soya too (up to 60% in non-IgE mediated CMA⁹). High energy oat milk was recommended as the milk substitute of choice for cooking. First line advice on eczema management in accordance with NICE¹⁰ and an eczema written action plan was provided¹¹. Mum was also advised to liaise with the GP regarding alternative antacid therapy.

Within 3 days of starting Omeprazole (proton pump inhibitor), Baby O's symptoms improved and mum stopped the Gaviscon Infant which resulted in looser stools, but they were mucousy and she was still suffering from problematic eczema, unresponsive to hydrocortisone. As a result, it was recommended to change to an alternative amino acid formula (SMA Alfamino) to see if tolerated any better, alongside ongoing Omeprazole. As soon as this occurred, mum reported improvement "feeds are now 100% more comfortable, with no arching, screaming or explosive burps. She is taking less feeds, but happier and fulfilled after drinking and napping in day as well. Eczema is clearing up and under control but, she has mucus in her stools and a red, sore bottom which she hasn't had before". Mum was advised to wait and see if symptoms settled down.

One week after changing amino acid formula she attended A&E with projectile, mucus vomiting, hiccups, wind, gagging, back arching and against mum's wishes the hospital advised to go back on Neocate LCP. Mum emailed to say "She is now back to screaming and having wet burps up to 4 hours after her bottle. She is projectile vomiting and becoming more sleepy and lethargic. Her eczema symptoms are coming back. I'm finding it hard to leave the house and it is making me increasingly emotional and mentally down which is not like me at all". Mum took her back to A&E who proved that she could keep water down without vomiting, so was discharged.

At 3 months of age, we recommended trialling her third amino acid formula, Neocate Syneo, and 3 weeks later mum emailed to say: "The first 3 days were horrendous squealing, not sleeping and copious amount of mucus in her stools. At first it was watery, by day 3 it was sloppy. It's almost as if her body was flushing itself out. By day 4 Baby O started settling down and day 5 stools are normal with no mucus, her eczema has also completely gone and I am just using CetraBen when washing her".

However, her reflux symptoms were becoming more problematic, so mum restarted Gaviscon, 1 sachet per bottle and states "It is stopping the silent reflux by 70% and seems to be filling her a little. The Neocate Syneo has settled her gut no end and she is currently having the best stools to date. She does however have a lot of bottom wind. Hopefully the Gaviscon will see her through for the next 2 weeks before we start introducing pureed root vegetables".

At 17 weeks of age mum updated me "I started to wean Baby O with pureed carrot 1tsp 3 times a day which has solved her hunger and is completely settled. Her bowels are normal, sleeping for naps in the day and taking 6 fl oz x 5 bottles Neocate Syneo plus 1 sachet of Gaviscon per bottle. She's never been so well and happy, such a pleasant baby now. I'm going to try her with broccoli next."

1 Year Review

Baby O has bouts of pain, food refusal, hiccups and coughs every 4-5 weeks for no obvious reason, although mum notes that her reflux is worse when teething. She has been weaning her off the Omeprazole and will hopefully be without it in the next few weeks. Mum started offering bread containing soya but she went off her food, screaming, offensive, mucousy stools which took her 2 weeks to recover from, so she will now be strictly avoiding soya for the time being. She is growing well, height has increased to the 98th centile, weight towards 91st centile, in keeping with observations from Meyer and colleagues that good nutrition on an exclusion diet can improve growth¹¹. Generally she eats really well, loves her food, self feeds and eats everything offered. Currently taking more formula than necessary and to aim for 600ml daily and to use oat milk in cooking/ on cereal. Mum will consider very careful baked cow's milk reintroduction when well and settled.

Discussion

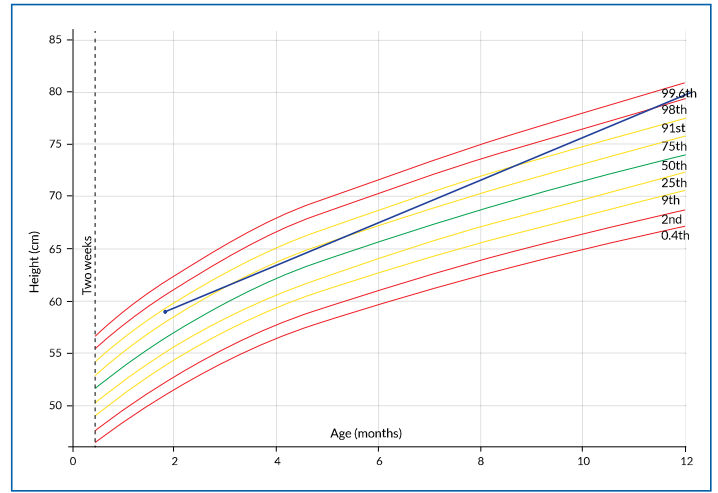
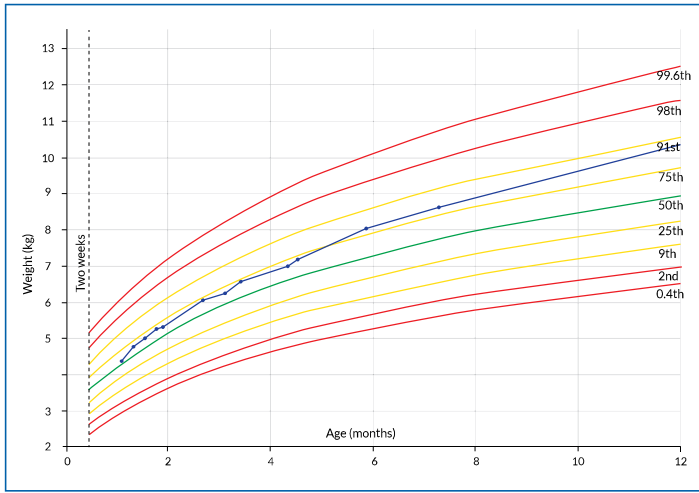
Until recently, there have been no probiotic formulas available for children with severe CMA who are unable to tolerate an EHF. These children tend to suffer from multiple system symptoms and often co-exist with GORD, making dietetic management very difficult.

There are concerns about the impact of antacids in infants, with an observational study suggesting that infants under 6 months using a proton pump inhibitor (PPI) have increased risk of fractures, possibly through effects on calcium absorption¹³. A retrospective, large cohort study found associations between the use of antacids in infants under 6 months of age and later development of allergic conditions¹⁴, which could be associated with the fact that PPI's have been shown to alter gut microbiota¹⁵. It has also been shown that partially hydrolysed formulas and the probiotic *Lactobacillus reuteri* decreased the frequency of regurgitation and increased gastric emptying¹⁶.

Evaluation of medication use in infants consuming a synbiotic containing amino acid formula (test) compared with the same formula without synbiotics (control) showed that a significantly lower number of subjects in the test group required 'drugs for functional gastrointestinal disorders' (test 4%, control 18%; $p=0.029$)¹⁷. Although there has been no research yet conducted on synbiotic containing amino acid formula for primary outcomes related to allergic/ atopic status, development of tolerance and symptom resolution, additional exploratory data on stool consistency and medications from the recently published ASSIGN trial using Neocate Syneo (amino acid formula with synbiotics) suggest a reduced incidence of ear infections; a symptom which tends to be found more frequently in infants with GORD, and lower usage of dermatological preparations¹⁸.

Neocate Syneo was the only amino acid formula tolerated by Baby O after a 5 day settling in period. The synbiotics tended to make her stools looser which is helpful if suffering from GORD, as constipation is likely to increase intra-abdominal pressure and therefore exacerbate reflux. Harvey and colleagues support this observation, where children taking an amino acid formula with synbiotics had softer stools more comparable to breast fed infants and less constipation compared with those on the same formula without synbiotics. Baby O's eczema has also been well controlled on Neocate Syneo compared with the same formula without synbiotics, suggesting that an amino acid formula containing synbiotics may better support some infants with multisystem allergic conditions and concomitant GORD. Her appetite whilst variable has not affected her enjoyment of a wide range of solids and textures, she is fully integrated into family meals and her growth has increased across the centiles for both weight and height.

Growth Charts for Baby O



Conclusion:

- The amino acid formula with synbiotics (Neocate Syneo) was better tolerated than other amino acid formulas in a child with multisystem symptoms of non-IgE mediated food allergies including eczema and primary gastro-oesophageal reflux disease requiring proton pump inhibition therapy.
- Neocate Syneo supported catch up growth in a child with complex non-IgE mediated cow's milk and soya allergy.

Product Usage

- ORAL NUTRITIONAL SUPPLEMENT
- TUBE FEED
- SOLE SOURCE OF NUTRITION
- SUPPLEMENT TO AN ELIMINATION DIET

CALORIE DENSITY: 0.68 KCAL/ML
(STANDARD CONCENTRATION)

Patient Profile

- ANAPHYLAXIS
- ATOPIC DERMATITIS (AD)
- FALTERING GROWTH
- MULTIPLE FOOD ALLERGIES (MFA)
- GI SYMPTOMS
- SYMPTOMATIC ON BREAST MILK
- SYMPTOMATIC ON AN EHF

References

1. EAAAI, 2015. Allergy focussed diet history Paediatric version https://static-content.springer.com/esm/art%3A10.1186%2F13601-015-0050-2/MediaObjects/13601_2015_50_MOESM1_ESM.pdf
2. Nottinghamshire Area Prescribing Committee. Guidance on the diagnosis and management of cow's milk allergy in infants and children. https://www.nottsapc.nhs.uk/media/1065/apc-full_nottinghamshire_guidelines-update-final-1016.pdf
3. Meyer R, Fleming C, Dominguez-Ortega G et al. Manifestations of food protein induced gastrointestinal allergies presenting to a single tertiary paediatric gastroenterology unit. WAO Journal 2013; 6:13
4. Venter C, Brown T, Meyer R et al. Better recognition, diagnosis and management of non-IgE mediated cow's milk allergy in infancy: iMAP – an international interpretation of the MAP (milk allergy in Primary care) guideline. Clin Transl Allergy 2017; 7:26
5. Luyt D, Ball H, Makwana N et al. BSACI guideline for the diagnosis and management of cow's milk allergy. Clin Exp Allergy 2014; 44: 642-672
6. Meyer R, Groetch M, Venter C. When should infants with cow's milk protein allergy use an amino acid formula? A Practical Guide: J Allergy Clin Immunol Pract 2018;6:383-99
7. NICE, 2015. Gastro-oesophageal reflux disease: recognition, diagnosis and management in children and young people. www.nice.org.uk/guidance/ng1
8. Rosen R, Vandenplas Y, Singendonk M et al. Pediatric Gastroesophageal Reflux Clinical Practice Guidelines: Joint Recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition. JPGN 2018;66: 516-554
9. Bhatia J & Greer F. Use of Soy Protein-Based Formulas in Infant Feeding. Pediatr 2008;121:1062
10. NICE, 2007. Atopic eczema in under 12's – diagnosis and management. Clinical guideline [CG57] <https://www.nice.org.uk/guidance/cg57>
11. University of Bristol Centre for Academic Primary Care. Eczema written action plan <http://www.bristol.ac.uk/primaryhealthcare/researchthemes/apache/ewap/>
12. Meyer R, De Koker C, Dzubiak R et al. The impact of the elimination diet on growth and nutrient intake in children with food protein induced gastrointestinal allergies. Clin Transl Allergy 2016; 6: 25
13. Lyon J. Study questions use of acid suppressors to curb mild infant reflux. JAMA 2017; 318 (15): 1427-8
14. Mitre E, Susi A, Kropp L et al. Association between use of acid-suppressive medications and antibiotics during infancy and allergic diseases in early childhood. JAMA Pediatr 2018. doi:10.1001/jamapediatrics.2018.0315. Published online April 2, 2018.
15. Jackson MA, Goodrich JK, Maxan M-E et al. Proton pump inhibitors alter the composition of the gut microbiota. Gut 2016; 65: 749-756.
16. Indrio F, Riezzo G, Giordano P et al. Effect of a partially hydrolysed whey infant formula supplemented with starch and Lactobacillus reuteri DSM 17938 on regurgitation and gastric motility. Nutrients 2017; 9: 1181
17. Burks AW, Harthoorn LF, Van Ampting MTJ et al. Synbiotics supplemented amino acid based formula supports adequate growth in cow's milk allergic infants. Pediatr Allergy Immunol 2015; 26: 316-322.
18. Fox AT, Wopereis H, Van Ampting MTJ et al. A specific synbiotic-containing amino acid-based formula in dietary management of cow's milk allergy: a randomized controlled trial. Clin Transl Allergy 2019; 9:5
19. Harvey BM, Langford JE, Harthoorn LF et al. Effects on growth and tolerance and hypoallergenicity of an amino acid based formula with synbiotics. Pediatric Research 2014; 75 (2): 343-351