COWS’ MILK PROTEIN ALLERGY IN INFANTS

Allergy has been called ‘the number one environmental epidemic disease facing children of the developed world’.1,2 Cows’ milk protein allergy (CMPA) is the most common food allergy found in children; with a worldwide prevalence of 1.9-4.9%3 and a UK prevalence of 2-3%.4,5 As milk is a key part of an infant’s diet, the nutritional management of this condition is crucial.

CMPA is a reproducible adverse immune response to one or more of the proteins found in cows’ milk, which usually presents before the age of one and is often outgrown by the age of five.6 The risk of CMPA increases when an infant has a history, or family history, of atopy; for example, eczema or asthma in the infant, or a family history of eczema, asthma, hay fever or food allergies.5

There is evidence that breastfed infants have a lower prevalence of CMPA, with about 7% of formula or mixed-fed infants developing CMPA compared to about 0.5% of exclusively breastfed infants. Furthermore, breastfed infants are reported to have less severe reactions if they do develop CMPA.3,6 The primary factor involved in the development of food allergy in infancy is genetic, with a parental atopic history (asthma, eczema and hay fever) significantly increasing the risk.8 Research has also identified contributing environmental factors, which include smoking during pregnancy, the infant’s gut microbiome which may be affected by route of birth (C-section versus vaginal birth), early antibiotic use and dietary diversity.9,20,21

CMPA is classified as either immunoglobulin E- (IgE) or non-IgE-mediated, depending on the type of immune response which occurs. IgE-mediated reactions occur when IgE antibodies form in response to cows’ milk protein, which causes the release of histamine from basophils and mast cells; whereas it is thought that non-IgE-mediated CMPA is caused by T-cells.5

IgE-mediated reactions have a quick onset, usually presenting within minutes to two hours and the symptoms can be severe, such as anaphylaxis, hives and facial swelling.5,9 Non-IgE-mediated reactions are more common, often have a more delayed onset (such as two hours to three days) and usually present with less acute symptoms, such as gastrointestinal and skin symptoms. See Table 1 (p28) for a full comparison of symptoms.5,9 Non-IgE-mediated CMPA tends to resolve by the age of three, whereas IgE-mediated CMPA more commonly resolves by the age of five.10

DIAGNOSIS

An allergy focused clinical history and physical examination based on the NICE guidelines for diagnosing food allergy in the under 19s is a crucial part of establishing whether CMPA is present, this usually includes gathering information on the following:11,17
• the suspected allergen (e.g. cows’ milk);
• the history of presenting symptoms (see Table 1) including: age of onset, speed of onset, duration of symptoms, severity of reactions, frequency of reactions, how many organs produced a reaction, locations the reaction has occurred, reproducibility of symptoms, how much of the food causes a reaction;
• medication and response to previous treatments;
• personal history of atopy (eczema, hay fever, dust allergies, asthma);
• family history of atopy;
• dietary intake, including cultural factors which affect food choice;
• history of infant feeding and weaning if applicable;
• history of response to the elimination and reintroduction of foods;
• growth and nutritional status.

As well as this allergy-focused history, there are validated tests which can be used to test a suspected IgE-mediated CMPA, such as: skin prick tests to check for IgE antibodies in the skin and specific IgE serum assays to test for circulating IgE antibodies. Oral food challenges are the gold standard to confirm diagnosis, especially if there is any uncertainty about this. For IgE-mediated reactions, these take place under medical supervision and can be open or blinded.

Non-IgE-mediated CMPA can be more difficult to diagnose as there are no validated tests to use, therefore diagnosis is based on a combination of an allergy-focused history and a trial elimination diet and ideally a subsequent reintroduction phase to monitor whether symptoms return.

It is important to note that there are types of complementary and alternative medicines which offer testing for CMPA, such as kinesiology and hair testing, but as these are not medically approved, they have no place in diagnosis of CMPA.

CMPA can be mistakenly diagnosed as lactose intolerance due to an overlap of symptoms (diarrhoea, abdominal pains, cramps, bloating, flatulence and nausea); however, lactose intolerance is a deficiency of the enzyme lactase rather than an allergy to the protein in cows’ milk, therefore a thorough allergy focused history can avoid misdiagnosis. Some patients may have secondary lactose intolerance as a result of damage to the gut lining when CMPA is untreated; however, this is usually a transient condition as long as a strict cows’ milk protein-(CMP) free diet is adhered to.
At the time of writing this article, the updated version of the Milk Allergy in Primary Care (MAP) guideline had not been released; this is called the international Milk Allergy in Primary Care (iMAP) guideline (due to be published on 16th August 2017), as it has been designed to suit an international audience. An updated iMAP six-step milk ladder is also due to be released.

**ELIMINATING COWS’ MILK PROTEIN**

CMP should be completely eliminated from the diet for two to six weeks to see whether the presenting symptoms improve. The NICE guidelines on food allergies in under 19-year-olds highlight that dietetic input is important in order to support with ‘nutritional adequacies, timings of elimination and reintroduction, and follow-up’.

Breastfeeding mothers are encouraged to continue to breastfeed, but to exclude cows’ milk from their diet, they also need to be assessed as to whether a daily calcium and vitamin D supplement is indicated, bearing in mind that a breastfeeding mother requires 1,250mg of calcium and 10mcg of vitamin D per day. Formula-fed infants need to switch to a hypoallergenic formula (see Table 2).

It is important to educate breastfeeding mothers, parents and carers of infants of weaning age and older children about interpreting food labels, which foods and ingredients contain cows’ milk protein (see Table 3). It is important to offer alternative food and drinks to ensure a balanced diet, especially in terms of calcium intake, and the duration,
safety and limitations of an elimination diet. It is also crucial to highlight that shop-bought CMP-free milks should be fortified with calcium, vitamin D and B vitamins. Unsweetened CMP-free milks are useful for weaning; however, if there is a concern with faltering growth, then a version with a higher calorie content may be a better choice. Higher calorie dairy-free milks also have an overall nutritional profile which is more similar to full fat cows’ milk and so may be a more suitable choice as a main milk drink from one to two years of age if CMP exclusion is still indicated.

Additional high energy high protein dairy-free options in the treatment of faltering growth include: oils, nut butters and dairy free spreads, creams, cheeses, ice creams and puddings. Further nutritional considerations often include general weaning support, minimising reflux, advice on avoiding other allergens where multiple food intolerances occur and aiming to avoid unnecessarily restrictive eating. Information and fact sheets on alternative dairy options can be obtained from the British Dietetic Association (BDA) website: www.bda.uk.com/

As CMPA resolves in the majority of cases, it is important that regular reviews need to take place with a healthcare professional to ensure that the child is developing tolerance to CMPA.4,9

For those with an IgE-mediated CMPA and Food Protein Enterocolitis Syndrome, a ward-based food challenge is needed to test whether tolerance to CMP has developed.4,9 This involves close medical supervision while introducing incremental dosages of cows’ milk.4 However, for mild to moderate non-IgE-mediated CMPA, advice can be given on the gradual reintroduction of cows’ milk using a milk ladder approach; this involves introducing small amounts of products containing well-cooked milk to begin with, as heat treatment alters the protein structure of CMP and reduces allergenicity, and eventually introducing fresh milk if tolerated.4,9 It is important that parents are advised to continue to include tolerated milk products in their child’s diet and when a step hasn’t been tolerated, to revert to the previous step on the ladder and continue including all foods up to this level, then periodically trying the next step to see if tolerance has been acquired.4,9 It is best to try reintroductions early in the day to avoid a reaction going unnoticed overnight and the amount of time needed on each step of the milk ladder varies; the MAP milk ladder highlights that this may be one day or one week depending on the individual.4,9

A milk ladder approach can also be used when a breastfeeding mother is reintroducing CMP into her diet to test for tolerance in her child. From clinical practice, it may be easier to start reintroductions via one route initially rather than introducing CMP to the mother’s diet and the infant’s diet at the same time.

**CONCLUSION**

As CMPA is a nutritionally complex condition, dietitians are central to the management of this, with our involvement spanning from diagnosis through to tolerance development in most cases. Therefore, it is important that we are aware of the full scope of CMPA, so that we can provide the best possible support for the families that we work with.

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**Table 3: Food items and ingredients that contain cows’ milk protein**

| Butter, butter fat, butter milk, butter oil, casein (curds), caseinates, hydrolysed casein, calcium caseinate, sodium caseinate, cheese, cheese powder, cottage cheese, cows’ milk (fresh, condensed, dried, evaporated, powdered, ordinary infant formulas, UHT, low fat), cream, artificial cream, sour cream, ghee, ice cream, lactalbumin, lactoglobulin, malted milk, some margarines, milk protein, milk powder, skimmed milk powder, milk solids, non-fat dairy solids, non-fat milk solids, milk sugar, whey, hydrolysed whey, whey powder, whey syrup sweetener, yoghurt, fromage frais, lactose |