Cow's milk protein allergy in children

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By Dr Rukhsana Hussain

CMPA

- **Cows' milk protein allergy** is an immune-mediated allergic response to proteins in milk
  - Milk contains casein and whey fractions, each of which have five protein components.
  - A person can be sensitized to one or more components within either group.

CMPA

- One of most common childhood food allergy worldwide.
- Affects 7% of formula or mixed fed babies.
- Highest prevalence in first year of life.
- Can affect exclusively breast fed babies but incidence much lower than formula fed and mixed formula and breast fed babies.

Possible risk factors

- Atopic co-morbidities – asthma/eczema for example
- Family history of atopy – an allergic predisposition is inherited not specific food allergies
- Some experts suggest that babies that are exclusively breast fed for 4-6 months are less likely to develop CMPA than those who are formula fed

Types of CMPA

- IgE mediated reactions – acute onset, up to 2 hours after ingestion milk, usually within 20-30 mins. Caused by release histamine and other mediators from mast cells and basophils.

- Non IgE mediated reactions – delayed and non acute. Manifest up to 48 hours or even 1 week after ingestion of cow's milk protein. Thought to be caused by T cells.

- Mixed IgE and non IgE mediated reactions

Prognosis

- Studies suggest that 53-57% with CMPA with IgE mediated allergy will be milk tolerant by age 5 years.

- Having asthma, allergic rhinitis, more severe reactions, larger reaction at skin prick test at diagnosis are poor prognostic factors suggesting a higher likelihood of the allergy persisting.

- Studies show that children with Non IgE mediated CMPA are most likely to be tolerant by 3 years of age.

Complications

- Poor nutritional intake or malabsorption leading to:

  Chronic iron deficiency anaemia

  Failure to thrive

- Anaphylactic shock

- Heiner's syndrome – a rare milk-induced pulmonary disease

Symptoms IgE mediated CMPA

- **Skin reactions**

  Pruritus
  Erythema
  Acute urticaria – localised or generalised
  Acute angioedema

- **GI symptoms**

  Oral pruritus
  Nausea
  Colicky abdominal pain
  Vomiting
  Diarrhoea

- **Respiratory symptoms**

  Lower respiratory tract symptoms (cough, chest tightness, wheeze, short of breath)

  Upper respiratory tract symptoms (nasal itching, rhinorrhoea or congestion (with or without conjunctivitis)

- **Other symptoms**

  Symptoms and signs of anaphylaxis or other systemic allergic reactions.

Symptoms Non IgE mediated CMPA

- **Skin reactions**

  Pruritus
  Erythema
  Atopic eczema

- **GI symptoms**

  GORD
  Loose or frequent stools
  Blood or mucus in stools
  Abdominal pain
  Infantile colic
  Food refusal or aversion

- **GI symptoms**

  Constipation

  Perianal redness

  Pallor and tiredness

  Failure to thrive with at least one or more GI symptoms listed

- **Respiratory symptoms**

  Lower respiratory tract symptoms – cough, wheeze, chest tightness or SOB.

Management suspected IgE mediated CMPA

- Refer secondary care/specialist services for skin prick test and/or specific IgE antibody blood test
- Inform parent/carer regarding what IgE mediated CMPA is and potential risk of severe allergic reaction

CMPA support website

Management of suspected non IgE mediated CMPA

- Consider referral to secondary care if:

  Failure to thrive with one or more GI symptoms

  One or more acute systemic reactions

  One or more severe delayed reactions

  Significant atopic eczema where multiple or cross-reactive food allergies are suspected by the parent or carer

  Persisting parental suspicion of allergy despite lack of supporting history

  Clinical suspicion of multiple food allergies

- If referral not indicated then :

  advise trial elimination of cow's milk from diet for 2-6 weeks followed by reintroduction to prove it is the cause of symptoms

  In **exclusively breast fed babies** advise mum to eliminate cow's milk protein from her diet and suggest 1000mg dietary calcium and vitamin d 400IU supplement daily.

  British Dietetic Association Milk allergy fact sheet

- **Mixed or formula fed babies**

  advise parents or carers to replace cow's milk formula with hypoallergenic infant formulas

- **In weaned infants or older children**

  advise parents or carers to eliminate cow's milk protein from the child's diet

  If symptoms do not improve despite elimination – refer

  If symptoms improve – reintroduce cow's milk and confirm allergy

Hypoallergenic infant formulas

- **Extensively hydrolysed formulas (eHFs)**

  whey or casein based – based on cow's milk but extensively broken down so less well recognised by immune system

  tolerated by 90 % of children and infants with CMPA

- **Amino acid formulas (AAF)**

  suitable for children who cannot tolerate eHFs or for children with severe symptoms or those who developed symptoms whilst exclusively breastfed

- **Soy protein-based formulas**

  not suitable first line or for children under 6 months. Absorption of minerals and trace elements may be lower due to phytate content and also oestrogenic content make them unsuitable.

- **Other milk substitutes**

  Rice milk – not advised before age 4.5 yrs

  Ready made soya, pea, oat or coconut or other milk substitutes may be used after 2 years of age

  Other mammalian milk proteins including unmodified cow's milk, sheep, buffalo, horses or goat milk **are not recommended** – because not adequately nutritious to provide sole source of food for infants **and** there is a risk of possible allergenic cross-reactivity with milk or formulas based on other mammalian milk proteins.

Extensive Hydrolysed formulas

Examples of prescribable eHfs are:

- Alimentum – suitable from birth
- Aptamil Pepti 1 – suitable from birth
- Aptamil Pepti 2 – suitable from 6 months
- Cow and Gate Pepti Junior – suitable from birth
- Nutramigen Lipil 1 – suitable from birth
- Nutramigen Lipil 2 – suitable from 6 months

Amino acid formulas

Examples of prescribable AAFs are:

- Alfamino – suitable from birth
- Neocate LCP – suitable from birth
- Neocate Active – suitable from 1 yr age
- Neocate Advance – suitable from 1 yr age for children who cannot eat other foods
- Nutramigen Puramino – suitable from birth

Note: EHF and AAF have an unpleasant taste and smell- serving in a closed cup or bottle or with a straw (depending on age) may improve tolerance. The milk has a greenish tinge when made up ready for use. Infant stools may be strong smelling and green in colour which is normal with hydrolysed feeds.

Confirmed non-IgE mediated CMPA management in primary care

- Eliminate cow's milk protein from diet for at least 6 months or until child is 9-12 months old

- Nutritional counselling/regular monitoring growth via dietitian

- Re-evaluate child's tolerance to cow's milk protein every 6-12 months – can be done at home if no indication for secondary care referral e.g. One or more systemic reactions

  re-introduce milk protein into diet and monitor for return of symptoms – use less allergenic baked products initially – if symptoms return, continue elimination diet and reassess 6-12 months

- Once tolerance established increase exposure using milk ladder

- Milk Ladder

References

- NICE CKS June 2015
- BMJ clinical review 2013
- CMPA support
- Prescribing specialist infant formula in primary care guidelines- updated July 2016 (useful tips from the South West Yorkshire Area Prescribing Committee when prescribing infant formulae for various conditions inc CMPA, GORD, lactose intolerance and faltering growth)