COW’S MILK PROTEIN ALLERGY IN CHILDREN

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By Dr Rukhsana Hussain
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)