Cow’s Milk Protein Allergy in Children (Cow’s Milk Protein Intolerance, CMPA) — Types and Treatment

Milk protein allergy or intolerance is characterized by an allergic reaction to the protein found in cow’s milk. It manifests as a variety of symptoms and signs which develop during infancy and regress by the fifth year. However, they are responsible for significant anxiety and parental distress leading to children being put on milk-free diets with subsequent nutritional deficiencies; therefore, it is important to diagnose this condition and counsel parents accordingly.

Epidemiology of Milk Protein Allergy in Children

Cow’s milk protein allergy (CMPA) or cow’s milk intolerance occurs in up to 4% of children. The highest prevalence rates are in infancy, with a resolution of symptoms in 50% of children by the age of one year, and in 90% by the age of five years.

Due to parental anxiety, more children are reported with CMPA despite their not suffering from it.
Principal Allergens in Cow’s Milk

The diagnosis of CMPA can be confusing to the doctor and the parents of the child. It is important to differentiate between lactose intolerance and CMPA. The later is characterized by a hypersensitivity reaction that is triggered by specific immunologic mechanisms and is what we are discussing here.

There are two main proteins in cow’s milk that can trigger an allergic reaction. They include casein and whey proteins. $\alpha_s1$, $\alpha_s2$, $\alpha_s3$, and $\kappa$-casein belong to the casein fraction of proteins and all of them can trigger an allergic reaction. $\alpha$-lactalbumin and $\beta$-lactoglobulin belong to the whey proteins’ family and they can cause allergies as well.

Types of CMPA

Two types of CMPA have been reported:

1. **IgE-mediated** (immediate allergic reaction): Immunoglobulin E associated CMPA is characterized by rhinorrhea, sneezing, hives, skin rash and wheezing within two hours of the child drinking cow’s milk
2. **Non-IgE mediated** (delayed allergic reaction) is characterized by allergic symptoms occurring approximately two to seven days after the child drinks cow’s milk. CM-induced enterocolitis syndrome, CM-induced enteropathy of the small bowel, and CM-induced proctitis and proctocolitis are non-IgE mediated.

Both these reactions can also occur in atopic eczema and Eosinophilic gastroenteritis confusing the clinical picture.

Presentation of Milk Protein Allergy in Children

The clinical manifestations of CMPA are varied, but predominantly involve the skin and gastrointestinal tract (GI). Dermatological symptoms include itching, hives, and eczematous reaction, while GI manifestations include nausea, vomiting, diarrhea, abdominal pain and hematochezia.

Other manifestations include irritability (especially in infants), poor feeding and growth retardation due to malabsorption of nutrients, facial edema and wheezing.

Workup of Milk Protein Allergy in Children

There are no specific tests to detect this condition. Diagnosis of CMPA is based on a detailed history of symptoms and a thorough physical examination. It is important for the physician to obtain details and the timeline of symptoms from the parents and confirm that they occur following the consumption of cow’s milk. In children with atopic dermatitis, if there is no direct relationship between cow’s milk consumption and symptoms, then no further testing is required.

In the case of a positive correlation, other tests in the workup include:

- **Skin prick test**: The negative predictive value of this test in more than 95%. However, a food challenge test is indicated to exclude atopic reactions.
- **Serum specific IgE test to cow’s milk protein**: This test may help only in 60% of children who have CMPA and positive IgE test.
- **Diet eliminating cow’s milk**: If CMPA is suspected, then the infant should be
fed a diet free of cow's milk for up to a month. A child without gastrointestinal symptoms can be fed extensively hydrolyzed formula (eHF) or soy formula (SF). Although amino acid formula (AAF) is non-allergenic, it is also expensive and is not tasty and therefore is not recommended.

In older children, EHF, SF, and AAF substitution are not required as there are several foods available to replace cow’s milk.

In infants with suspected IgE-mediated reactions, if there is an inadequate response with EHF or SF, then AAF substitution can be tried for two weeks.

An oral food challenge is indicated if symptoms improve following the elimination of cow’s milk.

Oral food challenge: This is the gold standard test. It must be performed in a specialized medical setting with facilities for resuscitation if required. In infants and children with immediate reactions of GI symptoms, anemia, and hypoalbuminemia with a direct relation to cow’s milk, OFC is not indicated.

**An Evaluation Algorithm of Infants Suspected to have CMPA**

1. If the infant shows symptoms and signs suggestive of CMPA that include anaphylaxis or a clear immediate type allergic reaction, CMP elimination diet and testing for specific IgE should be commenced. If specific IgE is positive, the diagnosis is confirmed and a therapeutic elimination diet should be used. If specific IgE is negative, a standardized oral challenge with CMP is recommended. If positive, the diagnosis is confirmed. If the negative, the diagnosis of CMPA is excluded.

2. If the infant’s symptoms and signs were not anaphylaxis or immediate type reaction, diagnostic elimination diet might be used. If the patient's patients improve, a standardized oral challenge with CMP is recommended and the interpretation of the results of this test is the same as in point 1. Specific IgE testing is not recommended for this group.

3. If the infant’s symptoms and signs did not improve after the commencement of a diagnostic elimination diet, the diagnosis of CMPA can be excluded and CMP elimination diet is not needed.

**Differential Diagnosis of Milk Protein Allergy in Children**

Infectious gastroenteritis should be excluded before carrying out allergy testing.

Infantile colic: CMPA is not associated with an irritable, crying infant with infantile colic

**Treatment of Milk Protein Allergy in Children**

Avoid SF in infants who have allergy symptoms and are under the age of six months or in children with GI symptoms. It is important to remember that soy milk can cause GI symptoms.

Children with mild atopic dermatitis and no history of cow’s milk protein reactions are not prescribed a diet.
Infants and children with CMPA should be prescribed a nutritionally balanced diet and calcium supplementation should be considered.

In breastfed infants with confirmed CMPA, the mother’s diet should be free of cow’s milk protein and eggs, etc for a month. If the infant improves, then the mother is asked to consume large amounts of cow’s milk for seven days to look for a re-occurrence of symptoms in the infant. If symptoms appear, then the mother should commence a diet without cow’s milk until the baby is weaned off. If there are no symptoms after the reintroduction of cow’s milk in the mother’s diet, then all foods which were previously excluded can be re-introduced in the mother’s diet one by one.

Substituting cow’s milk with goat’s or sheep’s milk will not help treat CMPA.

Several dairy foods like yogurt, butter, and cheese contain milk protein, and it may be necessary for parents to read the nutritional labels if their child has been prescribed a diet free of cow’s milk protein.

**Prognosis of Milk Protein Allergy in Children**

CMPA usually resolves within the first year of life and latest by the age of five years. Elimination of cow’s milk from the diet may be required for up to a year after confirming the diagnosis. Later, the child can be given the cow’s milk challenge with small amounts. If no reaction is noticed, then it can be resumed in the child’s diet.

**References**

- [Milk Allergy Diet for Children](https://www.stanfordchildrens.org) via stanfordchildrens.org
- [Cow’s Milk Protein Intolerance](https://www.gikids.org) via gikids.org

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