INVITED ARTICLE

Cow's Milk Protein Sensitive Enteropathy. Clinical and Histological Features in Infants

by

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Abstract

The terms "cow's milk allergy", "cow's milk protein intolerance", "cow's milk protein sensitive enteropathy", and "latent cow's milk intolerance" were discussed.

Cow's milk protein intolerance is thought to be due to sensitisation caused by macromolecular absorption.

Diarrhea with dehydration, electrolyte imbalance, malabsorption and failure to thrive in early infancy are the primary symptoms.

Histological changes can be found in the stomach and small intestine. The small intestinal mucosa exhibits a patchy enteropathy with villus atrophy, cellular infiltration and increased intraepithelial lymphocytes.

It has been shown that the assay of immunoglobulin and complement levels in the serum and duodenal juice is not useful in the diagnosis of CMPSE.

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Introduction

Cow's milk is the most common recognized cause of food allergy in children (Vaughan and Mc. Kay, 1979). Patients exhibit symptoms such as urticaria, wheezing and frequently other forms of allergic disease; there is also a high incidence of these problems in their close relatives. This condition is called cow's milk allergy.

Cow's milk protein intolerance implies an intolerance to cow's milk protein without reference to its etiology or pathogenesis. Symptomatology of CMP intolerance can be classified into "intestinal" such as diarrhoea and vomiting and "extra-intestinal" such as rhinorrhoea, anaphylactic shock, urticania etc. Intestinal symptoms of cow's milk protein intolerance is often associated with a small intestinal enteropathy. This enteropathy is called cow's milk protein sensitive enteropathy.

Symptoms of CMP intolerance usually occurs acutely after cow's milk ingestion, consisting of acute vomiting, diarrhoea, shock, dehydration and electrolyte imbalance. However a chronic form of CMP intolerance has also been recognized, consisting of abnormal stools, failure to thrive, rectal bleeding and intestinal colics (Kokkonen and Simila, 1980; Harris et al., 1977).

Kokkonen and Simila (1980) coined the term "Latent cow's milk intolerance" for a symptom complex thought to be different from cow's milk induced enteropathy. The criteria of diagnosis for this condition put forward by Kokkonen is: "Rapid lowering of the hemoglobin", "Guiac-positive stools", "Milk precipitins in the serum" during cow's milk ingestion and "recovery from anemia" after CMP withdrawal.

Pathogenesis.

The principal proteins in cow's milk are Casein, Beta Lactoglobulin, Alpha Lactalbumin and immunoglobulins. Of these. Beta lactoglobulins is thought to be most damaging. The enteropathy caused by CMP (cow's milk protein) is thought to be due to a local cell mediated immuno mechanism (Ferguson, 1979) or it is due to a direct chemical effect on an already damaged mucosa.

Iyngkaran et al., (1978) hypothesized that an acute infectious enteritis damage the gut mucosa with subsequent increased permeability. This post-enteritis increased permeability promotes macromolecular absorption resulting in sensitisation of the individual.

A subsequent challenge will then cause local CMI reaction of the small intestinal wall resulting in additional mucosal damage, malabsorption and continuing diarrhoea. Macromolecular absorption is more apt to occur in early infancy, IgA deficiency, lysosomal dysfunction, damaged mucosal barrier or abnormal intraluminal digestion.

The pathogenesis of the chronic form or the latent form of CMP intolerance, with rectal bleeding, is not known.

Pathology.

In CMP sensitive enteropathy histological changes can be found in the stomach and small intestines. Changes in the stomach includes degeneration of the surface epithelium and marked infiltration of the lamina propria (Kokkonen, 1979).

The small intestinal mucosa in CMP sensitive enteropathy frequently exhibits a patchy enteropathy (Manuel, 1979) with reduced mucosal thickness, reduced villus height, reduced villus cell : crypt-cell ratio, moderate increase in intra epithelial lymphocytes (Phillips et al, 1979), moderate elongation of crypts and infiltration of the lamina propria with polymorphs eosinophils, lymphoctytesi and plasma cells.

Diagnotic criteria

The original diagnotic criteria of Goldman (1963) which required positive reactions to three challenges with cow's milk is too rigid, dangerous and lead to underdiagnosis. It has largely been abandoned.

Iyngkaran et al., (1978) proposed a combined clinical and histological approach, i.e. :

1. Clinical disease while on CMP
2. Clinical improvement after CMP free diet
3. Normal jejunal mucosa 6 - 8 weeks after symptoms subside
4. Histological (with or without clinical) relapse after reexposure.

Cow's milk challenge (Walker-Smith, 1978) should only be attempted after a 6 - 8 weeks period with lactose and CMP free diet, and a normal prechallenge biopsy.

There after, 2 grams of lactose/kg BW in a 7% lactose solution should be given. A negative reaction rules out lactose intolerance and CMP challenge can be attempted. Small doses of 0.2 - 0.5 ml should be initially given, increasing the dose hourly.

A histological relapse with or without clinical symptoms is proof for the diagnosis of CMPSE.

Pre challenge alkaline phosphatase levels and one hour blood xylose levels were found by Iyngkaran (1979) to be good indicators for an abnormal mucosal finding (Iyngkaran, 1979).

Immunological investigations has received wide attention. However there is yet no sinile immunological investigation that is invariably positive in children with CMPSE. Antibodies to CMP perse in serum cannot be equated with clinical intolerance.

Burgin Wolff (1980) found the antibody levels against casein, Beta Lactoglobulin, Alpha Lactalbumin and bovine serum albumin, not useful in differentiating CMPSE from controls. Skin test or prick test are only positive in 59% of the patients (Walker-Smith, 1975) and is only useful to identify patients with skin reactions (Barnes et al, 1979).

The demonstration of immunoglobulin and complement deposits in the intestinal mucosa of infants with CMPSE

suggest that complement participates through its activation by antibody antigen complexes in the gut.

However it has been shown that the assay of immunoglobulin (IgE, IgA, IgM) and complement levels in the serum and duodenal juice, is not useful in the diagnosis of CMPSE (Yadav, 1979; Bulgin Wolff, 1980). A fall in serum IgG after CMP challenge was also not useful in differentiating between patients and controls.

Treatment

As soon as the diagnosis is suspected lactose and cow's milk protein should be totally withdrawn. Appropriate fluid and electrolyte should be administered. The first oral feeding should be an oral electrolyte mixture with a sodium concentration of 0.22%.

When diarrhoea has subsided breast milk should ideally be given (when available). Otherwise pregestimil in half strength dilutions should be tried. When breast milk is not available and diarrhoea persists despite pregestimil, parenteral feeding should be seriously considered.

The lactose free and cow's milk free diet should be maintained for at least 6 weeks.

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