

Cow's Milk Allergy among Children with Gastroesophageal Reflux Disease

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Background/Aims: Gastroesophageal reflux disease (GERD) and cow's milk allergy (CMA) are two common conditions that occur in infancy. This study was performed to investigate the frequency of CMA in a group of patients with GERD.

Methods: Eighty-one children with signs and symptoms of GERD were enrolled in this study. All subjects received omeprazole for 4 weeks after the initial evaluation. Empirical elimination of cow's milk from the diet was started for the patients who did not respond to the omeprazole treatment.

Results: Seventy-two cases presented with gastrointestinal signs and symptoms, whereas the remaining nine cases presented with respiratory complaints. After the initial treatment with omeprazole, two thirds of the cases (54 patients, 66.7%) responded well, and all of their symptoms were resolved. Cow's milk was eliminated from the diets of the remaining 27 patients. All signs and symptoms of GERD were resolved in this group after a 4 week elimination of cow's milk from the diet. **Conclusions:** A diagnosis of CMA was considered in one third of the pediatric cases with signs and symptoms of GERD. This finding shows that CMA can mimic or aggravate all signs and symptoms of severe GERD during infancy. (*Gut Liver* 2011;5:298-301)

Key Words: Cow's milk allergy; Food hypersensitivity; Gastroesophageal reflux disease

INTRODUCTION

Gastroesophageal reflux disease (GERD) and food hypersensitivity are two common disorders of infancy and childhood.^{1,2} Gastroesophageal reflux is an effortless retrograde movement of gastric contents into the esophagus, which could be considered as a normal physiologic process when lasting less than 3

minutes, occurring in the postprandial period, and causing few or no symptoms. However, when the reflux of gastric contents causes troublesome symptoms and/or complications, the diagnosis of GERD is made. The most common manifestations of GERD is distal esophagitis, followed by failure to thrive, esophageal peptic strictures, Barrett's esophagus, and pulmonary disease.^{3,4}

GERD is a multifactorial disease that frequently manifests during early infancy, and has a great tendency for spontaneous improvement during the first years of life, which might be as a result of feeding habits alteration as well as improved function of the lower esophageal sphincter (LES).^{1,5,6} Increased frequency of reflux in infants younger than age 4 months could suggest developmental immaturity of the LES,^{7,8} which seem to be the most common cause of gastroesophageal reflux in children.⁹⁻¹²

Association between GERD and cow's milk allergy (CMA) has been first described in infants and toddlers.¹³ Consequently, several studies were performed with controversial results on prevalence of CMA in infants with GERD,¹³⁻¹⁶ which could be due to different diagnostic criteria for either GERD or CMA among these studies.^{17,18}

This study was performed for the first time in our region to investigate the frequency of CMA in a group of infants with GERD.

MATERIALS AND METHODS

Eighty one patients who had been referred to the Children's Medical Center (Pediatrics Center of Excellence in Tehran, Iran) with signs and symptoms of GERD during 2006-2007, were enrolled in this study. There was no history of any previous underlying disease for the participants. Patients with associated diseases such as neurodevelopmental disorders, esophageal

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atresia and anatomical malformations were excluded from the study. The diagnosis of GERD was made based on clinical symptoms considering the medical history of patients and physical examination. Several questions regarding vomiting or regurgitation, crying, weight gain, respiration problems, cyanosis, apnea, pneumonia, bronchitis, chronic coughing, hiccups, and diarrhea were asked from the parents of patients.¹⁹ Barium swallow was also performed in some patients with intractable vomiting to evaluate esophageal stricture, hiatal hernia and/or intestinal obstruction.

All patients were treated with omeprazole 2 mg/kg/day divided in two doses for 4 weeks. The effect of omeprazole on GERD was assessed 4 weeks after treatment. For the patients who did not respond to this treatment, a trial of cow's milk elimination diet was considered for either infant or the mothers whom their child was breast fed for 4 weeks. The effect of cow's milk elimination was assessed after this 4-week period. Patients who respond to this elimination diet (including omitting cow's milk protein from diet) in addition to GERD treatment were assumed as CMA.

RESULTS

Forty two male and 39 female infants, with age range of 1 month to 2 years (median age of 12.5 months), were included in this study. Seventy two cases (88.89%) suffered from gastrointestinal signs and symptoms (such as nausea, vomiting, and irritability), whilst the remaining 9 cases (11.11%) presented with respiratory complaints (such as frequent cough, wheezing, asthma, and recurrent aspiration). Other less frequent symptoms were choking which was seen in 3 patients and apnea (less than 10 seconds) which were reported in 2 patients. The age distribution of all patients, participating in this study, is presented in Fig. 1.

After initial treatment with omeprazole, 54 out of 81 patient (66.67%) responded well to this treatment; all of their symptoms

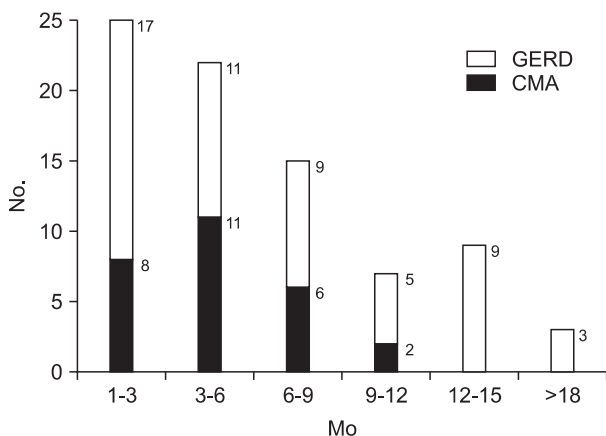


Fig. 1. Age distribution of the study patients with cow's milk allergy (CMA) and gastroesophageal reflux disease (GERD).

were resolved. These patients were diagnosed as GERD.

The remaining 27 patients (33.33%) underwent an elimination diet of cow's milk and reassessed for their symptoms after 4 weeks of this diet. All the signs and symptoms of these patients were resolved in this group after 4 weeks period of elimination of cow's milk from diet; thus the diagnosis of CMA was considered for these patients.

Among these 27 patients (15 male and 12 female) with CMA, 21 cases (77.78%) had gastrointestinal signs and symptoms, whereas 6 (22.22%) had respiratory symptoms. There was positive family history of allergy in at least one parent of 12 individuals (44.44%). The age distribution of patients with CMA in this study is summarized in Fig. 1.

DISCUSSION

GERD is a disease that commonly occurs during the first year of life; some forms of severe GERD have been shown to be associated with CMA.^{20,21} The pathogenesis of GERD is multifactorial and complex, involving the frequency of reflux, gastric acidity, gastric emptying, esophageal clearing mechanisms, the esophageal mucosal barrier, visceral hypersensitivity, and airway responsiveness.

In the present study, the CMA was diagnosed in one third of patients with sign and symptoms of GERD. A substantial part of these patients had family history of allergy or atopy. Although respiratory symptoms are expected to be seen in severe GERD, 6 out of 9 cases with respiratory symptoms were diagnosed as CMA. This finding shows that CMA can mimic all signs and symptoms of severe GERD.

The prevalence of food hypersensitivities in childhood and infancy is estimated about 7-8%.²² CMA is the most common one with prevalence of 2-3% in the infants.^{23,24} CMA can involve several organs, particularly skin and gastrointestinal tract. All parts of gastrointestinal lumen, including the esophagus, stomach, small intestine, colon and rectum, may be involved in CMA.^{20,21} It should be noted that in this study the trial of cow's milk elimination diet was not done in the infants who responded to omeprazole. So, the prevalence of CMA among GERD might be estimated to be lower than it really was.

Many questions about the causative relationship and the optimal diagnostic modalities of the GERD-CMA association have been remained unsolved until now.²¹ A trial of empiric elimination of cow's milk protein either in formula fed infants or breast fed infants mother has been considered as a diagnostic strategy for infants suspected to having food allergy, followed by either an open challenge or a double-blind, placebo-controlled food challenge (DBPCFC) to confirm or exclude a food allergy. However, DBPCFC should be conducted in adults and in children older than 3 years.^{20,21,23}

It should be noted that there are some differences between primary GERD or secondary GERD due to CMA. Although it is

not expected that the patients with CMA respond to omeprazole and diet elimination is necessary for treatment, a 24-hour esophageal pH monitoring could be recommended to determine the etiology of disease.²⁴

Although the gold standard therapy of GERD is proton pump inhibitors and H2 receptor blockers, the diagnostic strategy in infants who are suspected of having food allergy should involve 2-4 weeks elimination diet. It should be noted that adherence to a diet without proper guidance may have a negative effect on growth and development.²⁵⁻²⁷ It is important to diagnose CMA to avoid unnecessary elimination diets. The treatment of gastrointestinal manifestations of CMA relies on avoidance of cow's milk protein and dietary measures depending on the age of the child. Supportive treatment may also be included. Appropriate formula substitutes such as those containing extensively hydrolysed protein or, if not tolerated, amino acid-based formulas, should be used to secure appropriate energy and micronutrient needs.

In the present study, it has been shown that elimination of cow's milk product in the patients with diagnosis of refractory GERD resolved the problems. It seems that cow's milk product can either aggravate GERD symptoms (via dysmotility of gastrointestinal tract) or explain nonresponsive GERD to appropriate pharmacologic treatment.²⁸

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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