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Original Article

Pediatrics Section

# Cow's Milk Protein Allergy in Infants and Their Response to Avoidance

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## ABSTRACT

**Background:** Cow's milk Protein Allergy (CMPA) is the most common food allergy in infants and young children which affects 2% to 7.5% of the paediatric population. Although advanced immune regulatory medications were approved for the treatment, it seems that avoidance of cow's milk derivatives is the most effective therapeutic plan. In this study, we evaluated cow's milk protein allergy in infants with a positive family history and its response to the avoidance of cow's milk derivatives.

**Methods:** We conducted a cohort study on one hundred infants with the symptoms of CMPA who presented to the Najmiyeh Outpatients Clinic, Tehran, Iran, between 2008 and 2009. Other diagnoses were overruled and the CMPA treatment (avoidance of any cow's milk derivatives) was recommended. The children were followed up after two weeks of undergoing the Allergen Avoidance Regimen (AAR) and the efficacy of the regimen was assessed.

**Results:** Ninety three infants (mean age ± SD: 4.23±2.02 months, male: 54.8%) completed the study. A positive family history of atopy was observed in 77 (82.8%) children. Eighty eight infants (94.6%) showed a proper response to the AAR. There was no statistically significant correlation between the response to the AAR and the type of family history of the allergy, feeding and the clinical symptoms (P value of <0.05).

**Conclusion:** The common age of incidence of CMPA was a period between 3 and 6 months and the common symptoms of it were gastrointestinal symptoms. Regardless of the family history of the allergy or the types of clinical symptoms; the AAR was effective on the patients. However, the prevalence of the failure to the AAR was considerable.

**Key Words:** Cow's milk protein allergy, Infant, Avoidance, Atopy

## INTRODUCTION

Atopic diseases in infants and children have a prevalence of about 35%, which are the most important morbidity factors in industrialized countries [1-3]. Statistically, the incidence of these kinds of diseases is increasing and in western societies, it has been dramatically growing in recent decades [4]. 2.5%–15% of the infants show symptoms of cow's milk protein allergy (CMPA) [5-7]. In exclusively breast-fed infants, the incidence of CMPA is only about 0.5%, perhaps up to 1.5% at the most [8-9].

From the patho-physiological point of view, CMPA may be caused due to IgE-mediated and non- IgE-mediated processes [10]. Both of them trigger the inflammatory cascade, leading to cytokine release and the enhanced production of other inflammatory products. Finally, the symptoms appear in various organs such as the lung and the gut. Complex immune interactions are the cause of a postponed attack of the clinical symptoms. The gastrointestinal symptoms of an allergic interaction (especially the non-IgE-mediated form) are specified by the presence of isolated, blood streaked stools. A distinction between these two groups (IgE-mediated and non-IgE-mediated allergy) can be recognized by other symptoms, but the medical history is not adequate for this. Making this distinction is very important because IgE-mediated CMPA is accompanied by a higher risk of multiple food allergies and atopic conditions [11-15].

From the clinical point of view, CMPA in infants usually show symptoms which are similar to an allergic reaction in adults. These contain cutaneous symptoms such as skin rash, urticaria and pruritus, as well as respiratory symptoms such as cough and wheezing that are usually the symptoms of IgE-mediated CMPA [13].

In addition, CMPA may involve the gastrointestinal tract as a gastro-oesophageal reflux, showing the symptoms of delayed gastric emptying, colitis, gastritis, enteropathy, constipation and failure to thrive [14]. These symptoms may lead to paediatric colic and feed refusal in infants [16].

Various factors may contribute to the appearance of this allergy in infants such as diet, atopic symptoms and diseases, a family history of atopy, parental smoking, the number of siblings and furred household pets [17]. Although the incidence of the immunology based disorders have increased, the treatment of CMPA has progressed due to the developing medical technology. Although advanced immune regulatory medications were approved for the treatment, it seems that avoidance of cow's milk derivatives is the most effective therapeutic plan. In this study, we evaluated cow's milk protein allergy in infants with a positive family history and its response to the treatment.

## MATERIALS AND METHODS

We conducted a cohort study on infants with CMPA symptoms who visited the Najmiyeh Outpatients Clinic, Tehran, Iran, between February 2008 and November 2009. At first, we enrolled all the infants who were suspected to have CMPA; thereafter, CMPA was confirmed by applying an elimination challenge test on these infants.

Other diagnoses were overruled and the CMPA treatment was started for one hundred infants with a confirmed diagnosis CMPA. We assessed the patients for their demographic and clinical characterizations. The clinical signs and symptoms, a family history

of atopy, the nutrition of the infants and their mothers and the weight of the infants were assessed. A family history of atopy such as asthma, drug allergies, allergic rhinitis, food allergies, atopic eczema, and urticaria was exactly evaluated.

The patients were divided to three groups base on the type of their feeding. The first group was breastfed infants whose mothers were under a dietary regimen of avoidance of cow's milk products. The second group was infants who were fed with formula based cow's milk and soy; therefore, feeding with cow's milk and a soy based formula was avoided. The third group was breastfed infants who were also fed with cow's milk and the soy based formula or breastfed newborns whose mothers and they had used the complements. For the last group, the treatment plans of both the groups 1 and 2 were suggested. The patients were followed after a two week allergen avoidance regimen (AAR) and the efficacy of the regimen was assessed.

According to the response of the infants to the AAR after the first two weeks, the cases were divided into three groups again. The first group was patients who showed a good response to the AAR and so we suggested that they leave the regimen gradually (within 2-3 months). The patients who showed an improper response following the AAR were divided into two groups. The second group consisted of the children who had not followed the regimen. The third group consisted of infants who did not show a suitable response to the treatment plan anyway. The regimen in these last groups was continued for two weeks and the patients were followed after two weeks again. This study was approved by the ethical committee of the Baqiyatallah University of Medical Sciences. The SPSS software, 16th edition and the $\chi^2$ test were used for the analysis and a P value of $< 0.05$ was considered as significant.

## RESULTS

One hundred infants with a mean age of 4.23±2.02 months were enrolled in the study and 93 children completed the follow up (the loss to follow-up was 7%). 51 (54.8%) children who completed the survey were males and 42 (45.2%) were females. Bloody stool was the most common symptom which was seen in 74 (79%) infants, diarrhoea in was seen in 34 infants (36.6%), irritability was seen in 30 infants (32.3%), skin symptoms were seen in 20 infants (21.5%), vomiting was seen in 15 infants (16.1%), a gastro-oesophageal reflux (GER) was seen in 14 infants (15.1%), respiratory problems were seen in 6 infants (6.5%), anaemia was seen in 3 infants (3.2%), anal fissures were seen in 1 child (1.1%), diaper rash was seen in 5 infants (5.4%) and other symptoms were seen in 4 (4.34%) infants.

A family history of atopy was identified in 77 (82.8%) children. 28 (30.1%) children had a positive family history through their fathers only, 27 (29%) had it through their mothers, and 13(14%) had it through both their fathers and mothers. 1 (1.2%) infant had a family history through other first-degree family members and 8 (8.6%) had it through second-degree family members. Allergic rhinitis was the most common type of family allergy which was in 50 infants (53.8%), followed by food allergy (41.9%), atopic eczema (20.4%), asthma and respiratory problems (10.8%) and adverse reactions to the medication (7.5%) [Table/Fig-1].

60(71%) infants were fed by breast feeding solely, 9(9.7%) were fed by both breast feeding and formula, 4(4.3%) infants were fed only with formula, 3 (3.2%) infants were fed by breast feeding plus complement and finally, 2(2.2%) infants were fed with food only.

| Item | Finding |
|---|---|
| Age (mean±SD) | 4.23±2.02 months |
| Gender(male/female) | 54.8%/45.2% |
| Family allergy (ratio) | 77 (82.8%) |
| Commonest form of familiar atopy | Allergic rhinitis 50 (53.8%) |
| Commonest symptoms of CMPA | Bloody stool 74 (79%) |
| Commonest form feeding | Breast feeding (71%) |
| Commonest age period | 3-6 months (59.2%) |

**[Table/Fig-1]:** Base line characteristics

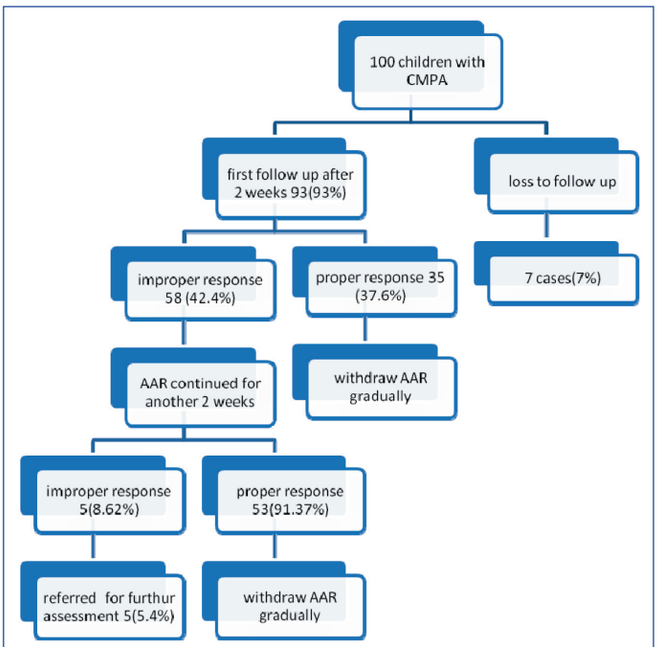
77 (82.8%) of the children had good weight gain, 10 (10.7%) had medial weight gain and 6 (6.5%) had weak weight gain.

The treatment plan was as follows: avoidance of cow's milk and its products for 76 (81.7%) mothers, avoidance of the complements which were based of cow's milk for 2 (2.2%) mothers, avoidance of formula based cow's milk or soya for 6 (6.5%) mothers, avoidance of dairy, cow's milk and its products for 2 (2.2%) mothers and avoidance of cow's milk for their infants; avoidance of cow's milk, and dairy products for 7 (7.5%) mothers and avoidance of formula or soya for their infants.

At their first visit after the treatment, 35 infants (37.6%) showed an excellent response and all their signs and symptoms were eliminated; therefore, the treatment plan was discarded within 2-3 months, gradually. 56 (60.2%) patients showed a relative response to the treatment, and 2 (2.2%) patients didn't show any response to the treatment; therefore, the treatment plan was continued with more attention being paid, for 2 weeks again.

At the second visit, 53 (91.37% of the total) patients who had shown an improper response to the treatment showed a proper response to the treatment and 5 (8.63% of the total) of them didn't show any response. Totally, 88 (94.6%) patients showed a suitable response to the treatment and 5 (5.37%) infants didn't show any response to the avoidance [Table/Fig-2].

Among 53 infants with CMPA who were only fed by breast feeding and who had a positive family history of allergy, 49 (92.4%) showed a proper response to the treatment and 4 (7.6%) of them didn't




**[Table/Fig-2]:** Response to avoidance

show any response to the treatment. Also, among 13 infants with CMPA who were only fed by breast feeding and who didn't have a family history of allergy, 12 (92.3%) showed a suitable response to the treatment. This difference was not statistically significant. (p >0.05) Out of 53 infants who were fed only by breast feeding and who had a family history of allergy, 49 (92.4%) showed good response to the treatment. Also, all the infants who were only fed by formula and who had a family history of allergy showed a good response to the treatment. This difference was not statistically significant (p>0.05).

Among 34 infants with diarrhoea, 32 (94.1%) showed a good response to the treatment and 2 (5.9%) didn't show a suitable response to the treatment. 69 (93.2%) of the 74 children with bloody stools showed a good response to the treatment. The response to the treatment was not affected by any of the underlying factors such as a family history of allergy, gender and age and clinical symptoms statistically. (p >0.05)

## DISCUSSION

In this study, a majority of the children (59%) were in the 3-6 months age group and this was similar to that in previous studies, which demonstrated the common age of CMPA [18-21]. Also, digestive symptoms were the most common symptoms in these patients (82.7%) that this was the same in other studies too [22-25]. Like in previous reports, other clinical symptoms and signs such as skin and respiratory symptoms were prevalent [18, 22-24]. In the present study, a family history of allergy was seen for 77 (92.7%) infants, although there was no correlation between the family history and the response to the AAR. This finding was similar to those of many other studies, whose findings reported a family history in up to 90% of the children who were studied [26-27].

More than one third of the infants in the first two weeks of the avoidance and more than half of the infants in the fourth week visit showed a proper response to the avoidance plan. Overall, 94.6% of the infants showed a good response to the treatment plan and 5.4% of them didn't show any response to the treatment. These were referred for further evaluation. The complete response to the avoidance in this study was similar to that which was seen in other studies [28-29].

In previous reports, the prognosis of CMPA was suitable generally, with a remission rate of nearly 85 to 90% without a specific treatment. In particular, the gastrointestinal symptoms, as compared to the other symptoms, showed a pleasant prognosis that was comparable to our findings [30]. Although the CMPA is a self limiting disorder, frequently and regressing along the time, its complications can affect the child'd growth. But this plan should be supervised closely because many of the parents don't respect it. On the other hand, the elimination of cow's milk from the dietary regimen may affect the growth of children and its avoidance must be done away with as soon as possible after establishing the therapeutic response [31]. Also, alternative options such as hydrolyzed milk or camel's milk may be useful for such children [32].

In other studies, a family history of allergy which was reported as a risk factor was shown to affect the infants with CMPA, but a correlation between CMPA in infants and a family history of allergy wasn't reported by them [32-35]. After surveying all the infants, we didn't find any reasonable correlation between CMPA in the breast-fed infants and a history of allergy in their parents. Also, a logical correlation between CMPA in the infants and the type of allergy in their families, such as allergic rhinitis and food allergies was looked for, but that wasn't seen, too. Recently, advanced immune-based medication was used for the treatment of CMPA, especially for the refractory cases and further studies may make its role clear soon [36-37]. In conclusion, a family history of allergy in infants with CMPA must be considered. Almost, all the children, regardless of the underlying factor, could benefit from a regimen which was free of cow's milk and its products. Therefore, the avoidance of these was recommended for all the children with CMPA, although the regimen should be respected and the response to the treatment should be followed closely.

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