

Cow's milk allergy in children: 9 years experience of Dr. Behçet Uz Children's hospital, Izmir

Çocuklarda inek sütü alerjisi: 9 yıllık deneyim Dr. Behçet Uz Çocuk Hastanesi, İzmir

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ABSTRACT

Objective: Cow's milk allergy is the most frequent food allergy in childhood. Delayed diagnosis may cause a number of systemic dysfunctions, while incorrect diagnosis may result in deficient nutrition of the mother and the child. As in other types of allergies, food allergy is also a growing problem in recent years. Our aim was to determine the characteristics of our patients allergic to cow's milk, and see if there was an increasing trend.

Material and Methods: The study was of retrospective and cross-sectional design. Patient data were collected from Pediatric Allergy Department patient files. Cases of food allergy were reviewed and patients fulfilling the criteria of cow's milk allergy were included in the study.

Results: A total of 105 cases with cow's milk allergy out of 264 food allergies who were followed up between 2003-2011 were investigated. Most of the patients were under 2 years of age (78.1%), were males (62.9%) and presented with a history of allergy (79.1%). IgE mediated cases constituted the majority (75.2%). More than half of the patients admitted in 2010 and 2011. This was mostly due to the increased number of patients less than twelve months of age (p=0.015). Most frequently involved system was skin (67.5%) and multisystem involvement was 15.7%

Conclusion: A detailed history is the key element of diagnosing cow's milk allergy. There is a considerable number of cases within the first year of life which may present with different signs and symptoms. Although not a life threatening situation, correct diagnosis is vital as nutrition is a key component in the development and growth of child.

Key words: Child, Infant, Clinical symptoms, Cow's milk allergy, Food hypersensitivity

ÖZET

Amaç: İnek sütü alerjisi çocukluk çağında en sık görülen gıda alerjisidir. Tanıda gecikme olduğunda sistemik reaksiyonlar ortaya çıkarken, yanlış tanı konulduğunda annenin ve çocuğun yetersiz beslenmesine neden olmaktadır. Diğer alerjik hastalıklar gibi besin alerjileri de son yıllarda giderek büyüyen bir sorundur. Amacımız, inek sütü alerjisi vakalarının özelliklerini saptamak ve sıklığının artıp artmadığını belirlemektir.

Gereç ve Yöntemler: Çalışmamız retrospektif ve kesitsel olarak planlandı. Hasta verileri Pediatrik Allerji Bölümü hasta dosyalarından toplandı. Gıda alerjisi tanısı konulan hastalar arasından inek sütü alerjisi saptanan hastalar çalışmaya alındı.

Bulgular: 2003-2011 yılları arasında gıda alerjisi tanısı ile takip edilen 264 olgu arasından inek sütü alerjisi tanısı alan 105 olgu çalışmaya alındı. Hastaların çoğu 2 yaşından küçük (%78,1), erkek cinsiyette (%62,9) idi ve anamnezinde süt alımı takiben kesin öykü vardı (%79,1). Olguların %75,2'sini IgE aracılı inek sütü alerjileri oluşturmaktaydı. Hastaların yarısından fazlası 2010 ve 2011 yıllarında başvuran hastalardı. Bu artıştan daha çok 1 yaş altındaki hastaların fazla olması sorumluydu (p=0.015). En sık tutulan sistem, deri (%67,5) ve multisistem (%15,7) olarak bulundu.

Sonuç: Detaylı bir öykü inek sütü alerjisi tanısında önemli bir rol oynar. Yaşamın ilk yılı içinde çok sayıda hasta çeşitli semptom ve bulgularla karşımıza çıkar. Genellikle hayatı tehdit eden bir durum olmamakla birlikte beslenme, çocuğun gelişimi ve büyümesinde rol oynadığı için doğru tanı çok önemlidir.

Anahtar kelimeler: Çocuk, infant, klinik belirtiler, inek sütü alerjisi, gıda aşırısı duyarlılık

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INTRODUCTION

Cow's milk is one of the most important nutrients in childhood. Cow's milk is also usually the first food following breast milk which is given to infant which makes cow's milk proteins the first foreign proteins introduced to the baby ⁽¹⁾. On the other hand cow's milk allergy (CMA) is the most common food allergy in infants affecting 2-3% of the infants and young children in general population ⁽²⁾. When this reaction is immune-mediated, it is defined as allergy, when the reaction is non-immune mediated it is defined as intolerance. Onset of CMA is usually within the first year of life and tolerance is achieved in the first few years. But in a recent study 21% of CMA patients were found to be still allergic at the age of 16 years ⁽³⁾.

Allergic reactions to cow's milk may be divided into IgE-mediated and non IgE-mediated types ⁽⁴⁾.

A prompt and correct diagnosis of CMA is vital. When the diagnosis is delayed it may impair the growth and quality of life, it may even be life threatening ⁽⁵⁾. On the other hand eliminating cow's milk from the child's diet depending on an incorrect diagnosis of CMA may interfere with the nutritional status of the child ^(5,6). As in other food allergies CMA is a growing problem in recent decade ^(7,8).

In this study we try to identify the CMA cases of Dr Behcet Uz Children's Hospital Department of Pediatric Allergy outpatient clinic and demonstrate their characteristic features.

MATERIAL and METHODS

Our study was cross-sectional and the study group was selected from the patients who were followed by Department of Pediatric Allergy in Dr Behcet Uz Children's Hospital, Izmir Turkey. Data were collected from the patient files. All files of the years from 2003 to 2011 were evaluated by the researchers and patients with food allergy were selected. Cases who had, 1) History of anaphylaxis with cow's milk and milk products 2) A positive history of allergic reacti-

on following milk protein ingestion plus specific IgE levels/skin prick test results above positive predictive values or 3) Positive open challenge with milk, were included in the study group.

Skin prick test was performed by using commercial milk extract (ALK, Abello) and fresh cow's and goat's milk ⁽¹⁾. Determination of cow's milk specific IgE was performed by Immuno CAP system (Pharmacia, Uppsala, Sweden).

For the diagnosis of CMA, European guidelines were used: A skin prick test wheal diameter over 3 mm was considered to be positive. In case of a wheal diameter more than 6 mm up to two years of age and a wheal diameter more than 8 mm after 2 years of age, milk challenge test was not performed. When specific IgE was used for diagnosis, levels above 0.35 kU/L was considered to be positive. Challenge test was not performed above 5 kU/L up to 2 years of age and over 15 kU/L after 2 years of age ⁽¹⁾. When there was a history of anaphylaxis with milk and milk products, challenge test was not performed.

Since oral challenge test is not performed routinely on all suspected food allergy cases we did not consider oral challenge test results as an inclusion criteria, although it was used in our clinic for diagnosis of non-IgE mediated CMA.

Files with insufficient data were not included into the study group (n=14). Data collected from the files were analyzed in three main groups: demographic characteristics (age, sex, data of admission), clinical features (age at admission, history, involved system in allergic reaction) and laboratory findings (eosinophil count, IgE levels, skin prick test, specific IgE levels). All necessary ethic committee approvals were obtained.

Statistical analysis was done using SPSS 15.0.

RESULTS

Among a total number of 11271 files found in the archives of Department of Allergy in Dr Behcet Uz Children's Hospital Izmir Turkey, study group con-

sisted of 105 children.

The majority of the CMA patients were boys (62.9%). IgE mediated CMA was significantly more among boys ($p=0.04$) compared to girls.

Great majority of the patients were younger than 2 years of age (78.1%) and 38.1% were within the first year of their lives. When the child has a history of anaphylaxis that is, an anaphylactic reaction following ingestion of milk or milk products, we considered the child as having CMA. Of the 105 patients 11 (10.5%) had anaphylaxis with cow's milk. The diagnosis in 47 of the remaining patients was based on positive skin prick test and positive specific IgE values. Skin prick test was positive in 28 patients and specific IgE levels were above positive predictive value by European guidelines in 19 patients. Open challenge test result was positive in 44 patients, 3 patients with equivocal open challenge test results were further evaluated by double-blind placebo controlled challenge test.

Of the 105 CMA patients 79 (75.2%) was IgE mediated which was considered by specific IgE levels and skin prick tests. Demographic and clinical features of IgE mediated and non-IgE mediated children are given in Table 1.

There was no difference in IgE mediated CMA between younger (less than 3 years of age) and older (3 years or older) children ($p>0.05$). New diagnosed

cases of CMA showed a significant increase in years 2010 and 2011, when compared to previous years, that is 55 new patients in the last 2 years, 50 new patients in remaining 6 years. Most of these new patients were under 1 year of age, that is, 47.4, and 26% of these cases were identified as allergic between years 2010-2011, and 2003-2009, respectively ($p=0.015$).

When there is a certain history of CMA, the symptoms were either dermatologic (67.5%), gastrointestinal (10.8%), respiratory (6.0%) or multisystemic (15.7%). Some of our patients had positive history, specific IgE and/or skin prick test results for one or more food allergens besides cow's milk. We have 30 cases (28.6%) with multiple food allergies. Most frequent accompanying food allergen was hen's egg (22 cases, 20.9%). By the year 2010, goat's milk became commercially available, so our patients with CMA started to try goat's milk as an alternative. As a result of this demand, we included goat's milk to our prick testing panel. A total of 19 cases had goat's milk in their skin prick test panel, and 14 had goat's milk allergy (73.7%). All of these 14 patients had positive skin prick test results for cow's milk also.

DISCUSSION

CMA was prevalent in male gender in our study

Table 1. Demographic and clinical features of the study group.

		IgE Mediated (n)	Non-IgE Mediated (n)	Total (n)
Gender	Boys	54 (68.4%)	12 (46.2%)	66 (62.9%)
	Girls	25 (31.6%)	14 (53.8%)	39 (37.1%)
	Total	79 (100.0%)	26 (100.0%)	105 (100.0%)
Age	0-1 years	48 (60.8%)	14 (53.8%)	62 (59.1%)
	1-2 years	22 (27.8%)	7 (27%)	29 (27.6%)
	>2 years	9 (11.4%)	5 (19.2%)	14 (13.3%)
	Total	79 (100.0%)	26 (100.0%)	105 (100.0%)
Presenting symptom	Skin	44 (55.7%)	12 (46.2%)	
	Respiratory	3 (3.8%)	2 (7.7%)	
	Gastrointestinal	2 (2.5%)	7 (26.9%)	
	Multi system presenting	8 (10.2%)	5 (19.2%)	
	No symptoms	22 (27.8%)	0 (0.0%)	
	Total	79 (100.0%)	26 (100.0%)	105 (100.0%)

population, which was reported to be a result of greater male gender prevalence of allergic disease in male until adolescence⁽⁹⁾, although this was not a consistent finding in all studies⁽¹⁰⁾.

Majority of our patients were under 3 years of age. CMA is usually regarded as a problem in early ages⁽¹¹⁾, and even under one year of age⁽¹²⁾.

In our study, diagnosis of CMA was not made based on double-blind, placebo controlled food challenge test results because of a number of practical issues. Instead, when there is a convincing history of CMA accompanied by a positive cow's milk specific IgE test results (either by elevated serum levels of specific IgE or positive skin prick test results) the patient was considered to have IgE mediated CMA. The diagnosis of IgE mediated cow's milk allergy was based on production of high specific IgE levels against cow's milk antigen, where diagnostic decision points were set to >95% PPV to predict cow's milk allergy. For the remaining cases, firstly, cow's milk was eliminated from the diet. If there was a symptomatic improvement followed by the symptoms when cow's milk was introduced again, the patient was considered to have non-IgE mediated CMA. This diagnostic approach was used in a number of studies^(13,14).

In our study population, majority of the patients were IgE mediated (>75%). Most of our patients had skin manifestations (>67%), followed by gastrointestinal and respiratory symptoms. A considerable percent of presentations were multisystemic (15%). Other studies have revealed similar results^(10,15). The most frequently seen symptom was cutaneous manifestations (67.5%). Kvenshagen et al. reported gastrointestinal, cutaneous and respiratory symptoms in 66, 37, and 37% of their patients which is quite different from our results but their non-IgE mediated CMA cases was also very high when compared to our data (99% vs 24.8%)⁽¹¹⁾. There were also many studies which demonstrated similar results⁽¹⁶⁾. It was also reported that, although infrequently symptoms in CMA may overlap⁽¹⁷⁾.

IgE mediated CMA has been reported to be found in 14-73% of the cases^(11,18). Although in some of the studies IgE mediated CMA was found to be lower, in some studies similar results as ours have been reported⁽¹²⁾.

There were more CMA cases in recent years, as shown in other studies^(7,8). This increase was probably due to the increase in cases younger than 1 year of age. There was a significant increase in 0-1 age group ($p=0.015$). This may be a result of increased awareness of CMA cases which resolves before age 2.

We had a considerable number of food allergy cases which were nearly 1/3 of the total cases of allergics. Although goat's milk was considered as a substitute in CMA, in most cases there is a cross-reaction to goat's milk as well⁽¹⁹⁾. We had higher rates (73.7%) of cross-reaction to goat's milk. On the other hand using goat's milk as an alternative in the remaining one quarter of the children was an important support for nutritional status. But this assertion should be taken with caution and oral challenge with goat's milk should be performed when possible.

A detailed history is the key element of diagnosing CMA. There is a considerable number of cases within first year of life which may present with different signs and symptoms. Although not a life threatening situation, correct diagnosis is vital as nutrition is a key component in the development and growth of a child.

KEY MESSAGES

Cow's milk allergy should not be overlooked, as it may interfere with a healthy growth and development. On the other hand, when cow's milk allergy was overdiagnosed, child may deprive of a very important nutrient, and subsequent growth impairment may result.

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