Cow’s milk allergy (CMA) is one of the most common food allergies to occur in infants and children under 3 years of age. The incidence in early childhood varies between 2% and 7.5%. \(^1\) Studies carried out in different regions in Turkey have recorded an incidence of between 0.55% and 1.55%. \(^2\) Clinical symptoms of CMA manifest in infants fed with breast milk generally within the first months of life, and in infants fed with formula containing cow’s milk, it may be seen in just days or weeks following formula intake. \(^5\)

Clinically, skin findings reflecting an allergic reaction are observed in 50% to 60%, gastrointestinal system symptoms are seen in 50% to 60%, and respiratory system symptoms appear in 20% to 30% of CMA patients. \(^6\), \(^7\) Immunoglobulin E (IgE)-mediated reactions typically occur within 1 to 2 hours after ingestion of cow’s milk, and non-IgE-mediated reactions may be seen some 2 hours after intake. Due to the role of cellular and humoral mechanisms in mixed-type reactions, the symptoms may be acute or chronic. \(^6\) There are at least 20 protein compo-
The symptoms generally occur before 6 months of age, but may rarely be seen after 12 months. For this reason, it is important for clinicians to consider CMA in patients younger than 2 years of age. Making a correct diagnosis is critical for treatment, follow-up, and the prognosis of the disease.

The objective of this study was to determine the knowledge level of pediatric residents and pediatricians about CMA and to evaluate the effect of in-service training.

**Methods**

Pediatric residents and pediatricians working in the children’s health clinic of a training and research hospital were surveyed for this study. All of the respondents were fully informed about the study. The plans for the use of the results obtained were explained to the participants, and they were assured about the confidentiality of the information gathered. Written, informed consent forms were obtained from all of the participants. No compensation was provided for participation in the study. Respondents were asked to complete a questionnaire of 10 questions related to CMA to assess their knowledge before and after receiving training on the subject. The content of the questionnaire forms was not disclosed prior to the initial response. The respondents were given 10 minutes to complete the pre-training questionnaire, which was then followed by a 60-minute training course on CMA. The same questionnaire form was distributed after the training session and the results were evaluated.

The CMA questionnaire administered in this study was prepared by a researcher who is a pediatric allergy and immunology specialist. General information was collected, as well as responses specifically related to treatment using the current practical guidelines on cow’s milk protein allergy. There were 3 questions requesting socio-demographic data, followed by a total of 10 true/false questions, 4 of which were general information about CMA and 6 were related to treatment and management.

Statistical analysis was performed using the 2007 NCSS statistical software program (NCSS, LLC, Kaysville, UT, USA). In addition to descriptive statistical methods (mean and SD), an independent t-test was performed for pairwise comparison of variables with normal distribution, while pairwise comparison of variables with non-normal distribution was conducted with a Mann-Whitney U test. A chi-square test was used for the comparison of qualitative data. P<0.05 was accepted as the level of significance.

**Results**

A total of 45 physicians, 31 pediatric residents and 14 pediatricians, were enrolled in the study. The mean age of the pediatric residents was 27.4±1.28 years, and the mean age of the pediatricians was 41.92±5.37 years. There were 20 (64.5%) female and 11 (35.5%) male pediatric residents, and 8 (57.1%) female and 6 (42.9%) male pediatricians enrolled in the study. The mean length of professional experience was 2.3 years in the pediatric resident group and 8.9 years in the pediatrician group. The mean number of correct answers of a possible score of 10 before the training was 8.32±1.37 in the resident group and 7.5±1.69 in the pediatrician group. There was no significant difference between the groups in the results of the pre-evaluation (p=0.09). In the assessment using the same questionnaire after training, the pediatric resident group had a mean correct score of 10 and the pediatrician group had a mean correct response rate of 9.71±0.6. The difference in the score within the groups after training was significant (p=0.01).

Intragroup evaluations of pre- and post-training responses indicated a significantly greater number of correct responses after receiving training. (p=0.001) (Table 1).

The rate of correct responses to the questions in the survey forms before and after the training for both study groups are presented in Table 2.

| Table 1. Analysis of variables related to cow’s milk allergy |
|-------------------------------------------------------------|
| Group | Pediatric residents (n=31) | Pediatricians (n=14) | p |
| Gender (%) | | | |
| Female | 20 (64.5) | 8 (57.1) | 0.63 |
| Male | 11 (35.5) | 6 (42.9) | |
| Age (years) | 27.4±1.28 | 41.92±5.37 | 0.001 |
| Number of correct answers before training | 8.32±1.37 | 7.50±1.69 | 0.09 |
| Number of correct answers after training | 10.0±0.001 | 9.71±0.61 | 0.01 |
| Intragroup change | 8.32±1.37 | 7.50±1.69 | 0.001 |
| Pre test-post test | 10.0±0.00 | 9.71±0.61 | |
Discussion

Because CMA often appears early in childhood, it is important that pediatricians be aware of the circumstances and be prepared to make a correct diagnosis and use current approaches to treatment and management. The lack of studies of those working in the field of pediatrics makes it necessary to evaluate the current knowledge level of physicians on this subject. However, there are a few noteworthy studies about the knowledge and practices of pediatricians regarding food allergies.\[10, 11\]

A study related to food allergies that included 407 pediatricians and primary care physicians conducted by Gupta et al.\[10\] revealed that the general knowledge level of physicians was scored at an average level and that fewer than 30% of the participants felt comfortable performing follow-up of children with a food allergy. Krugman et al.\[11\] demonstrated that pediatricians did not receive adequate training in the diagnosis or treatment and management of anaphylaxis due to food allergy. A study that enrolled 126 family physicians working in the province of Malatya, Turkey, found that the knowledge level of the study participants about diagnosis and treatment of CMA and adrenaline autoinjector use was insufficient.\[12\]

The foundation of CMA treatment consists of the removal of cow’s milk and foods containing cow’s milk from the diet.\[5\] Goat’s milk is sometimes perceived as an alternative to cow’s milk and is recommended by physicians for patients with CMA; however, goat’s milk has a similar sequence homology to cow’s milk, and therefore the rate of reaction is very high among those with CMA and consumption is not recommended.\[8, 13\] Our survey question inquiring if goat’s milk is an appropriate alternative to cow’s milk. In 13% to 20% of the children with CMA, there is also an allergy to beef.\[14\] Elimination of beef from the daily diet is not generally recommended; however, in children who develop a reaction, an allergy specialist may decide to recommend this course. In our study, 64.5% of the pediatric residents answered a question about the elimination of beef from the diet correctly, and 57.1% of the pediatricians responded correctly. A question related to the removal of dairy products such as yogurt, cheese, and butter, was answered correctly by 74.1% and 64.2% of the residents and pediatricians, respectively. These results indicate that there is a lack of awareness of current information among pediatricians on these issues and that it is necessary to be more mindful about the elimination of milk products from the diet and to work with allergy experts. In their study, Topal et al.\[12\] reported that almost 3 of 4 among 126 family physicians knew that milk and milk products should be removed from the diet in patients diagnosed with CMA. The results of our study indicate a similar awareness among physicians regarding recognition of the necessity to eliminate products containing cow’s milk.

Children with CMA should be monitored at regular intervals and the development of tolerance should be investigated. In recent years, research has shown that consumption of baked milk products, such as muffins or pizza containing cheese, can accelerate the development of tolerance.\[5\] Seventy-five percent of children with CMA can tolerate baked milk.\[15\] In our study, the question about the consumption of baked products was answered correctly by 61.2% of the pediatric residents and 50% of pediatricians. These results show that the respondents had insufficient knowledge of the contribution of milk products to the development of tolerance.

Probiotics are live microorganisms that affect the health of the host positively when consumed in sufficient amounts.

| Table 2. Correct answers before and after training |
|-----------------------------------------------|
|                                    | Pediatric resident, n (%) | Pediatricians, n (%) |
|                                  | Pre training | Post training | Pre training | Post training |
| Treatment of anaphylaxis          | 22 (70.9)    | 31 (100)     | 9 (64.2)    | 14 (100)     |
| Administration route of adrenaline in anaphylaxis | 21 (67.7)    | 31 (100)     | 9 (64.2)    | 13 (92.8)    |
| Choice of anaphylaxis formula     | 20 (64.5)    | 31 (100)     | 8 (57.1)    | 12 (85.7)    |
| Routine use of probiotics         | 22 (70.9)    | 31 (100)     | 7 (50)      | 14 (100)     |
| Calcium supplement                | 19 (61.2)    | 31 (100)     | 8 (64.2)    | 14 (100)     |
| Is goat’s milk an alternative treatment for CMA? | 21 (67.7)    | 31 (100)     | 8 (64.2)    | 13 (92.8)    |
| Routine elimination of beef from diet | 20 (64.5)    | 31 (100)     | 8 (57.1)    | 14 (100)     |
| Mostly known food allergy         | 25 (80.6)    | 31 (100)     | 13 (92.8)   | 14 (100)     |
| Consumption of baked products     | 19 (61.2)    | 31 (100)     | 7 (50)      | 13 (92.8)    |
| Knowledge of elimination diet     | 23 (74.1)    | 31 (100)     | 8 (64.2)    | 14 (100)     |
Experimental studies have shown that probiotics can regulate allergy responses by facilitating the response of T1 lymphocytes to the immune system and by suppressing the production of IgE-type antibodies. However, it is emphasized in the national guidelines for food allergies that the use of probiotics provides no additional improvement of CMA. Importantly, our study results also indicated that the question regarding the routine use of probiotics in the treatment of CMA was answered correctly by 70.9% of the pediatric residents and 50.0% of the pediatricians before the study training session.

The greater awareness of the pediatric residents is likely a result of studies during their rotation in an allergy clinic with specialists. There was a significant increase in the rate of correct responses after receiving training.

Anaphylaxis is a sudden onset reaction that progresses rapidly and is potentially life-threatening. Due to the risk of death, physicians must be able to recognize and properly treat anaphylaxis. Adrenaline should be injected intramuscularly into the anterolateral aspect of the thigh (vastus lateralis muscle). The survey question of whether the first option in the treatment of anaphylaxis in a child with CMA is antihistamines was answered correctly by 70.9% of the pediatric residents and 64.2% of the pediatricians. Topal et al. reported that 64.3% of the family physicians surveyed knew that an adrenaline autoinjector should be prescribed for patients who developed anaphylaxis due to cow’s milk protein, and questions about adrenaline autoinjector use, the injection site, and dosage were responded to correctly by 34%, 34.1%, and 30.2% of the family physicians, respectively. Importantly, our study results also indicated that pediatricians lack knowledge about anaphylaxis.

In patients with a history of anaphylaxis due to cow’s milk, the first choice is an amino acid-based formula. The choice of formula is critical for the prevention of anaphylaxis. In our study, this question was answered correctly by 64.5% of the pediatric residents and 57.1% of the pediatricians. These results are important in that they reveal pediatricians’ preference for other cow’s milk or goat’s milk-based formulas rather than an amino acid-based formula. The fact that our study was a single-center questionnaire with a small sample size is a limitation. This was small-scale observational research to investigate the knowledge, perceptions, and experience of pediatricians regarding CMA. Data from a multi-center study could more generally reflect pediatricians.

In-service academic training significantly increased the level of knowledge related to CMA. The inclusion of subjects related to the treatment and management of CMA in the academic program will increase the knowledge level of pediatricians.

Disclosures

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – C.C., N.A.; Design – C.C., V.S., K.B.; Supervision – N.H., S.H.; Materials – C.C.; Data collection &/or processing – V.S.; Analysis and/or interpretation – C.C., V.S.; Literature search – N.A., K.B., L.B.; Writing – C.C.; Critical review – L.B., N.H., S.H.

References

1. Torkaman M, Amirsalarli S, Saburi A, Afsharpaiman S, Kavehmanesh Z, Beiraghdar F, et al. Cow’s milk protein allergy in infants and their response to avoidance. J Clin Diagn Res 2012;6:615–8.
2. Altintas D, Guneser S, Evliyaoğlu N, Yüksel B, Atici A, Serbest M. A prospective study of cow’s milk allergy in Turkish infants. Acta Paediatr 1995;84:1320–1.
3. Kucukosmanoglu E, Yazi D, Yesil O, Akkoc T, Gezer M, Ozdemir C, et al. Prevalence of immediate hypersensitivity reactions to cow’s milk in infants based on skin prick test and questionnaire. Allergol Immunopathol (Madr) 2008;36:254–8.
4. Doğruel D. Alerjik hastalıkların sıkılığı ve gelişmesindeki risk faktörleri: Doğum kohort çalışması. Adana: Çukurova Üniversitesi; 2012.
5. Yavuz T, Sаçkеsеn C. İnek sütu alerjisi. Katkı Pediatri Dergisi 2012;34:81–90.
6. Sicherer SH, Sampson HA. Food allergy: Epidemiology, pathogenesis, diagnosis, and treatment. J Allergy Clin Immunol 2014;133:291–307.
7. Burks AW, Tang M, Sicherer S, Muraro A, Eigenmann PA, Ebisawa M, et al. ICON: food allergy. J Allergy Clin Immunol 2012;129:906–20.
8. Fiocchi A, Brozek J, Schünemann H, Bahna SL, von Berg A, Beyer K, et al. World Allergy Organization (WAO) Diagnosis and Rationale for Action against Cow’s Milk Allergy (DRAcMA) Guidelines. World Allergy Organ J 2010;3:57–161.
9. Karakoç GB. İnek sütu Alerjisi. In: Sekerel BE, editor. Çocukluğça alerji, astım, immunoloji. 1st ed. Ankara: Ada Basın Yayın; 2012. p. 619.
10. Gupta RS, Springer EE, Kim JS, Smith B, Pongracic JA, Wang X, et al. Food allergy knowledge, attitudes, and beliefs of primary care physicians. Pediatrics 2010;125:126–32.
11. Krugman SD, Chiaramonte DR, Matsui EC. Diagnosis and management of food-induced anaphylaxis: a national survey of pediatricians. Pediatrics 2006;118:e554–60.
12. Topal E, Çatal F, Özdemir R, Karadağ A, Yıldırım N, Ermiştekin H, et al. Measuring the primary care physician’s knowledge about diagnosis and treatment of cow’s milk allergy and adrenaline auto injector usage. Asthma Allergy Immunol 2014;129–14.
13. Restani P, Ballabio C, Di Lorenzo C, Tripodi S, Fiocchi A. Molecular aspects of milk allergens and their role in clinical events. Anal Bioanal Chem 2009;395:47–56.
14. Martelli A, De Chiara A, Corvo M, Restani P, Fiocchi A. Beef allergy in children with cow’s milk allergy: cow’s milk allergy in children
16. Kutlu T. Prebiotics and probiotics. Turk Arch Ped 2011;46 Suppl:59–64.
17. Altıntaş DU, Büyüktiryaki B. Besin alerjisi Türk ulusal rehberi 2017. Asthma Allergy Immunol 2017;15:92.
18. Cavkaytar Ö, Tuncer A. Anafilaksid klinik, tedavi ve korunma. Katki Pediatri Dergisi 2012;34:53–68.
19. Simons FE, Gu X, Simons KJ. Epinephrine absorption in adults: intramuscular versus subcutaneous injection. J Allergy Clin Immunol 2001;108:871–3.
20. Sekerel BE. İnek sütü protein alerjisinde rasyonel formula kullanımı. In: Sekerel BE, editor. A’dan Z’ye İnek Sütü Protein Alerjisi. 1st ed. Ankara: Ankamat Basım; 2016. p. 54.