EDITORIAL

Cow's milk allergy: how to deal with it

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Cow's milk allergy (CMA) is one of the most frequent allergic pathologies in early childhood, affecting up to 7.5 % of infants[1,2]. Epidemiologically, it has been noted that those children who present with IgE-mediated CMA not only have a higher incidence of inhalant sensitisation, but they also show a general higher incidence of other food allergies, including egg proteins[3].

The study by Garcia-Ara et al. in this issue of Allergologia et Immunopathologia[4] underlines the fact that even a small amount of milk may elicit allergic reactions. The clinical picture, including gastrointestinal, dermatologic, respiratory symptoms, or even systemic anaphylaxis, may appear from the first weeks of life even in exclusively breastfed children[5] and, even though most patients become tolerant during the first years of life, 15 % of infants with IgE-mediated CMA retain their sensitivity through their second decade of life. Moreover, 35 % express allergic reactions to other foods[6]. On the other hand, it has been discovered that those who become tolerant show a mucosal induction of tolerance against dietary antigens that is associated with the development of CD4+ CD25+ regulatory T (Treg) cells[7]. These cells are expressed at higher frequencies in this group of patients if compared with children who maintain clinically active CMA. Also, as found in the research developed by Martorell et al. and published in this issue[8], it seems that the population who may become tolerant to cow's milk protein presents, when first tested, a lower concentration of specific serum IgE, if compared with the population with lasting allergy.

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In clinical practice, when a patient needs to be investigated for suspected CMA, the allergist collects a detailed history, that should be followed by a Skin Prick Test (SPT) and by the detection of specific IgE to cow's milk, which is considered as a good method for predicting clinical reactivity at a specific moment[8]. Especially in the paediatric population, quantification of specific IgE against cow's milk proteins is a useful test in the diagnosis of symptomatic CMA and has proved to be a useful method to predict the outcome of oral food challenge test; thus as pointed out in both the studies by Garcia-Ara and by Martorell, it could eliminate the need to perform oral challenges tests in a significant number of children[4,8].

Yet, in those cases in which the history reported by the patient is highly predictive of CMA, and the SPT and the search for specific IgE to cow's milk are negative, an elimination diet and a challenge test are required.

In general, though the gold standard for the diagnosis of CMA is a food challenge after a period of elimination, which is actually the only definitive way to establish or exclude food allergy. This technique has positive and negative predictive accuracies in excess of 95 %[6]. The test, following a subjective assessment, requires a lot of time and is associated, even though not so frequently, to the risk of anaphylactic shock. Protocols start with low-doses of milk that are increasingly administrated in a short period of time, until the given dose is considered as a maximum of intake. When performing the challenge, an allergic response may occur in different organ systems, such as skin, upper and lower respiratory tract and gastrointestinal tract. At the end of the test, though, the allergist can actually confirm the tolerance or the presence of a clinical reactivity to cow's milk. The main problem related with such a proce-

dure, though, is the cost of it in terms of both time and money.

Nonetheless, clinicians know that a challenge is not risk free[9], which could represent a problem both for those doctors who perform the test and for the patient or his/her parents. Several attempts have been made to find a test result that could avoid the oral challenge. An interesting method is suggested by Garcia-Ara[4]: in his study, the author, by retrospectively analysing the results of positive oral challenge tests in patients with milk allergy, finds an inverse association between the dose of the challenge test able to elicit an allergic reaction and the level of specific IgE to milk. His data confirm that patients with higher cow's milk specific IgE are more likely to present a positive oral challenge test, even when low doses of milk are administered. Moreover, these patients are more likely to have respiratory symptoms appearing during the test.

Thus, in order to avoid oral challenge, on the basis of previous tests, Martorell[8] suggests monitoring specific cow's milk IgE levels since these are actually good predictors of tolerance or clinical reactivity.

Other studies have actually focused on the relationship between specific IgE to cow's milk and the outcome of the challenge with milk, validating a strong association mainly in children younger than 2.5 years. However, these studies have considered cut-offs that were considerably different[10]. The European Academy of Allergology and Clinical Immunology (EAACI) has indeed stated that "*food challenge may be avoided in selected cases where positive test results make challenge unnecessary as is the case in children with positive skin prick test to egg and specific IgE (CAP) above a certain level from 0.35 to 17.5 KUA/l, in which the probability of a positive challenge outcome exceeds 95 %*"[11]. Thus, what could be stated at last is that, even though food challenge is a very important tool in detecting milk allergy and in reaching a definitive diagnosis, the clinical picture, together with the SPT and the specific IgE detection may be sufficient, especially in children under 2.5 years of age.

As for the definitive treatment of milk allergy, the matter remains unsolved. The avoidance of milk, dairy products, and milk-containing food is first of all very difficult, especially in infants and adolescents, and secondly it could induce psychological problems[12]. In the literature, there is little evidence of specific oral tolerance induction as a possible intervention in humans. Moreover, oral food desensitisation does not always solve the problem completely. In those cases in which clinical tolerance is not definitively reached, it could actually last as long as the patients keeps consuming milk on a regular base. Furthermore, even a partial tolerance, when reached, results in a striking improvement in quality of life[13].

Nowadays, physicians are increasingly asked to evaluate patients for possible food allergy. In any case in which a child presents with a suspicion of CMA and with gastrointestinal, respiratory and/or cutaneous symptoms, diagnosis should be considered. Clinicians need to reach an accurate diagnosis, which is essential, in order to reassure parents and also to set an adequate treatment which can actually decrease the risk of allergic reactions.

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