Revista de Gastroenterología de México. 2020;85(4):379–381

REVISTA DE GASTROENTEROLOGÍA DE MÉXICO
www.elsevier.es/rgmx

EDITORIAL

# Cow's milk protein allergy in pediatric patients: The vision of the Latin American Society for Pediatric Gastroenterology, Hepatology and Nutrition☆

## Alergia a proteínas de leche de vaca en pacientes pediátricos: visión de la Sociedad Latinoamericana de Gastroenterología, Hepatología y Nutrición Pediátrica

Cow's milk protein allergy (CMPA) is a clinical entity associated with an adverse immune response to some of cow's milk protein fractions.[1] It is a frequent problem in pediatric clinical practice and its complexity lies both in its pathophysiology, in which gut-associated lymphoid tissue (GALT) is involved, and in a broad clinical spectrum, which besides gastrointestinal manifestations, can be expressed in the skin and upper and lower respiratory tracts.[2,3]

In a recent issue of the *Revista de Gastroenterología de México*,[4] an original article was published, in which a survey was applied to explore the knowledge of pediatric gastroenterologists (PGs), members of the Latin American Society for Pediatric Gastroenterology, Hepatology and Nutrition (LASPGHAN), regarding international consensuses and diagnostic guidelines on CMPA in pediatric patients, as well as the application of that knowledge in their clinical practice. A Latin American consensus and the diagnostic-therapeutic guidelines on CMPA formulated by PGs and published in 2012 and 2014, respectively, were the reference parameters utilized to determine the results of the survey.[3,5] The central finding related to knowledge of the two documents was that, even though 79% of the physicians surveyed were familiar with them, only 17% used them as guides in their daily diagnostic-therapeutic approach. The knowledge of Latin American PGs about the international guidelines developed by expert academic groups in North America and the European Union[6,7] was 37 percentage points lower than the knowledge of the reference documents. Rather than being a result of insufficient understanding, the lack of strict adherence to the parameters could be explained by a process of adaptation to the local and regional availability of diagnostic resources, such as skin prick testing (SPT), which identifies IgE-mediated allergy,[3] and serum IgE quantification against the protein fractions of cow's milk, or by not having the option of consulting with a pediatric allergist. The heuristic thinking that clinicians develop in their daily practice is a largely unconscious and automatic mental process for resolving problems based on theoretic knowledge and daily clinical experience[8] that ultimately guides their diagnostic and therapeutic approach. The lack of adherence to clinical practice guidelines or consensuses is not an unusual situation and has been described in other pathologies of pediatric gastroenterology, such as gastrointestinal functional disorders.[9] Pragmatically, diagnostic guidelines and consensuses could be considered general guides for supporting the clinician in his/her diagnostic-therapeutic approach, within the context of available resources and clinical experience.

The oral food challenge deserves special attention. Despite its limitations and the difficulty in interpreting subjective manifestations in infants and preschoolers, as well as the absence of a comprehensive biologic marker, it is a clinical diagnostic alternative that has remained a reference parameter over time, enabling adequate diagnostic decisions to be made in the majority of cases.[3,10] The non-ratification of the diagnosis of CMPA by means of a challenge test can be consequential in relation to the immediate and middle-term nutritional intervention, because the patient will not receive the specialized formula that is indicated, most likely increasing the institutional or family costs of his/her treatment.[11] In the present survey, the frequency of use of the oral food challenge was reasonably high, albeit not

☆ Please cite this article as: Larrosa-Haro A. Alergia a proteínas de leche de vaca en pacientes pediátricos: visión de la Sociedad Latinoamericana de Gastroenterología, Hepatología y Nutrición Pediátrica. Revista de Gastroenterología de México. 2020;85:379–381.

greatly systematized. The published information on when, where, with what, and how to perform that test of clinical calculation differs importantly among diverse authors or organizations. Despite the fact that there are solid proposals in the different clinical practice guidelines and consensuses, there is still no universal and systematized approach that enables the experience between groups managing pediatric patients with CMPA to be compared.[3] The double-blind, placebo-controlled food challenge test[12] is considered the reference standard but it is not very practical and is used in selected cases and research protocols. In clinical practice, the simple oral food challenge test is a feasible and efficacious alternative.[3]

One-fourth of the PGs surveyed performed an upper endoscopy in the evaluation of almost half their cases. Even though patients with CMPA can have inflammatory changes and other alterations, such as nodular lymphoid hyperplasia and flattened villi,[13] endoscopy is not considered a diagnostic method for CMPA, given that those alterations can be related to other clinical entities. In such a context, it is important to consider that clinical practice guidelines are based on an established object of study, in this case CMPA, as well as on predetermined pathophysiologic conditions, such as IgE-mediated and non-IgE-mediated allergy. Nevertheless, the clinician receives patients that are not diagnosed with CMPA, but rather that present with specific clinical manifestations that are interpreted and explained in different ways by the parents. Therefore, the decision to perform upper endoscopy could be related to the clinical suspicion of entities different from CMPA that can have similar clinical signs, such as gastroesophageal reflux disease, eosinophilic esophagitis, or the need to take duodenal biopsies when celiac disease is suspected.

CMPA is an interesting pathophysiologic model, in the sense that the initial event is related to the exposure of cow's milk protein fractions to the intestinal immune system at the level of the apical membrane of the enterocytes, and that the core idea of the intervention is the temporary elimination of those macronutrients from the patient's diet, or that of the mother, if breastmilk-mediated allergy is suspected. The therapeutic approach of the PGs surveyed reasonably adhered to the recommendations regarding treatment intention and formula selection. However, significant difficulties identified by the survey were the specific lack of availability of specialized formulas, such as the extensively hydrolyzed formulas and those based on amino acids or hydrolyzed rice protein, in certain regions of Latin America, or the economic difficulty of the parents or healthcare institutions to acquire the prescribed formula.

The survey conducted by the Food Allergy Working Group of the LASPGHAN[4] can be considered an exploratory study, which together with the 2014 survey, appears to constitute the beginning of a process of research and medical education on CMPA, in an ambitious attempt to encompass the complex universe that is Latin America. Despite being a study with a non-representative sample, by not having carried out random, stratified sampling that would have enabled a representative and proportional sample of the participating countries, it clearly identified the position of the PGs surveyed, with respect to their knowledge and application of the current diagnostic-therapeutic guidelines and consensuses on CMPA, complying with the aim of the working group. In fact, exploratory studies are a way to frame a study objective and are the first level of awareness of a problem, enabling the proposal of questions for the following stages.

The development of methodology for analyzing the quality of medical evidence has revolutionized diagnostic processes and medical decision-making, placing medical practice guidelines and consensuses at the highest levels as performance tools in the context of evidence-based medicine.[14] From that viewpoint, exploring the position on CMPA of the PGs that belong to the LASPGHAN provides a starting point for carrying out medical education and clinical and epidemiologic research. In a recent publication of the World Allergy Organization Diagnosis and Rationale for Action against Cow's Milk Allergy (DRACMA) clinical practice guidelines,[15] a flexible diagnostic and therapeutic approach is proposed that enables current evidence to be adapted to the particular conditions of the patients, which can be pertinent in the Latin American pediatric population. Carrying out that task throughout the extensive territory of Latin America, made up of countries with enormous cultural diversity and different levels of development, is complex but can be supported by the free or low-cost digital communication resources currently available.

## Financial disclosure

No financial support was received in relation to this article.

## Conflict of interest

The authors declare that there is no conflict of interest.

## References

1. Flom JD, Sicherer S. Epidemiology of cow's milk allergy. Nutrients. 2019;11:1051, http://dx.doi.org/10.3390/nu11051051.
2. Fiocchi A, Dahda L, Dupont C, et al. Cow's milk allergy: towards an update of DRACMA guidelines. World Allergy Organ J. 2016;9:35, http://dx.doi.org/10.1186/s40413-016-0125-0.
3. Montijo-Barrios E, López-Ugalde MV, Ramírez-Mayans J, et al. Guía latinoamericana para el diagnóstico y tratamiento de alergia a las proteínas de la leche de vaca (GL-APLV). Rev Invest Clín. 2014;66:S9–72. PMID: 25706585.
4. Toca MC, Roman-Riechmann E, Vázquez-Frías R, et al. Conocimiento sobre el diagnóstico y el tratamiento de la alergia a las proteínas de la leche de vaca por un grupo de gastroenterólogos pediatras en Iberolatinoamérica: resultado de la encuesta del Grupo de Trabajo de Alergia Alimentaria de la Sociedad Latinoamericana de Gastroenterología, Hepatología y Nutrición Pediátrica. Rev Gastroenterol Mex. 2019, http://dx.doi.org/10.1016/j.rgmx.2019.08.002.
5. Toca MC, Sosa PC, Furnes R, et al. Consenso ibero latinoamericano en el diagnóstico y tratamiento de la alergia a la proteína de leche de vaca. J Food Allergy. 2012;1:353–66.
6. Boyce JA, Assa'ad A, Burks AW, et al. Guidelines for the diagnosis and management of food allergy in the United States: report of the NIAID sponsored expert panel. J Allergy Clin Immunol. 2010;126:S1–58, http://dx.doi.org/10.1016/j.jaci.2010.10.007.
7. Koletzko S, Niggemann B, Arato A, et al. Diagnostic approach and management of cow's milk protein allergy in infants and children: ESPGHAN GI Committee practi-

cal guidelines. J Pediatr Gastroenterol Nutr. 2012;55:221–9, http://dx.doi.org/10.1097/MPG.0b013e31825c9482.
8. Marewski JN, Gigerenzer G. Heuristic decision making in medicine. Dialogues Clin Neurosci. 2012;14:77–89. PMID: 22577307.
9. Jang HJ, Chung JY, Seo JH, Moon JS, Choe BH, Shim JO. Nationwide Survey for Application of ROME IV Criteria and Clinical Practice for Functional Constipation in Children. J Korean Med Sci. 2019;34:1–11, http://dx.doi.org/10.3346/jkms.2019.34.e183.
10. Järvinen K, Sicherer SH. Diagnostic oral food challenges: Procedures and biomarkers. J Immunol Methods. 2012;383:30–8, http://dx.doi.org/10.1016/j.jim.2012.02.019.
11. Álvarez-López MC, Larrosa-Haro A, Vásquez-Garibay EM, Cepeda-Vélez A. Frecuencia de alergia/hipersensibilidad a proteínas de leche de vaca en niños menores de 36 meses de edad con síntomas de enfermedad por reflujo gastroesofágico. Rev Gastroenterol Mex. 2009;74 Supl. 2:156.
12. Sampson H, van Wijk R, Bindslev-Jensen C, Sicherer S, Teuber S, Burks W, et al. Standardizing double-blind, placebo-controlled oral food challenges: American Academy of Allergy, Asthma & Immunology-European Academy of Allergy and Clinical Immunology PRACTALL consensus report. J Allergy Clin Immunol. 2012;130:1260–74, http://dx.doi.org/10.1016/j.jaci.2012.10.017.
13. Coello-Ramírez P, Larrosa-Haro A. Gastrointestinal occult hemorrhage and gastroduodenitis in cow's milk protein intolerance. J Pediatr Gastroenterol Nutr. 1984;3:215–8 http://www.ncbi.nlm.nih.gov/pubmed/6707841
14. Sox HC, Higgins MC, Owens DK. Medical Decision Making. 2nd ed Oxford: John Wiley & Sons; 2013.
15. Dahdah L, Arasi S, Valluzzi RL, Fierro V, Fiocchi A. How guideline can shape clinical practice globally: the diagnosis and rationale for action against cow's milk allergy experience. Curr Opin Allergy Clin Immunol. 2019;19:185–91, http://dx.doi.org/10.1097/ACI.0000000000000513.

A. Larrosa-Haro*
*Instituto de Nutrición Humana, Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara, Mexico*

*Corresponding author at: Instituto de Nutrición Humana, Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara, Salvador Quevedo y Zubieta # 350, Col. Independencia, CP 44340, Guadalajara, Jalisco, Mexico.
*E-mail address:* alfredo.larrosa@academicos.udg.mx