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Case Report

Oral Desensitization in Nursling with Cow's Milk Allergy

Abstract

Food allergy is a major public health problem affecting nearly 10 % of children in most industrialized countries. Unfortunately, there are no effective therapies for food allergy, relegating patients to simply avoid the offending foods and treating the reactions which occur on accidental exposure. Recently however, studies suggest that food immunotherapy may provide a promising new approach to food allergy, particularly using the oral form of immunotherapy (OIT). Enthusiasm for this approach though must be tempered because of the significant allergic reactions that often occur with OIT that tends to limit its use to patients with less severe disease. Actually this technique of desensitization is applied in child with ages over 5 years old, because many investigators think that this is the frontier from which the allergy is persistent all the life, and before this age the possibilities of natural tolerance to milk is very much probability. In contrast to this, are few investigational groups dedicated to try to desensitize children under 1 years old, and less in the first 6 months of the life, due to the high possibilities of secondary reactions, especially anaphylaxis.

Clinical Case

Nursling with 6 months old who is send to the Pediatric Allergy Unit from his Health Center for having presented, with 5,5 months old an urticarial reaction with great wheals and angioedema areas in the face, after the eating artificial feeding.

In the first visit at our Unit come both parents and they said that they were witnesses when the reaction happened. They referred that until this moment, the nursling was eating exclusive breastfeeding and they had introduced, only, natural orange juice diluted with water, in small amount two or three times in a day.

In the moment of the birth, they decided the breastfeeding although the first days of the infant life he received infant cow's milk in Maternity Unit of the hospital while the mother was in the Intensive Care Unit due to complications that arose at the end of the gestation.

Familiar history

The parents said that they had some family members with different allergies (rhinitis, asthma, etc.). The father presented an allergy asthma and rhinoconjunctivitis process with sensitization to Dermatophagoides pteronissinus and Dermatophagoides farinae, besides grass and olive pollen. The mother presented an allergy rhinitis with sensitization at the same mites, and she was diagnosed of Oral Allergy Syndrome when she ate shrimps, and this process had worsened during the pregnancy due to Tropomiosins sensitization.

Paternal and maternal grandparents also referred symptoms of respiratory illnesses due to allergy process.

They have other child of 4 years old without allergy problems.

Other illnesses in family history were Insulin Dependent Diabetes.

History of Present Illnes

The pregnancy of the mother was physiological and she referred

vomiting episodes in the three first months of the pregnancy, without medication need for the control. The mother had healthy life with sport activity and without tobacco cigarette, alcohol and other drugs.

The newborn presented APGAR 9-10-10 (1st-5th-10th minutes of life), with amniotic liquid with blood, and without need cardiopulmonary resuscitation. After the birth he was transport in incubator to the Neonatology Unit where, and when the nurses were sure that the mother cannot gave maternal lactation, the infant received artificial milk beginning with 30 ml amount each three hours and 40 ml the next day. In total he received 12 intakes of milk with a total quantity of 400 ml of milk which would correspond to 540 grams of milk proteins.

During within the first intakes the parent didn't refer any presence of complications or dermatological problems.

After the recovery of the mother, the infant began exclusively breast feeding. The maternal feeding had been variety and healthy without restriction of milk foods.

They did not observe atopic dermatitis, although the mother said that in some moments she used in the newborn skin body cleansing wipes that one of the components was milk and she saw that the areas where she applied these wipes began to be irritated during few minutes.

Case History

The parent decided to give at the infant artificial feeding. The first day the feeding bottle was prepared with continuation artificial feeding, also with cow milk prepared, using 180 milliliters of water with six scoops of milk without wheals.

The mother observed that with the first sucking movements, the child began to cry and reject the bottle, which she thought was due to the bottle nipple, insisting in the take. Five minutes later the mother saw that her child presented a reaction with facial erythema most

intensive around the mouth and with a fast evolution in crane caudal direction and the emergence of hives of different sizes that tended to meet in the skinfolds. Also the lesions of the face had a purplish color with white center and the lips began to inflame. In that moment the mother stopped the bottle feeding and the child was urgently taken to the Emergency Unit where after explore at the patient, the doctors decided to inject intramuscular corticosteroid (metilprednisolone). The child had, at all times, respiratory and cardiac frequencies in normal values moreover an oxygen level in blood between 98-100% breathing ambient air, without need oxygen supplementary.

After the finish of this process and with the suspect of Cow's Milk Protein Allergy the doctors of the Emergency Unit banned the feeding with cow milk, and the indicated a special formula with hydrolyzed casein formula.

The infant was derivate to the Pediatric Allergy Unit with preference and he was visit 3 days after. There, after talking with the mother, the nurse made a Prick test using a drop of whole milk, alfalactoalbumin, betalactoglobulin and casein. The result of this diagnostic method, using a commercial kit of Stallergens laboratory® (Lactotest®) and after 20 minutes, was consider positive with a diameters hives of 4x5 millimeters (mm) for whole milk, 3x3 mm for alfalactoalbumin, 3x4 mm for betalactoglobulin and 6x5 mm for casein with a positive control (histamine) of 3x3 mm [1].

Due to this test positivity was practice an analysis of blood at the infant and to determinate the levels of alfalactoalbumin (Bos d4), betalactoglobulin (Bos d5), casein (Bos d8), serum albumin (Bos d6) and dlactoferrin (Bos lac) with Phadiatop proceeding. The results was the next:

- n Bos d4: 13.4 UI/ml
- n Bos d5: 16.8 UI/ml
- n Bos 6: 9.76 UI/ml
- n Bos d8: 25.6 UI/ml
- n Bos lac: 4.31 UI/ml

Although the data got in Phadiatop test together with the patient clinic status give us the diagnostic of Cow's Milk Protein Allergy [2,23], it was necessary, after the parents sign the legal authorization, that the patient was subjected with an oral provocation using 1 ml of commercial milk. 2 hours after the administration of the milk, the patient presented an urticarial generalized state without breathing, digestive or cardiac symptoms, so it was no classified as anaphylaxis. The order was give him 2,5 ml of Dexclorfeniramine (Polaramine®) and the skin lesions disappeared in 10 minutes [3].

The parent were informed about the diagnostic of Cow's Milk Allergy and we offered the possibility of a novel treatment. The parent had two possibilities: in first place they could eliminated the cow's milk and foods than had this protein changing for a hydrolyzed milk, as they had been doing until that moment and having at their home adrenaline autoinjectors for administrate in case of anaphylaxis [4,18].

The second option was began in that moment the desensitization

process, thereby to get the tolerance to the milk of the infant, decreasing the risk of anaphylaxis [5].

The parent chose for the desensitization technique so that we proceeded to give at the infant dilutions of milk and water according to a protocol established in our Pediatric Allergy Unit. After give one dosage of 2,5 ml of Dextromethorphan and with precharged adrenaline for if we can need it, the first day we prepared a dilution 1/100 (1 ml of milk and 100 ml of water) administering 1 ml by the mouth and checking the infant was free of allergy symptoms. After this, and each 1 hour, we gave at the infant dosage of 2-4-8 and 16 ml of the same dilution. The symptoms presented by the baby was mild facial exanthema that stopped with a new dosage of antihistamine.

During the rest of the day the infant was under clinic vigilance in Pediatric Unit with cardiac and respiratory monitoring and we could check absence of allergy symptoms.

The second day, and using the same milk dilution 1/100 we gave him 16 ml and one hour after 32 ml with presented symptoms. Later we did a new dilution 1/10 (1 ml of milk and 10 ml of water) giving him 6-12-24 ml each hour, and the baby was asymptomatic all the day, with cardiac and respiratory frequency between normal values.

The third day we began with 24 ml of 1/10 dilution and one hour after 24 ml more, this was a total accumulative dosage of milk of 5 ml with normal tolerance.

After these three days the infant returned at his home with the parent and with the order of taken 5 ml of milk, during the mornings in the first take of the day and the rest of the food using the hydrolyzed milk avoiding new foods in the baby diet.

After one week the baby and his parent return at the Pediatric Hospital Day proceeding to administrate 10 ml of milk, en twice of 5 ml separated one hour between them. Two hours after the last dosage he presented mild facial erythema which disappeared after gave him Dexclorfeniramine.

The baby had been coming at our Hospital each week with successive increases of 20 ml, 40 ml and nowadays he is in the time of taking 60 ml of baby milk and having introduced other foods like vegetables, chicken, turkey, veal and gluten without allergy symptoms none of them. Actually we have get the total amount of 240 ml of cow milk and if the baby needs to receive more milk the diet is complementary with hydrolyzed milk. In the next weeks we are going to increase this quantity until the total amount of 500 ml of milk in a day.

Discussion

The cow's milk protein is the first antigen which a baby take contact in his life, either by transmission by the maternal milk due that these proteins includes in the normal diet of the mothers have the ability to cross the milk ducts, or due to be the first non-autologous antigen different at the maternal milk protein that the babies receive in their lives in great quantities.

Cow's Milk Protein Allergy is the name to all those clinical cases in which is possible to demonstrate an immunological mechanism [6], and must exist a direct relation between the ingestion of cow's

milk and the appearance of the symptoms. It is therefore that the immediately hypersensitivity reactions or mediated by IgE are which presented a common symptomatology, easily recognized and ascertainable.

Sometimes the infants are diagnosed of Non Mediated IgE Cow's Milk Protein Allergy. The majority of the patients present principal digestive symptoms with mild or few cutaneous reactivity, and these infants are without symptoms when the milk is retired of the diet. In these patients are more striking the diarrhea with mucus and blood, intestinal colic, gastroesophageal reflux and insomnia with risk of malnutrition.

The epidemiological dates show a variability between 2-3% with an incidence of adverse reactions of 0.5-7.5% during the first year of life. Studies developed in Spain described that the cow's milk allergy is the third cause of food allergy after egg and fish. The cow's milk present a composition with more than 40 proteins that can act as antigens. The principals allergens are betalactoglobulin, casein with different subunits, alfalactoalbumin and seroalbumin; betalactoglobulin is a protein which do not exist in the maternal milk but is eliminated in the maternal milk due the diet of the mother (this is the cause that this protein is the first awareness of the babies) [13].

In most cases the symptomatology appear when the infant start the artificial feeding after a period of maternal feeding. This is the reason why the age of beginning the symptoms is related with the age of beginning the artificial feeding, with a peak incidence between 3-4 months of life, and exceptional after the second year of life.

The reactions can be classified, as time of start, in immediately (is easy to demonstrate the role of IgE), intermediate and late. The symptoms are varied, but is possible to resume in cutaneous (erythema or perioral urticarial), digestive symptoms (diarrhea with mucus and blood or vomiting) related with the levels of alfalactoalbumin protein, respiratory symptoms (stridor, cough, nasal or ocular pruritus); and by last, the most serious cases can present anaphylaxis [12].

The diagnosis besides a complete clinical history in which is necessary to demonstrate the relation between the ingestions of cow's milk and the appearance of the clinical symptoms, we can use various techniques to help us in the confirmation of this diagnostic, although this is not all that we can do [6].

In first place one of the most simples, easier, comfortable and cheap techniques to do is Prick- Test. This technique consist on the placement of different extracts of proteins (alfalactoalbumin, betalactoglobulin, casein) besides whole milk and compare with a positive (histamine) and negative control (physiological whey) [1]. After is necessary to use a lancet and puncture the skin with the lancet crossing the drop of liquid that contains the allergen and arrive at epidermis to allow that the above allergen penetrates and contact with antigen presenting cells (APG), starting so the hypersensitive reaction and forming a wheal between 5-20 minutes later. Once elapsed time one proceeds to measure the size of the different wheals, starting with positive and negative control (the presence of a positive control without wheal indicates two situations; first and the most common is the taking of an antihistamines, or the second options are the diagnostics of anergia, special situation of the babies in which is

possible the absence of histamine in the skin; while the presence of a negative control with a wheal indicates the opposite, hyperergia due to excess of histamine in the skin in such the dermis reacts forming a wheal as consequence of low traumatism). This technique only indicates sensitization of the patient at the cow's milk protein and never must be considered allergy [7].

A second technique in the diagnostic is the determination of specific antibodies levels using quantification and that nowadays are commercialized for alfalactoalbumin, betalactoglobulin, casein, seroalbumin and lactoferrin [8]. The presence of high levels of this antibodies indicate us, like Prick-Test, sensitization of the patient; but if we want to certificate the allergy in the patient we need a correlation with the clinical history, or in case of doubt we need to do a Controlled Oral Challenges Test Food (COCTF) [9].

The COCTG consists of administering the food that we are studying as cause of the patient allergy, in small quantities trying to relate the food ingestion to the presentation of the symptoms of the allergy. Is a technique not exempt or risks and must be made only in recognized Pediatric Allergy Units, with training professionals (doctors, nurses) and with all the means appropriated for avoiding dangerous situations (high anaphylaxis, respiratory disorders, etc.) [19,20].

If the COCTG is positive, that is the patient suffers a reactions, we have two options. Until a few years these patients have forbidden the ingestion of milk or food with possibilities of containing these proteins, which cause several problems in the quality of life of the patients and their families. They might be sure that the food will not have milk and they might transport autoinjectors of adrenaline to puncture in case of anaphylaxis. And they had to use hydrolyzed milk, or if the infant had more than one year old he could drink soy milk, with the possibility of new allergic reactions at soy protein.

There are many studies published in which the authors demonstrate the incidence in quality of life and how impact in the familiar economy, increasing costs [17].

From ten years ago, we have a therapeutic weapon based on the concept of desensitization. The Specific Oral ImmunoTherapy (SOIT) also named as Specific Oral Tolerance Induction (SOTI) consists in administering milk dilutions with concentrations each higher, starting with dilution with water 1/100 (1 milliliter of milk and 100 ml of water) and increasing the total quantity of milk protein offered at the patient, changing the dilution and arriving the moment in which the patient take whole milk, depending of the tolerance capacity of the patients, sometimes is possible to arrive at the end of the technique taking 240 ml of whole milk, or sometimes the infant or child cannot increasing the dosage due to undesirable side effects [10,11,26,27].

Undoubtedly this is a technique in which we can quantify in every moment the quantity of milk proteins that we are given at the patient, different each one and depending the tolerance capacity; so some patients could tolerate 5 ml/day, others 24 ml/day or 240 ml/day (exits conversion tables with foods that contains lacteal derivate such as cheese, yogurts, etc.) [14].

Though the SOTI technique began to develop the patients were

selection with more than 5 years old, nowadays the Pediatric Allergy units accept patients under this age, coming near to desensitization in breastfed babies of 6 months old (as we show in our case). This technique has a continuous develop, and once the patient reaches the maximum tolerance dosage is necessary that all the days take the same dosage for keep the immunological memory of tolerance. Other investigations groups are trying to demonstrate that if the child stop drink of milk and after he the patient is submitted at a Controlled Oral Challenges Test Food, is possible that allergy symptoms don't show, reaching the total tolerance [15,16,22].

Conclusion

Although OFD may sometimes be successful and may be considered a valid alternative to an elimination diet, further randomized controlled trials are needed, in order to clarify some controversial points, such as the characteristics of the child undergoing OSIT, and the methods of food preparation and administration. Moreover, further studies should further investigate OSIT safety, efficacy and costs [17,24,25].

References

- Saarinen KM, Suomalainen H, Savilahti E. (2001) Diagnostic value of skin-prick and patch tests and serum eosinophil cationic protein and cow's milk-specific IgE in infants with cow's milk allergy. *Clinical and Experimental Allergy*, 31: 423-429
- Miceli Sopo S, Radzik D, Calvani M (2007) The predictive value of specific immunoglobulin E levels for the first diagnosis of cow's milk allergy. A critical analysis of pediatric literature. *Pediatr Allergy Immunol* 18: 575-582
- Alonso-Lebrero E1, Fuentes V, Zapatero L, Pérez-Bustamante S, Pineda F, et al. (2008) Goat's milk allergies in children following specific oral tolerance induction to cow's milk. *Allergol Immunopathol* 36; 180-1
- Plaza Martín AM1, Martín Mateos MA, Giner Muñoz MT, Sierra Martínez JI, et al. (2001) Challenge testing in Children with allergy to cow's milk proteins. *Allergol Immunopathol* 29: 50-4
- Järvenpää J, Paasilta M, Salmivesi S, Sannisto T, Niitty S, et al. (2014) Stability of parent-reported food allergy in six and 7-year-old children: the first 5 years of the Finnish allergy programme. *Acta Paediatr*. 12:1297-300
- Sommanus S, Kerddonfak S, Kamchaisatian W, Vilaiyuk S, Sasisakulporn C, et al. (2014) Cow's milk protein allergy: immunological response in children with cow's milk protein tolerance. *Asian Pac J Allergy Immunol* 32(2): 171-7
- Imai T, Yanagida N, Ogata M, Komata T, Tomikawa M, et al. (2014) The skin prick test is not useful in the diagnosis of the immediate type food allergy tolerance acquisition. *Allergol Int*. 63(2): 205-10
- Amin MR, Khoury JC, Assa'ad AH. (2014) Food-specific serum immunoglobulin E measurements in children presenting with food allergy. *Ann Allergy Asthma Immunol*. 112(2): 121-5
- Host A, Halken S. (2014) Cow's milk allergy: where have we come from and where are we going?. *Endocr Metab Immune Disord Drug Targets*. 14(1): 2-8
- Elizur A, Goldberg MR, Levy MB, Nachshon L, Katz Y. (2015) Oral immunotherapy in cow's milk allergic patients: course and long-term outcome according to asthma status. *Ann Allergy Asthma Immunol*. 114(3): 240-244
- Horimukai K, Hayashi K, Tsumura Y, Nomura I, Narita M, et al. (2015) Total serum IgE level influences oral food challenge tests for IgE-mediated food allergies. *Allergy*. 70(3): 334-7
- Petrus NC, Schoemaker AF, van Hoek MW, Jansen L, Jansen-van der Weide MC, et al. (2014) Remaining symptoms in half the children treated for milk allergy. *Eur J Pediatr*. 4(6): 759-65
- Jung-Wu S. (2014) Formula Selection for Management of Children With Cow's Milk Allergy Influences the Rate of Acquisition of Tolerance: A Prospective Multicenter Study. *Pediatrics*. 3: S154-5
- Calatayud CM, García AM, Aragonés AM, Caballer Bde L. (2014) Safety and efficacy profile and immunological changes associated with oral immunotherapy for IgE-mediated cow's milk allergy in children: systematic review and meta-analysis. *J Investig Allergol Clin Immunol*; 24(5): 298-307
- Lifschitz C, Szajewska H. (2015) Cow's milk allergy: evidence-based diagnosis and management for the practitioner. *Eur J Pediatr*. 174(2): 141-50
- Machinena-Spera A1, Giner-Muñoz MT, Alvaro-Lozano M, Iniesta-Benedicto R, Lozano-Blasco J, et al. (2014) Can total IgE/specific IgE ratio predict tolerance in cow's milk allergic children?. *Pediatr Allergy Immunol*. 25(8): 823-6
- Diamanti A, Fiocchi AG, Capriati T, Panetta F, Pucci N, et al. (2015) Cow's milk allergy and neonatal short bowel syndrome: comorbidity or true association? *Eur J Clin Nutr*. 69(1): 102-6
- Mehr S, Turner PJ, Joshi P, Wong M, Campbell DE, et al. (2014) Safety and clinical predictors of reacting to extensively heated cow's milk challenge in cow's milk-allergic children. *Ann Allergy Asthma Immunol*. 113(4): 425-9
- Vandenplas Y1, Abuabat A2, Al-Hammadi S3, Aly GS4, Miqdady MS, et al. (2014) Middle East Consensus Statement on the Prevention, Diagnosis, and Management of Cow's Milk Protein Allergy. *Pediatr Gastroenterol Hepatol Nutr*. 2014 Jun; 17(2):61-73. doi: 10.5223/pghn.2014.17.2.61. Epub 2014 Jun 30. Review. Erratum in: *Pediatr Gastroenterol Hepatol Nutr*. 17(3): 201.
- Vandenplas Y, De Greef E, Devreker T. (2014) Treatment of Cow's Milk Protein Allergy. *Pediatr Gastroenterol Hepatol Nutr*. 17(1): 1-5
- Pajno GB, Caminiti L, Salzano G, Crisafulli G, Aversa T, et al. (2013) Comparison between two maintenance feeding regimens after successful cow's milk oral desensitization. *Pediatr Allergy Immunol*. 24(4): 376-81
- Luyt D, Bravin K, Luyt J. (2014) Implementing specific oral tolerance induction to milk into routine clinical practice: experience from first 50 patients. *J Asthma Allergy*. 28: 7:1-9.
- Castro AP, Pastorino AC, Gushken AK, Kokron CM, Filho UD, et al. (2015) Establishing a cut-off for the serum levels of specific IgE to milk and its components for cow's milk allergy: Results from a specific population. *Allergol Immunopathol (Madr)*. 43(1): 67-72
- Nicolaou N, Tsaouri S, Priftis KN. (2014) Reintroduction of cow's milk in milk-allergic children. *Endocr Metab Immune Disord Drug Targets*. 14(1): 54-62.
- Dupont C. (2013) How to reintroduce cow's milk? *Pediatr Allergy Immunol*. 24(7): 627-32.
- Meglio P, Caminiti L, Pajno GB, Dello Iacono I, Tripodi S, et al. (2015) The oral food desensitization in the Italian allergy centres. *Eur Ann Allergy Clin Immunol*. 47(3): 68-76.
- Umetsu DT, Rachid R, Schneider LC. (2015) Oral immunotherapy and anti-IgE antibody treatment for food allergy. *World Allergy Organ J*. 8(1): 20.

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