Cow`s milk protein allergy (CMPA) Causes , Effects and Diagnosis

Isha Gupta[1]
[1]*Faculty Department of Applied sciences, Chandigarh University, Gharuan, District Mohali , Punjab, India*
Pin Code-140413
ishagupta1695@gmail.com

Abstract

Food allergy is increasing with the advancing time. CMPA is a type of gastrointestinal food allergy that develops in response to a particular milk protein that serves as an antigen. There is large scale use of cow`s milk as a feed from long time back and it`s manufacturing has been increased to many fold during and after the white revolution. In response to a particular protein there is production of antibodies which is known as IgE-mediated response. Allergy to cow milk can also be non IgE-mediated. during earlier times techniques to diagnosis of CMPA was not well developed but now there is advancement in diagnostic techniques with the development of science. CMPA is most common in developed countries than developing ones and it also depends on age group of a particular individual and is more common in infants than adults as it`s effects decreases with increase in age. IgE-mediated CMPA is more common and is easy to diagnose than non IgE - mediated. The purpose of this article is to review adverse effects of cow`s milk (non human milk)on our lives , and how it is diagnosed. So, this review article favours breast feeding over the non-human sources of milk during early stages of life. This article also informs about when and how to conclude that there is a need to eliminate CMP (cow milk protein) from the diet os the suspected individual.

Keywords: *Atopic, Cutaneous, GALT, GERD, Immunoglobulin, MHC, RAST .*

1.Introduction

Condition in which the body of the infected person`s immune system reacts to some allergen is called allergy. Common allergens are dust, pollen and mould. Adverse immune responses to dietry antigens leads to gastrointestinal food allergy. This allergy is a great problem for clinician because of the lack of diagnosis and variable symptoms appear in different patients. According to the latest research there is an increase in the food allergies in both developed and developing countries. Food allergy is very prevalent as much as 10% in western countries and the most affected are children. Among the developing countries children of china and Africa are most affected. The most important food allergens are cow`s milk and egg.[1] our main area of interest is cow`s milk protein allergy (CMPA). CMPA allergy depends on both the condition and age of the patients. It is more prevalent in infants than adults. Due to the increase in cases of patients with CMPA with the advancement in time it is required to be further studied.

2. Diagnosis

During the last decade we have developed various diagnostic techniques for food allergen. Basis of food, allergy diagnosis is the responses of the body against presence or elimination of a particular antigen (food article)[**2]**. In the future the advanced diagnosis can be done by microarray technology and by using epitopes**[3]**. The allergic reactions can affect functioning of different body organs, either skin, gastrointestinal or respiratory system. Therefore to identify the risk of a particular allergen to the affected patient it is necessary to have a broad knowledge**[4]**. It was very difficult to diagnose CMPA/CMPI before 1950. Since 1970, from 1.8% to 7.5% have been reported. In developing countries the incidence of CMPA/CMPI in infants is about 2-5%**[5].**

Corresponding author:- ishagupta1695@gmail.com

The most common symptoms of CMPA/CMPI is Atopic dermatitis (AD). Various tests and challenges were performed on AD children and approximately one third of them was having CMPA/ CMPI .Many of these children may develop immunity against CMP (cow`s milk protein) in few years, But many may develop other allergic diseases as well. It is suggested that genetic, immunologic and environmental factors play an important role in allergic responses **[6].** Even a very small amount of foreign / non self protein in human milk can induce immne activation and leads to allergic reactions. In majority of infant`s cord blood immunoglobins specific to cow`s milk proteins are detected that are the main causes of allergic activities. To prevent this allergic sensitization we can induce prenatal sensitization in infants. So, it is required to have intrauterine education. Allergy can be recovered upto 45-56% at first year of life , 60-77% at second year and upto 71-87% at third year [7].
The impact of CMPA is generally nonspecific. Due to which it is not easy to distinguish between gastroesophageal reflux disease (GERD) and CMPA and infants by simple physical observation. In infants it is generally confused with symptoms of GERD and also with dyspepsia or abdominal pain, (gastrointestinal disorders or lactose intolerance) . Therefore, it is a great challenge to distinguish between these and make a correct treatment [8].

3. Effects of CMPA on the gastrointestine of humans

Our gut has developed various barriers to prevent us from various foreign antigens. Barriers can be specific or non specific. The non specific or non-immunological mechanisms include the intestinal mucosal barrier, the intestinal motility, secretion of mucus, gastric acidity, enzymes etc. The specific barriers include the production of various immunoglobulins that interact with antigen and protect us from them. This antigrn and antibody interaction occurs in Gut Associated Lymphoid Tissue (GALT). Inside the GALT there are present various immune cells like- antigen presenting cells, dendritic cells etc, these cells play an important role in the development of a immune response. These cells helps in proceesing of these foreign antigens and these act as presenting cells i.e they present it on a major histocompatibility complex (MHC) class II receptor to the T cells, due to which naïve T cells are transformed into the active T-cells ,that result in immune response activation.

Recent studies have suggested that there is a role of human enterocytes in capturing soluble antigens and selective activation of CD 8+ T cells with has suppressive function. According to recent studies it is suggested that enterocytes can help in regulation of speed and kind of absorption of these ingested antigens. Mucus also has an important function as it can also act as a barrier. M cells (Microfold cells) which are present in the duodenum, also helps these protein antigens to cross the epithelial barrier by transcytosis]. There is paracellular diffusion of food proteins through the epithelial layer, that leads tonproduction of various proinflammatory cytokines**[9].**
All these responses will ultimately leads to the activation of our immune system and various allergic reactions.

4. Exploration of Literature

Immune reaction against food allergies can be either IgE-mediated, non-IgE-mediated (T-cell-mediated) and combined IgE- and T-cell-mediated**.** CMPA is the IgE-mediated reactions and CMPI (cow`s milk protein intolerance) is a non-IgE- mediated immune response against CMP (cow milk protein). The diagnosis of IgE-mediated immunity is much easier than the IgE-non mediated**[10].** IgE-mediated responses are basically the imunological mechanisms and are better identified than non-IgE-mediated and the development of symptoms are also rapid i.e after the contact with the antigen it may take from several minutes to several hours . Therefore, it is referred as " Immediate Hypersensitivity"[9].

In one research 2 groups of infants were observed, first group included the infants which reacted to little amount of cow`s milk in few minutes or less than an hour, these give positive results on skin prick test

and RAST (radioallergosorbent test). The second group included the infants with development of allergic reactions against cow`s milk in one hour or longer time period, the reactions shown by them not IgE-mediated. therefore the result of development of cow`s milk allergy is dependent on both atopic constitution and age of a particular infant[11]. Prevalence of the allergy is estimated at age group of 2 and it decreases with the increase in age (approx 5% higher in children).[2]· Prevalence of food allergy is 2% in adults and 6% of young children[12]. In one research 1,633 newborn babies are observed for first year of their life :- out of them 56 i.e 3.3% showed adverse reactions and 6 (0.36%) were confirmed with cow`s milk. Out of the total children with cow milk allergy 83% were having first degree relatives with the same disease and 19% were without it. The result of the experiment was that, the probability of allergy increases with the first degree relative having the same **[13].** Prick test, the method of diagnosis of allergies was done on infants infected with CMPA. 2 different procedures were carried out for 3 and 1 day respectively. 409 infants were investigated and the test was done on 286 (70%) infants only. Out of them 234 (58%) infants was confirmed wth IgE-mediated allergy and 15(4%) were confirmed with IgE-non mediated allergy. 3.5 months was the average age of the reaction against cow`s milk. In 95% infants within first weeks symptoms appeared, and cutaneous signs appeared most frequently ,within 30 min of feed[14]. So, it is concluded that IgE- mediated allergy is more frequent than IgE-non mediated.

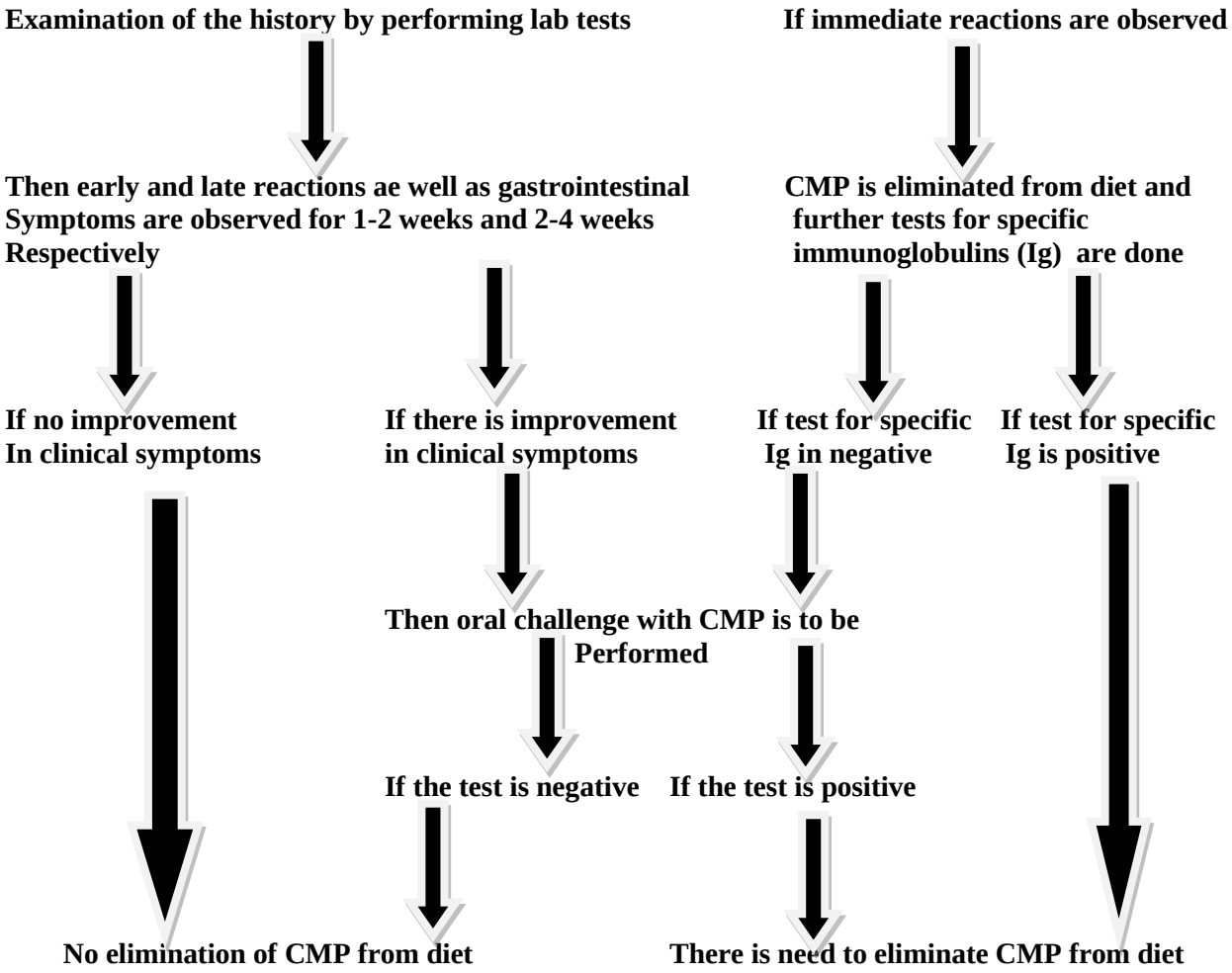
Between march 1, 2000 and February 28, 2001 infants suspected with CMPA were studied by the pediatric services of Hospital La Paz. Total births were 5367 and out of them the adverse reaction was observed in 185 infants. Among them allergy due to CMP was present in 101 (54%) infant. The incidence of CMPA was 101/5356 (1.9 %)**[15].**

In 1996 a research to determine the link between skin tests and the amount of IgE-mediated antibodies againt cow`s milk protein was done. In this 143 infants below the age of 2 years were diagnosed. In this experiment IgE against CMP was measured, followed by prick and patch tests. Out of 143 , 72 (50%) infants showed positive reactions. 22 out of these 72 showed immediate type of reactions and50 showed delayed-onset of reactions. Of the 72 infants with CMPA, elevated IgE concentrations to CMP was shown by 26% of infants, skin prick test was positive in 14% , and 44% showed positive patch test. Interestingly, in most of the patch test-positive patients, the prick test for cow's milk was not positive. Therefore the patch test is more sensitive test than prick test or RAST to detect CMPA[16].

Conclusion

CMPA is either IgE-mediated or non IgE- mediated, of which IgE-mediated is more common and is easily detected. More common in infants and developing countries. It is most prevalent at the age of 2. It`s allergic responses can affect other organs of the body as well. Most common symptom is Atopic Dermatitis (AD) or cutaneous signs. CMPA is the most prevalent of all the food allergies. Chances of an infant to have this allergy increases if his/her first order relative is diagnosed with it So, this allergy depends on the genetic constitution of that particular children. To detect the CMPA patch test is more appropriate than skin prick test and RAST. To, prevent the CMPA we should prefer breast-feeding over the milk from non- human sources.

If the symptoms revelant to CMPA are visible then there is an immediate need to eliminate the CMP from the diet of that particular individual. So, there is a procedure to diagnose as the CMPA and when it is to be eliminated from the diet of the patient.



References

[1] W. Loh and M. Tang, "The Epidemiology of Food Allergy in the Global Context", International journal of Environmental Research and Public Health., vol. 15, no. 9, **(2008)**, pp. 2043.

[2] T. Ahmed and G. J. Fuchs, "Gastrointestinal allergy to food : a review" , Journal of Diarrhoeal Research., vol. 15, no. 4, **(1997),** pp. 211-223.

[3] A. Host and S. Halken, " Cow`s milk allergy : where have we come from and where are we going? " , Endoceine, Metabolic & Immune Disorders – Drug Targets., vol. 14, no. 1, **(2014),** pp. 2-8.

[4] M. I. Fogg and J.M. Spergel, " Management of food allergies" , Expert Opinion On Pharmacotherapy., vol. 4, no. 7, **(2003),** pp. 1025-1037.

[5] A. Host , " Cow`s milk protein allergy and intolerance in infancy. Some clinical, epidermiological and immunological aspects " , Pediatric Allergy And Immunology., vol. 5, no. 1, **(1994),** pp. 1-36.

[6] E. Novembre and A. Vierucci, "Milk allergy/ intolerance and atopic dermatitis and childhood" , Journal of allergy ., vol. 56, no. 67, **(2001),** pp. 105-108.

[7] A. Host and H. P. Jacobsen, " the natural history of cow`s milk protein allergy/intolerance", European Journal of clinical Nutrition., vol. 49, no. 1, **(1995),** pp. 8-13.

[8] S. Koletzko, B. Niggemann, A. Arato, J. A. Dias, R. Heuschkel, S. Husby, M. L. Mearin, A. Papadopoulou, F. M. Ruemmele, A. Staiano, M. G. Scha¨ppi, and Y. Vandenplas, "Diagnostic Approach and Management of Cow's-Milk Protein Allergy in Infants and Children", Journal of Pediatric Gastroenterology and Nutrition., vol. 55, no. 2, **(2012),** pp. 221-229.

[9] V. Giovanna, C. Carla, C. Alfina, P. A. Domenico and L. Elena, "The immunopathogenesis of cow's milk protein allergy (CMPA)" , Italian Journal of Pediatrics., vol. 38, **(2012)**, pp. 35-38.

[10] V. Vigi and S. Fanaro, " Food allergies in early childhood. 1. General concepts, etiopathogenesis, and main clinical features", Journal of Pediatrics., vol. 52, no. 4, **(2000),** pp. 215-25.

[11] T. Foucard, "Development of food allergies with special reference to cow`s milk allergy", Journal of Pediatrics., vol. 75, **(1985),** pp. 81-177.

[12] H. A. Sampson, "Food Allergy", Journal of Allergy and Clinical Immunology., vol. 111, no. 2,**(2003),** pp. 7-540.

[13] S. Ortega, M. Aragonés , M. Gómez and N. García, "incidence of IgE-mediated allergy to cow`s milk proteins in the first year of life", Anales De Pediatria., vol. 54, no. 6,**(2001),** pp. 9-536.

[14] A. Martorell, A. M. Plaza, J. Boné, S. Nevot , M. C. García ,L.Echeverria, E. Alonso, J. Garde, B. Vila, M. Alvaro, E. Tauler , V. Hernando and M. Fernández " cow`s milk protein allergy.Amulti- center study: clinical and epidermiological aspects" , Allergologia et immunopathologia- journal., vol. 34, no. 2, **(2006)**, pp. 46-53.

[15] M. C. García , B. Martínez, D. Pena, M. Muñoz, P. Marcos, G. Sánchez and M. Esteban, "incidence of allergy to cow`s milk protein in the first year of life and its effect on consumption of hydrolyzed formulae", Journal of pediatrics., vol. 58, vol. 2, **(2003)**, pp. 5-1oo.

[16] H. Majamaa, P. Moisio, K. Holm, H. Kautiainen And K. Turjanmaa , " cow`s milk allergy: diagnostic accuracy of skin prick and patch tests and specific IgE", Allergy Journal., vol. 54, no. 4, **(1999)**, pp. 346-351.