

RETROSPECTIVE STUDY OF MANAGEMENT OF COW MILK PROTEIN ALLERGY IN INFANTS AND CHILDREN

By

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ABSTRACT

Background: Cow's milk protein allergy (CMPA) represents one of the leading causes of food allergy in infants and young children. The immune reaction mainly due to casein and β -lactoglobulin protein. Many systems are affected specially GIT, respiratory system and skin.

Aim of the work: To evaluate management of cow milk protein allergy in infant and children retrospectively.

Patient and methods: This was Retrospective study that carried out on children who admitted in Al-Azhar Assiut University Hospital and Assiut Genetic Counseling Centre. During a period between 1st January 2019 and 28th February 2021.

Result: Among the studied 150 case there were 119 (79.3%) with diarrhea, 54 (36%) with vomiting, 18 (12%) with constipation, 46 (30.7%) with abdominal distension, 53 (36%) with abdominal colic, 32 (21.3%) with eczema and 13 (8.7%) with respiratory distress, 60(40%) with occult blood in the stool, 100(66.6) with +ve prickly test, the mean cow milk related symptoms score (Co Miss score) of the studied cases was 18.95 (± 4.72 SD) with range (12-32), number of children who used amino acids based formula has affordable response 130(97%) and the number of children who used extensively hydrolyzed formula has affordable response 18(90%).

Conclusion: Treatment by formulas has significantly reduced the morbidity associated with CMPA. The long-term management of CMPA involves prevention of inadvertent allergen exposure, and implementation of precautions against anaphylaxis. Patients require at least annual reassessment for tolerance development, as well as monitoring of dietary intake and growth parameters. If appropriately managed, the prognosis of CMPA is excellent.

Keyword: Food allergy, Milk allergy, Formula types, prognosis.

INTRODUCTION

Food allergy is an adverse health effect arising from a specific immune response that occurs after exposure to some foods. The immune reaction may be immunoglobulin (Ig) E mediated, non-IgE mediated, or mixed. Cow's-milk protein (CMP) is the most common cause of food allergy in young children smaller than 3 years (**Sicherer SH, 2011**). However, CMP allergy (CMPA) with gastrointestinal tract symptoms and signs can be diagnosed in all age groups. Gastrointestinal tract symptoms and signs of CMPA are nonspecific. In infants, history and physical examination may not differentiate between gastroesophageal reflux diseases (GERD) and CMPA. In any younger children, CMPA may present with symptoms of GERD but also with abdominal pain, and may be easily confused with functional gastrointestinal diseases or lactose intolerance. Therefore, the challenge is to make a correct diagnosis (**Nielson RG et al., 2004**). Diagnosis of cow milk protein allergy is based on the personal history of some allergen, skin prick test (SPT), patch test, and measurement of milk protein specific serum IgE. SPT and IgE have a sensitivity of around 88% but specificity of 68%,

respectively, meaning these tests may be detect a milk sensitivity but may also be false-positive for other allergens (**Soares-Weiser K et al., 2014**). Mothers must be encouraged to continue breast-feeding while avoiding all milk or milk products from their own diet. This usually requires qualified dietary counseling to fully exclude most sources of CMP. If the infant receives any complementary feedings or drugs, these should be free of CMP. If the personal history suggests an immediate reaction, then the maternal elimination diet must be maintained for only 3 to 6 days. If delayed reactions are suspected (eg, allergic proctocolitis), then the diet must be continued for up to 14 days. If there is no improvement, the diagnosis is other than CMPA and the child should be further evaluated. If symptoms improve, then reintroduction of CMP into the mother's diet should then be performed. Should this challenge prove positive and the mother should continue breast-feeding while maintaining a CMP-free diet. In some breast-fed infants, proteins other than CMP (eg, soy, egg) may cause allergic reactions (**Isolauri E et al., 2005**). If the diagnosis of CMPA is confirmed, then the infant must be maintained on an elimination diet using a

therapeutic formula for at least 6 months or until 9 to 12 months of age. Infants with severe immediate IgE-mediated reactions may remain on the elimination diet for 12 or even 18 months before they are rechallenged after repeated testing for specific IgE (**Dupont C et al., 2012**). Soy protein-based formulae are tolerated by a lot of infants with CMPA, but between 10% and 14% of affected infants react to soy protein, with higher proportions in infants younger than 6 months (**klemola Tet al., 2002**). Children with CMPA that continues beyond the first 12 months of age need individualized nutritional advice (**Laitinen K et al., 2005**).

AIM OF THE WORK

The aim of this study is to evaluate management of cow milk protein allergy in infant and children retrospectively.

Ethical consideration:

1. A written informed consent was obtained from patients or their legal guardians.
2. An approval by the local ethical committee was obtained before the study.
3. The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

4. All the data of the patients and results of the study are confidential, and the patients have the right to keep it.
5. The authors received no financial support for the research, authorship, and/or publication of this article.

PATIENTS AND METHODS

This study was a Retrospective study carried at Al-Azhar Assuit University Hospital and Assuit Genetic Counseling Centre include 150 cases (80males and 70 females) diagnosed clinically and laboratory as cow milk protein allergy from 1st January 2019 and 28th February 2021.

Inclusion Criteria:

Infants and children diagnosed clinically and laboratory as cow milk protein allergy below the age of 2 years.

Exclusion Criteria:

All Children above the age of 2 years. Children with lactose intolerance, metabolic diseases and other food allergy clinically and laboratory excluded.

All the studied cases were conducted to the following:

1. **History taking:** personal history, complain, history of present illness, family history, developmental history, nutritional history (breast feeding or artificial

feeding, other food (contain animal protein or not), type of formula (Extensively hydrolyzed formula, Amino acid free formula).

2. Application of Cow milk related symptoms score (CoMiss):

The scoring ranges from 0 to 33. Each symptom has a maximal score of 6, except respiratory symptoms where the maximal score is 3.

If final score ≥ 12 , the symptoms are likely cow milk related. This could be CMPA.

If final score <12 , the symptoms are less likely cow milk. Look for other causes.

3. Examination:

General examination; pulse, respiratory rate, BP, temperature,

local examination, skin manifestation and anthropometric measures.

4. Investigation: stool analysis, prick test, CBC.

Statistical analysis:

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean, standard deviation, median and interquartile range (IQR). Significance of the obtained results was judged at the 5% level.

RESULTS

Table (1): Demographic data of studied patients with CMPA:

Demographic data	Cases(Total 150)	
Age (months)		
Range.	10-24	
Mean \pm SD.	18.01 ± 3.84	
Sex	No.	%
Female	70	46.7
Male	80	53.3
Residence	No.	%
Rural	64	42.7
Urban	86	57.3
Duration of illness (weeks)		
Range.	1 – 7	
Mean \pm SD.	4.11 ± 2.06	
Family history of allergy	No.	%
+ve	124	82,8

Table (2): Clinical data of studied cases with CMPA:

Clinical data	Cases(Total 150)	
Symptoms	No.	%
Diarrhea	119	79.3
Vomiting	54	36.0
Constipation	18	12.0
Abdominal colic	53	36.0
Signs	No.	%
Abdominal distension	46	30.7
Eczema	32	21.3
Respiratory distress	13	8.7

Table (3): Anthropometric measurements of studied cases with CMPA:

Anthropometric measurements	Cases (Total 150)
Weight(kg)	
Range.	2.5 – 4.1
Mean ± SD.	3.29 ± 0.51
Height(cm)	
Range.	70.7 – 87.6
Mean ± SD.	79.8 ± 3.6

Table (4): Distribution of studied cases of with CMPA according to CoMiss score:

CoMiss score	Cases (Total 150)
Range.	12 – 32
Mean ± SD.	18.95 ± 4.72

Table (5): Distribution of studied cases of with CMPAaccording to lab finding in studied cases:

Test	Case(Total 150)	
	No.	%
Occult blood in the stool	60	40
Skin prickle test	100	66,6

Table (6): Formula types and response to them in studied cases with CMPA:

Formula	Cases(Total 150)	
	No	%
Amino acid based formula	86,6	130
Response to it	97	126
Extensively hydrolyzed formula	13,4	20
Response to it	90	18

DISCUSSION

(CMA) is one of the most common FAs among children. CMA is defined as a reproducible adverse reaction to one or more cow's milk (CM) protein (usually casein or serum β -lactoglobulin) (**Giannetti, A et al., 2021**).

Diaferio et al., 2020 said that, Most of the patients were females (58%), and the remaining patient were male (42%), In agreement with our study which said that 70 (46.7%) females and 80 (53.3%) male.

In disagreement with our study, **Torkaman et al., 2012** study said that 51 (54.8%) children who completed the survey were males and 42 (45.2%) were females.

In our study there were 124 (82.7%) of them with positive family history of allergy ,In agreement with, **Torkaman et al., 2012** study showed that family history of atopy was identified in 77 (75%) children. 28 (27.1%) children had a positive family history through their fathers, 27 (25%) had it through their mothers, and 13(14%) had it through both their fathers and mothers. 1 (1.2%) infant had a family history through other first-degree family members and 8 (8.6%) had it through second-degree family members. Allergic rhinitis was the most common

type of family allergy which was in 50 infants (53.8%), followed by food allergy (41.9%), atopic eczema (20.4%), asthma and respiratory problems (10.8%) and adverse reactions to the medication (7.5%).

Also **Zeng Y et al., 2019** showed that among 24 affected infants definitely diagnosed with CMPA, there were 18 infants (75%) with eczema, 15 infants (62.5%) with bloody stools and 15 infants (62.5%) with diarrhea, in agreement with our study which said that, 119 (79.3%) with diarrhea, 32 (21.3%) with eczema and 60(40%) with occult blood in the stool.

In agreement with our study, **Vandenplas et al., 2015** study suggested that the findings resonate that a CoMiSS>12 may be a vital cutoff value to recognize symptoms related to CMPA in infants. A low CoMiSS even after absence of cow's milk protein and its derivatives for one month can have a considerable risk of a positive challenge test.

In agreement with our study, **Rance et al., 2010** said that the skin prick test is the most widely used test for detecting IgE-mediated food hypersensitivity. his study aimed to define firstly the correlations between results obtained with prick tests using

commercial extracts and fresh foods, and secondly the correlations between these results and those obtained with oral challenge. We compared the wheal diameters read at 15 min with commercial extracts and fresh foods, for four foods, in 430 children with suspected food allergy. For cow's milk, wheal diameters were larger with commercial extracts, but the difference was not significant. Conversely, wheal diameters were significantly larger with fresh foods for the other food allergens. Skin prick tests were positive in 40% of cases with commercial extracts and in 81.3% with fresh foods.

In agreement with our study, **E Isolauri E et al., 2018** study included 22 infants with a mean age of 6 months (95% confidence interval, 4 to 7), who were fed an extensively hydrolyzed whey formula, and 23 infants with a mean age of 17 (95% confidence interval, 4 to 7) months, who were given an amino acid-derived formula and show that hydrolyzed formulas are safe and effective for most infants; an amino acid-derived formula may be preferable for infants with multiple food allergies, especially for the maintenance of normal growth.

CONCLUSION

Treatment by formulas has significantly reduced the morbidity associated with CMPA. The long-term management of CMPA involves prevention of inadvertent allergen exposure, and implementation of precautions against anaphylaxis. Patients require at least annual reassessment for tolerance development, as well as monitoring of dietary intake and growth parameters. If appropriately managed, the prognosis of CMPA is excellent.

RECOMMENDATIONS

Further studies on large geographical scale and on larger sample size to emphasize our conclusion.

REFERENCES

1. Diaferio, L., Caimmi, D., Verga, M. C., Palladino, V., Trovè, L., Giordano, P., ... & Miniello, V. L. (2020): May Failure to Thrive in Infants Be a Clinical Marker for the Early Diagnosis of Cow's Milk Allergy?. *Nutrients*, 12(2), 466.
2. Dupont C, Chouraqui JP, de Boissieu D, et al. (2012): Dietary treatment of cows' milk protein allergy in childhood: a commentary by the Committee on Nutrition of

- the French Society of Paediatrics. Br J Nutr 2012; 107:325–338.
- 3. EisolauriE, Y Sütas, S Mäkinen-Kiljunen, S SOja, R Isosomppi, K Turjanmaa. (2018):** Efficacy and safety of hydrolyzed cow milk and amino acid-derived formulas in infants with cow milk allergy. 3476(95)70111-7.
 - 4. Giannetti, A., ToschiVespasiani, G., Ricci, G., Miniaci, A., diPalmo, E., &Pession, A. (2021):** Cow's Milk Protein Allergy as a Model of Food Allergies. Nutrients, 13(5), 1525.
 - 5. Isolauri E, Tahvanainen A, Peltola T, et al. (2005):** Breast-feeding of allergic infants. J Pediatr 2005; 134:27–32.
 - 6. klemola T, Vanto T, Juntunen-Backman K, et al. (2002):** Allergy to soy formula and to extensively hydrolyzed whey formula in infants with cow's milk allergy: a prospective, randomized study with a follow-up to the age of 2 years. J Pediatr 2002; 140:219–224.
 - 7. Laitinen K, Kalliomaki M, Poussa T, et al. (2005):** Evaluation of diet and growth in children with and without atopic eczema: follow-up study from birth to 4 years. Br J Nutr 2005; 94:565–574.
 - 8. Nielsen RG, Bindslev-Jensen C, Kruse-Andersen S, et al. (2004):** Severe gastroesophageal reflux disease and cow milk hypersensitivity in infants and children: disease association and evaluation of a new challenge procedure. J PediatrGastroenterolNutr, 2004; 39: 383 – 391.
 - 9. Rancé, F. Juchet, A. Brémont, F. Dutau, G (2010):** Department of Respiratory and Allergic Diseases in Children and Adolescents, University Hospital Purpan, Toulouse, France 2010: 52 (10), p 1031–1035.
 - 10. Sicherer SH (2011):** Epidemiology of food allergy. J Allergy Clin Immunol 2011; 127:594–602.
 - 11. Soares-Weiser K, Takwoingi Y, Panesar SS, Muraro A, Werfel T, Hoffmann-Sommergruber K, Roberts G, Halken S, Poulsen L, van Ree R, Vlieg-Boerstra BJ, Sheikh A (2014):** "The diagnosis of food allergy: a systematic review and meta-analysis" 69 (1):7686. doi:10.1111/all.12333. S2CID 21493978.

- 12. Torkaman, Mohammad & S, Afsharpaiman&Amirsalari, Susan & Saburi, Amin. (2012):** Cow's Milk Protein Allergy in Infants and Their Response to Avoidance. Journal of Clinical and Diagnostic Research. 6. 615-618.
- 13. Vandenplas Y, Dupont C, Eigenmann P, et al. (2015):** A workshop report on the development of the Cow's Milk-related symptom score awareness tool for young children. *Acta Paediatr.* 2015; 104: 334–9.
- 14. Zeng Y, Zhang J, Dong N (2019):** Assessment of Cow's milk related symptom scores in early identification of cow's milk protein allergy in Chinese infants. *BMC Pediatr.*, 19: 191-195.