Growth of Infants with Cow's Milk Allergy Fed Chicken-Based Formula

Channagan Kangwanpornsiri MD*,
Pipop Jirapinyo MD*, Narumon Densupsoontorn MD*, Jiranat Poungkaew MD*,
Renu Wongarn BA*, Nuchnoi Thammonsiri BSc*, Channarong Jatutipsompol MSc*

** Division of Nutrition, Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*

Background: *The recommended formulas for treatments of cow's milk allergy (CMA) in infants are hydrolyzed protein-based and amino acid-based formulas. However, they are not always affordable. Furthermore, some patients are still allergic to these formulas. Therefore, chicken-based formula has been innovated and used as an alternative formula to treat CMA in these infants.*
Objective: *To assess the growth of infants with CMA who consumed chicken-based formula compared to normal infants.*
Material and Method: *A prospective study was performed in 34 infants aged 3 to 24 months diagnosed as CMA at Siriraj Hospital. All subjects consumed the chicken-based formula for at least three months. The growth parameters were recorded.*
Results: *Manifestations occurred in dermatological (78.6%), respiratory (67.9%), and gastrointestinal (53.6%) systems. Mean (±SD) chicken-based formula intake was 77 (±39.6) kcal/kg/d. Weight gains are higher (35.7%), equal (10.8%), and lower (53.5%) than those of normal infants. In addition, length gains were higher (38%), equal (5%), and lower (57%) than those of normal infants. However, the difference of weight and length in chicken-based fed, cow's milk-allergic infants, and normal infants were not statistically significant ($p = 0.141$, $p = 0.192$). None of these infants had severe complications.*
Conclusion: *Growth parameters of infants fed with chicken-based formula are not different from those of normal infants.*

Keywords: *Growth, Infant, Milk allergy, Synthetic diet, Thailand*

J Med Assoc Thai 2013; 96 (1): 20-5
Full text. e-Journal: *http://jmat.mat.or.th*

Cow's milk allergy (CMA) is one of the most parent-concerned eating problems in infants. Its prevalence in infants might be between 2% and 3% and marginally lower in older children[1,2]. However, CMA was diagnosed by the symptom criteria and the clinical response after cow's milk elimination[3]. There has not been any report of the prevalence of CMA in Thailand. Ngamphaiboon et al reported that the most common symptoms of CMA in Thai children were respiratory system, followed by gastrointestinal (GI), and skin manifestations. Less common symptoms included failure to thrive, anemia, delayed speech due to chronic serous otitis media and anaphylactic shock[4].

In the aspect of treatment, in addition to avoidance of cow's milk and dairy products, exclusively breastfeeding with reducing maternal allergen load is recommended[5]. In formula-fed infants, there are special formulas used instead of cow's milk formula i.e. soy formulas, extensively hydrolyzed protein formulas (EHF) and amino acid-based formula (AAF). In 2006, the Committee on Nutrition of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) recommended that soy protein formulas should not be used in infants with CMA during the first six months of life because of the higher rate of adverse reactions to soy protein. This committee also recommended that, when soy formula is used to treat CMA in infants over six months of age, tolerance to soy-based formula be established by clinical challenge[6]. Most infants with IgE-mediated-CMA can tolerate soy-based formula, whereas almost 50% of those with non IgE-mediated-CMA react to soy[7,8]. Although hen eggs are commonly reported to be high immunogenic in infants suspected food allergy, chicken meat is rarely reported as a contributing factor to an allergic reaction. Chicken meat is a cheaper material and available throughout the world; therefore,

Correspondence to:
Kangwanpornsiri C, Division of Nutrition, Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, 2 Prannok Road, Bangkoknoi, Bangkok 10700, Thailand.
Phone: 0-2419-7000 ext. 5946, Fax: 0-2411-2535
E-mail: channagan.kan@mahidol.ac.th, teckz@mahidol.ac.th

it can be the alternative choice for infants with CMA who develop intolerance to soy-based formula and EHF. This leads to the tailor-made alternative formula or synthetic diet using chicken meat as a major ingredient. The advantages of the chicken-based formula are not only lactose-free formula but also the lower osmolarity and better palatability than EHF and AAF as well[9].

The authors' previous study showed that the chicken-based formula could be used more effectively than soy-based formula in infants with CMA[9]. The present study, which is a continuing part of the previous study, has two objectives composed of assessing of growth of infants with CMA who consumed the chicken-based formula compared to those of normal infants, and tracing any complications occurring during taking such formula.

Material and Method

Subjects

The study protocol was approved by the Siriraj Ethical Committees. Written informed consent was obtained from a parent or a caregiver of each subject. A prospective study was performed between August 2007 and May 2009 in 34 infants aged between 3 and 24 months diagnosed as CMA at Siriraj Hospital, Bangkok, Thailand. The infants had been diagnosed as CMA based on clinical criteria that symptoms would disappear after elimination of cow's milk protein and recur when cow's milk products were reintroduced again. The additional criterion was an improved clinical response after receiving EHF or AAF. Moreover, the infants who had a history of chicken meat allergy, chronic infection, systemic diseases, genetic diseases, and moderate to severe protein energy malnutrition were excluded from the present study. All subjects consumed the chicken-based formula for at least three months. The authors reviewed the presenting symptoms, family history of atopic disease in the first degree relatives, the amount of consumed milk per day, other complementary foods, and complications that occurred after being fed on chicken-based formula. Body weight and length of each subject were measured by using a Seca 767 balance scale (accuracy ±0.01 kg; Seca Corporation Weighing and Measuring Systems, MA, USA) and length-board (accuracy ±0.1 cm; Seca Corporation Weighing and Measuring Systems, MA, USA). Then comparison of the growth parameters between these subjects and normal infants by using the standard references of weight and height in Thai people aged 1 day to 19 years was performed[10].

Formula

The chicken-based formula was made from homogenizing chicken meat added with vegetable oil, glucose polymer, vitamins, and minerals in order to contain compositions as recommended by ESPGHAN Coordinated International Expert Group for Infant Formula (Table 1)[11]. The energy content of the formula was measured by bomb calorimetry. Fat was extracted by a standard method and nitrogen content was measured by micro-Kjeldahl. All vitamins and mineral contents of such formula were analyzed by the Department of Science Service, Ministry of Science and Technology, Bangkok, Thailand.

Table 1. Compositions of the chicken-based formula used in this study compared to the global standard for the composition of the infant formula

Compositions (per 100 kcal)	Chicken-based formula	Infant formula*
Energy (kcal/dL)	67.0	60.0-70.0
Protein (g)	2.0	1.8-2.0
Fat (g)	4.0	4.4-6.0
Carbohydrate (g)	7.0	9.0-14.0
Sodium (mg)	42.0	20.0-60.0
Potassium (mg)	68.0	60.0-160.0
Chloride (mg)	66.0	50.0-160.0
Calcium (mg)	90.0	50.0-140.0
Phosphorus (mg)	46.0	25.0-90.0
Magnesium (mg)	7.0	5.0-15.0
Iron (mg)	1.3	0.3-1.3
Zinc (mg)	0.9	0.5-1.5
Iodine (μg)	44.0	10.0-50.0
Copper (μg)	60.0	35.0-80.0
Vitamin A (μg)	80.0	60.0-180.0
Vitamin E (mg)	1.7	0.5-5.0
Vitamin C (mg)	12.0	8.0-30.0
Vitamin B1 (μg)	90.0	60.0-300.0
Vitamin B2 (μg)	90.0	80.0-400.0
Vitamin B6 (μg)	50.0	35.0-175.0
Niacin (mg)	1.1	0.3-1.5
Folic acid (μg)	14.0	8.0-30.0
Pantothenic acid (μg)	0.4	0.4-2.0
Biotin (μg)	1.8	1.5-7.5

* Adapted from the table of proposed compositional requirements of infant formula in ESPGHAN recommended standards for the composition of infant formula[11].

Statistical analysis

The data were analyzed by using SPSS version 13 (SPSS Inc., Chicago, IL). While the growth parameters of infants before and after being fed on the chicken-based formula were compared by using the Wilcoxon signed rank test, the growth of infants who consume chicken-based formula compared to normal infants was assessed by using Mann Whitney U Test. The demographic data and complications after feeding on chicken-based formula were described by descriptive statistics. The statistically significant p-value was less than 0.05

Results

The 34 study-participants were categorized by sex, family history of atopic disease and presenting symptoms (Table 2). The infants, who participated in this study, were 18 males and 16 females. The average age of the participants was 9.3±1.1 months (aged 3-24 months). Seventy percent of the infants had a history of CMA in the first-degree relatives. The presenting symptoms were mainly in three systems i.e. skin (82.3%), respiratory (64.7%), and gastrointestinal systems (56%). However, most of the participants had presenting manifestations in more than single system involvement. The most common symptoms in skin, respiratory, and gastrointestinal system were eczema, rhinitis, and diarrhea, respectively. The average daily amount of consumed chicken-based formula was 580 ml per day (78 ml/kg/day). Additionally, all the solid foods for infants were restricted to cow's milk products, soybean, egg, peanut, wheat, and seafood.

Average weight and length at baseline and after 3-month treatment with chicken-based formula were 7.6 kg (SD = 0.3) and 9.5 kg (SD = 0.3); 69.6 cm (SD = 1.56) and 76.6 cm (SD = 1.57), respectively. Weight gains are higher (35.7%), equal (10.8%) and lower (53.5%) than those of normal infants and length gains are higher (38%), equal (5%) and lower (57%) than those of normal infants as well. Both weight and length of the participants at the end of a 3-month study were statistically greater than those at baseline ($p<0.001$, $p<0.001$). In accordance with growth percentiles, the participants had both changes in weight and length. They had proclivities of nearly normal-range weight and length after three months ($p<0.001$, $p = 0.009$). It would be concluded that the growth parameters of the infants had been increasing continuously with statistically significance. When the authors compared the weight and length status at 3-month study with the standard references of those in Thai children and adolescents aged 1 day-19 years by using Mann Whitney U Test, there were no significant differences ($p = 0.141$, $p = 0.192$). Additionally, the increments of weight and length (growth velocity) of the participants during a 3-month study demonstrated that they did not significantly differ from those of normal infants ($p = 0.258$, $p = 0.296$). Although there was a case that still had persistent wheezing, no one had a complication after being fed on the chicken-based formula.

Table 2. Demographic data of 34 infants with CMA

Demographic data	n (%)
Sex	
Male	18 (52.9)
Female	16 (47.1)
Age at entry	
0-6 months	17 (50.0)
7-12 months	6 (17.6)
>12 months	11 (32.4)
Family history of atopic disease	
Yes	24 (70.6)
No	10 (29.4)
Clinical presentation	
Dermatological	28 (82.3)
Respiratory	22 (64.7)
Gastrointestinal	19 (56.0)

Discussion

In the present study, the authors diagnosed CMA from participants' compatible presentations. The other criteria is the improving and disappearing of those symptoms after elimination of cow's milk. The presenting symptoms in this study were mainly involved in three systems i.e. skin, respiratory, and GI respectively. These data were similar to the reviewed study for the years 1967 through 2001[12]. However, this prevalence differed from the previous study in Thai children, which found that the most common symptoms were respiratory, GI, and skin respectively.

In the modalities of the treatment in cow's milk allergy, strict elimination of cow's milk and its product is very crucial. Furthermore, other foods that are highly-allergic should be avoided. Hill et al reported on infants who were allergic to cow's milk, soy, extensively hydrolyzed formula, and several protein-containing foods such as egg, wheat, peanut, and fish. He called it "multiple food protein intolerance of infancy" (MFPI)[13]. The hypoallergenic formulas that now have been accepted for infant's feeding are only EHF and AAF, although approximately 10% and

1% of the infants with CMA are still allergic to these formulas[14]. A systemic review about comparisons of AAF with EHF showed that both formulas are equally efficacious for relieving the symptoms of CMA. However, the infants in specific subgroups (e.g. non-IgE mediated food-induced gastro-enterocolitis-proctitis syndromes with failure to thrive, severe atopic eczema, or with symptoms during exclusive breastfeeding) were likely to benefit from AAF[15]. Because most of these formulas have bitter taste, many infants often reject to drink them. They prefer their previous infant formulas, which cost much more. Therefore, many parents cannot afford them in the long-terms. The alternative formula, chicken-based, was innovated for the infants who have such problems.

There was a recent study of growth in infants with CMA after being fed on soy formula and extensively hydrolyzed whey formula. It showed that both nutritional status and growth were well in references. Although the soy formula group had low transferring receptor, there were no any statistical differences in hematologic abnormalities[16]. The other interesting study was performed to evaluate growth and tolerance comparing between a new extensively hydrolyzed formula containing lactose and an amino acid formula. The data revealed that there were no significant differences between the two groups in any of the growth measurements. Length and head circumference were similar to Euro-growth standards, but weight was slightly lower. Infants fed on EHF had significantly less vomiting than infants fed on AAF but a significantly higher frequency of soft stools[17]. Furthermore, there has not been any data about the nutritional status, growth, and safety in infants with CMA taking chicken-based formula.

While the present study is continuing from the previous study by Jirapinyo et al comparing the chicken-based formula and soy-based formula in infants with CMA that resulted in higher efficacy and effectiveness of chicken-based formula than soy based formula[9]. The presented data showed the follow-up of growth of infants fed on chicken-based formula for at least three month after starting this project. The authors found that the growth parameters (weight and length) of participants were not significantly different from those of normal infants. Additionally, the infants had normal growth velocities and no one had side effect or adverse reaction from this alternative formula. Consequently, it would be implied that the chicken-based formula might be used to be an alternative formula for infants with CMA.

However, there are some limitations to the present study such as a small number of recruited participants and short-term 3-month duration for growth and developmental outcomes. Additionally, cow's milk-allergic infants fed on modular diets as the chicken-based formula should be assessed biochemical parameters of nutritional status such as albumin, hemoglobin, and amino acid profiles that may be performed in the further study.

Conclusion

Growth parameters of infants fed on chicken-based formula are not different from those of normal infants who are not allergic to cow's milk.

Acknowledgement

This study was supported by a grant of the Siriraj Research Development Fund, Faculty of Medicine Siriraj Hospital, Mahidol University. The authors wish to thank Mr. Sutthipol Udompanthurak and Ms. Julaporn Pooliam for statistical assistance.

Potential conflicts of interest

None.

References

1. Dean T. Prevalence of allergic disorders in early childhood. Pediatr Allergy Immunol 1997; 8: 27-31.
2. Kneepkens CM, Meijer Y. Clinical practice. Diagnosis and treatment of cow's milk allergy. Eur J Pediatr 2009; 168: 891-6.
3. Host A. Cow's milk protein allergy and intolerance in infancy. Some clinical, epidemiological and immunological aspects. Pediatr Allergy Immunol 1994; 5: 1-36.
4. Ngamphaiboon J, Chatchatee P, Thongkaew T. Cow's milk allergy in Thai children. Asian Pac J Allergy Immunol 2008; 26: 199-204.
5. Crittenden RG, Bennett LE. Cow's milk allergy: a complex disorder. J Am Coll Nutr 2005; 24: 582S-91S.
6. Agostoni C, Axelsson I, Goulet O, Koletzko B, Michaelsen KF, Puntis J, et al. Soy protein infant formulae and follow-on formulae: a commentary by the ESPGHAN Committee on Nutrition. J Pediatr Gastroenterol Nutr 2006; 42: 352-61.
7. Zeiger RS, Sampson HA, Bock SA, Burks AW Jr, Harden K, Noone S, et al. Soy allergy in infants and children with IgE-associated cow's milk allergy. J Pediatr 1999; 134: 614-22.

8. Burks AW, Casteel HB, Fiedorek SC, Williams LW, Pumphrey CL. Prospective oral food challenge study of two soybean protein isolates in patients with possible milk or soy protein enterocolitis. Pediatr Allergy Immunol 1994; 5: 40-5.
9. Jirapinyo P, Densupsoontorn N, Wongarn R, Thamonsiri N. Comparisons of a chicken-based formula with soy-based formula in infants with cow milk allergy. Asia Pac J Clin Nutr 2007; 16: 711-5.
10. Division of Nutrition, Department of Health, Ministry of Public Health. The standard references of height and weight in Thai people aged 1 day - 19 years [Internet]. 2001 [cited 2009 Aug 14]. Available from: http://nutrition.anamai.moph.go.th
11. Koletzko B, Baker S, Cleghorn G, Neto UF, Gopalan S, Hernell O, et al. Global standard for the composition of infant formula: recommendations of an ESPGHAN coordinated international expert group. J Pediatr Gastroenterol Nutr 2005; 41: 584-99.
12. Host A. Frequency of cow's milk allergy in childhood. Ann Allergy Asthma Immunol 2002; 89: 33-7.
13. Hill DJ, Cameron DJ, Francis DE, Gonzalez-Andaya AM, Hosking CS. Challenge confirmation of late-onset reactions to extensively hydrolyzed formulas in infants with multiple food protein intolerance. J Allergy Clin Immunol 1995; 96: 386-94.
14. de Boissieu D, Matarazzo P, Dupont C. Allergy to extensively hydrolyzed cow milk proteins in infants: identification and treatment with an amino acid-based formula. J Pediatr 1997; 131: 744-7.
15. Hill DJ, Murch SH, Rafferty K, Wallis P, Green CJ. The efficacy of amino acid-based formulas in relieving the symptoms of cow's milk allergy: a systematic review. Clin Exp Allergy 2007; 37: 808-22.
16. Seppo L, Korpela R, Lonnerdal B, Metsaniitty L, Juntunen-Backman K, Klemola T, et al. A follow-up study of nutrient intake, nutritional status, and growth in infants with cow milk allergy fed either a soy formula or an extensively hydrolyzed whey formula. Am J Clin Nutr 2005; 82: 140-5.
17. Niggemann B, von Berg A, Bollrath C, Berdel D, Schauer U, Rieger C, et al. Safety and efficacy of a new extensively hydrolyzed formula for infants with cow's milk protein allergy. Pediatr Allergy Immunol 2008; 19: 348-54.

การเจริญเติบโตของทารกที่มีภาวะแพ้โปรตีนนมวัวหลังรับประทานนมเนื้อไก่

ชนกานต์ กังวานพรศิริ, พิภพ จิรภิญโญ, นฤมล เด่นทรัพย์สุนทรม, จิรนัฏ พวงแก้ว, เรณู วงษ์อาน, นุชน้อย ธรรมนศิริ, ชาญณรงค์ จตุทิพสมพล

ภูมิหลัง: *สูตรนมซึ่งได้รับการแนะนำให้ใช้ในการรักษาภาวะแพ้โปรตีนนมวัวอันได้แก่ นมซึ่งมีการย่อยโปรตีนอย่างละเอียด และนมกรดอะมิโนนั้นมีราคาค่อนข้างสูงในประเทศไทย นอกจากนี้ยังพบว่าในผู้ป่วยแพ้โปรตีนนมวัวบางรายอาจมีอาการแพ้ต่อนมเหล่านี้ได้ ดังนั้นการผลิตนมจากเนื้อไก่จึงเป็นทางเลือกหนึ่งในการรักษาภาวะแพ้โปรตีนนมวัวในผู้ป่วยเหล่านี้*

วัตถุประสงค์: *เพื่อประเมินการเจริญเติบโตในทารกซึ่งมีภาวะแพ้โปรตีนนมวัวและได้รับประทานนมเนื้อไก่เปรียบเทียบกับการเจริญเติบโตในทารกปกติ*

วัสดุและวิธีการ: *เริ่มศึกษาติดตามการเจริญเติบโตในทารกวัย 3-24 เดือน จำนวน 34 ราย ซึ่งได้รับการวินิจฉัยว่ามีภาวะแพ้โปรตีนนมวัวที่โรงพยาบาลศิริราช และทารกทุกรายได้รับประทานนมเนื้อไก่ติดต่อกันเป็นเวลาอย่างน้อย 3 เดือน โดยคณะผู้นิพนธ์ได้ทำการบันทึกข้อมูลการเจริญเติบโตต่าง ๆ ของผู้ป่วยไว้*

ผลการศึกษา: *อาการของภาวะแพ้โปรตีนนมวัวนั้นพบได้ใน 3 ระบบหลัก ได้แก่ ระบบผิวหนัง ระบบหายใจ และระบบทางเดินอาหาร โดยคิดเป็นร้อยละ 78.6, 67.9 และ 53.6 ค่าเฉลี่ยพลังงานจากนมเนื้อไก่ที่รับประทานต่อวันเท่ากับ 77±39.6 กิโลแคลอรีต่อน้ำหนักตัวหนึ่งกิโลกรัมต่อวัน นอกจากนี้จำนวนผู้ป่วยที่มีอัตราการเพิ่มของน้ำหนักมากกว่ากลุ่มทารกปกติคิดเป็นร้อยละ 35.7 เท่ากับกลุ่มทารกปกติคิดเป็นร้อยละ 10.8 และน้อยกว่ากลุ่มทารกปกติคิดเป็นร้อยละ 53.5 ตามลำดับ แต่ไม่มีความแตกต่างของนัยสำคัญทางสถิติ (p = 0.141) ขณะที่จำนวนผู้ป่วยที่มีอัตราการเพิ่มของส่วนสูงมากกว่ากลุ่มทารกปกติคิดเป็นร้อยละ 38 เท่ากับกลุ่มทารกปกติคิดเป็นร้อยละ 5 และน้อยกว่ากลุ่มทารกปกติคิดเป็นร้อยละ 57 และไม่มีความแตกต่างของนัยสำคัญทางสถิติเช่นเดียวกัน (p = 0.192) และในกลุ่มผู้ป่วยที่ทำการศึกษานั้นไม่พบภาวะแทรกซ้อนรุนแรงหลังรับประทานนมเนื้อไก่แต่อย่างใด*

สรุป: *การเจริญเติบโตของทารกซึ่งมีภาวะแพ้โปรตีนนมวัวและได้รับประทานนมเนื้อไก่นั้น ไม่มีความแตกต่างจากการเจริญเติบโตของทารกปกติ*