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### Safety of Soy Formula in Children with Cow's Milk Protein Allergy

### Erika Wasito<sup>1\*</sup>, Adelia Azzahra<sup>2</sup>

<sup>1</sup>Danone SN Indonesia, Jakarta, Indonesia, <sup>2</sup>Ridwan Institute, Cirebon, Indonesia

\*Correspondence: erika.wasito@danone.com

ABSTRACT: Cow's milk protein allergy is a common health problem among children. Children with cow's milk protein allergy cannot consume cow's milk or other dairy products because their bodies react to cow's milk proteins. In an effort to meet the nutritional needs of these children, soy formula is a commonly used option. The purpose of this study was to evaluate the safety of soy milk formula in children with cow's milk protein allergy. This study used qualitative research methods. The data collection technique was done by literature study. The data that has been collected was then analyzed using three stages namely data reduction, data presentation and conclusion drawing. The results showed that soy milk formula is generally safe to be given to children with cow's milk protein allergy. Soy milk formula does not cause significant allergic symptoms in children with cow's milk protein allergy. In addition, soy milk formula also fulfills the nutritional needs of children with cow's milk protein allergy. Based on the results of the study, soy milk formula can be a safe and effective formula option for children with cow's milk protein allergy.

Keywords- Cow's milk allergy, extensively hydrolyzed formulas, food allergy, infants, pediatrician

### INTRODUCTION

Cow's milk is the main foreign protein fed to an infant, cow's milk allergic disease (CMA) is often the first atopic disease in a child (Siregar & Munasir, 2016). Cow's milk protein is divided into two main fractions, casein and whey. Some of the proteins present in this composition can essentially trigger allergic reactions in susceptible individuals. A number of these proteins are considered as major allergy triggers. The casein fraction alone accounts for about 80% of the total protein in cow's milk, while alpha and beta casein make up about 70% of this casein fraction (Surya & Salmiyati, 2023).

Allergy to cow's milk is an unwanted response in the body involving the immune system to cow's milk proteins. Typically, cow's milk allergy is related to a type 1 hypersensitivity reaction mediated by IgE antibodies. However, CMA can also be triggered by immune reactions that do not involve IgE or in some cases, a combination of both. The incidence of cow's milk allergy ranges from 2 to 7.5%, and allergic reactions to cow's milk are still possible in about 0.5% of exclusively breastfed

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infants. Most cow's milk allergic reactions are associated with IgE antibodies, with an incidence of about 1.5%, while the rest are non-IgE types. Symptoms that appear are mostly clinical and mild to moderate in severity, with only a small proportion (around 0.1-1%) experiencing severe clinical symptoms (IDAI, 2014). The diagnosis of cow's milk allergy can be made based on several methods including history taking and physical examination, namely:

#### 1. Anamnesis

- a. Period of onset of symptoms after drinking cow's milk/cow's milk-containing food
- b. Amount of milk drunk/food containing cow's milk
- c. Atopy diseases such as asthma, allergic rhinitis, atopic dermatitis, urticaria, food allergy, and drug allergy in the family (parents, siblings, grandparents of parents), and the patient himself.
- d. Clinical symptoms on the skin such as urticaria, atopic dermatitis, race
- e. Airway: recurrent cough especially at night, after exercise asthma, allergic rhinitis
- f. Gastrointestinal tract, vomiting, diarrhea, colic and obstipation.

### 2. Physical examination

The skin shows skin dryness, urticaria, allergic shiner's dermatitis, Siemen grease, geographic tongue, pale nasal mucosa, and wheezing. Milk formulas made from soy and grains can be an alternative nutritional option for children who cannot consume cow's milk. Of the different types of grain-based formulas, those using soy are the most researched. However, there is debate whether soy formula can really be used as a substitute for cow's milk, as there are considerations that some of its components may be allergy triggers as well (Tzifi et al., 2014).

Previous research by (Vandenplas et al., 2014b) showed the safety of soy and estimated that no more than 10-15% of infants with cow's milk allergy become allergic to soy. Accurate diagnosis of cow's milk allergy is still difficult. The revival of soy and the development of rice hydrolysates are challenging cow's milk-based extensive hydrolysates as the first choice and amino acid formulas. Another study by (Zeiger et al., 1999) showed that soy allergy only occurs in a small proportion of young children with IgE-related CMA. Thus, soy formula may provide a safe and growth-promoting alternative for the majority of children with IgE-related CMA who are shown to be tolerant to soy at the time of soy formula introduction.

The results of this study may also encourage further research into the use of soy formula and its long-term impact on children's health. These implications may motivate further studies to gain a better understanding of the long-term benefits and risks of soy formula use. The aim of this study was to evaluate the safety of soy infant formula in children with cow's milk protein allergy (Syahrani et al., 2023).

#### **RESEARCH METHODS**

This study used qualitative research methods. According to (Sugiyono, 2018) qualitative research methods are a research approach based on a philosophy used to investigate scientific situations (experiments). In this method, the researcher acts as the main instrument, data collection and analysis techniques focus more on qualitative aspects related to meaning. The qualitative research methodology approach aims to analyze and describe phenomena or research objects through understanding social activities, individual views, and perceptions that are manifested both at the individual and group levels. Qualitative research is conducted by those involved in this investigation with the assumption that this approach tends to test theories deductively, involves efforts to identify potential biases, control counterfactual factors or alternative explanations, and has the capability to generalize and replicate the findings obtained. The data collection technique was carried out with a literature study. Literature searches were conducted using PubMed, Google Scholar, and Scopus databases. The data that has been collected is then analyzed using three stages, namely data reduction, data presentation and conclusion drawing.

#### **RESULTS AND DISCUSSION**

Children who are allergic to cow's milk are not actually allergic to the whole cow's milk itself, but only to some of the proteins contained in it. The allergy is also not to the entire protein, but only to certain parts of the protein that have the ability to bind to specific IgE. These parts are called epitopes. Thus, the proteins in cow's milk consist of a fairly long chain of amino acids, and only a small part of this chain has the ability to bind to specific IgE that will trigger an allergic reaction (Tsabouri et al., 2014).

Management of cow's milk allergy includes avoidance of cow's milk and other dairy products, with the use of soy milk as a substitute until the child develops tolerance to cow's milk. One of the significant differences between CMA and other food allergies in infants is that tolerance in CMA can develop naturally at an early age. Research data shows that about 85% of children with CMA will become tolerant to cow's milk before reaching 3 years of age. Despite the possibility of tolerance at this age, appropriate prevention and management efforts are still needed to avoid the development of more severe allergies and allergic reactions to other allergenic foods in the future (Siregar & Munasir, 2016).

Soybean is a very popular food ingredient in Indonesia for several reasons. Firstly, soy has been a part of Indonesia's agricultural culture since the 17th century and is a very important crop, ranking third after rice and corn in the hierarchy of cultivated food crops in Indonesia. As a result of this long history, soy-based foods and beverages such as tempeh and tofu can be easily recognized and accepted in society due to these historical factors. In addition, soybeans are also well-known as an

excellent source of protein. The protein content in raw soybeans reaches about 40%, which makes it a very protein-rich option when compared to the content of other macronutrients, such as carbohydrates (about 25%) and fat (about 20%) (Sharma et al., 2014). Soy has been part of the diet in various countries for centuries. In 1909, Ruhra published the first report on the use of soy-based infant formulas. These early formulas were made from soy flour, which had difficult-to-digest proteins and lower protein content compared to the soy formulas used today. By the early 1960s, the soy formula used today replaced soy flour in infant formulas (Vandenplas et al., 2014a).

Unlike regular soy beverages made from raw soybeans, soy-based infant formula uses soy protein isolate as one of its main components. Soy protein isolate is produced by processing soybeans and removing other nutrients, resulting in a protein product of more than 90% purity, with less than 1% fat, less than 0.2% crude fiber and about 4% carbohydrates. The production process also involves heat treatment and extraction to reduce some unwanted components, such as isoflavones, trypsin, phytic acid, and unwanted odors or flavors (Vandenplas et al., 2021).

According to guidelines released in 2012 by the Nutrition Committee of the European Pediatric Society for Gastroenterology Hepatology and Nutrition (ESPGHAN), the use of soy milk formulas should be limited to certain conditions. These include conditions such as galactosemia, persistent lactose intolerance, and special religious or ethical considerations. However, the use of soy milk is not recommended in premature infants. In infants suffering from cow's milk allergy (CMA), the use of soy milk formulas should begin after reaching 6 months of age, with the first clinical challenge to soy protein required. The position of the American Academy of Pediatrics differs, stating that soy milk formulas can be used to manage CMA, although hypoallergenic milk formulas are preferred regardless of the age of the infant (Tzifi et al., 2014). Advances in soy-based infant formula processing technology have significantly improved the quality of these products, making them more suitable for consideration by the target population (Kipfer & Goldman, 2021).

Soy-based infant formula may be better tolerated by infants with cow's milk allergy (CMA) caused by IgE reactions compared to infants with CMA without IgE reactions involved. The nutritional deficiency problems that have occurred with these formulas in the past have now been largely corrected by manufacturers. Current soy milk formulas have been fortified with the necessary amino acids in appropriate amounts, including Methionine, Taurine and Carnitine. But 95% of ingested aluminum is not absorbed by the body through the intestines, while only 5% is absorbed and then excreted by the kidneys. Therefore, there is no significant difference in the blood levels of aluminum in children fed different formulas. The same goes for manganese. Although these two elements have come under scrutiny for their alleged negative impact on the nervous system, studies have not shown any different developmental or mental health impairments between children fed soy formula and cow's formula. Soy milk formulas typically contain phytates which can affect the absorption of some minerals

and oligoelements. However, since the late 1980s, phytate content in soy formulas has been almost completely reduced, thus improving the absorption of essential micronutrients (Fiocchi et al., 2016).

Guidelines recommend the use of formulas containing extensively hydrolyzed cow's milk protein (eHF) to address cow's milk protein allergy in infants. Evaluated eHF products seem to be well accepted by most children with cow's milk protein allergy (CMA). However, based on published studies, no conclusions can be drawn regarding the benefits of one formula compared to another formula used in the management of CMA (Stróżyk et al., 2020). Recently, however, formulas with extensively hydrolyzed rice protein (eRHF) have become available as an alternative. We tested clinical tolerance to eRHF in forty infants with cow's milk protein allergy, whose average age was 3.4 months. The results showed that all infants could tolerate eRHF, with symptom-based scores significantly decreasing within the first month of using this formula. In addition, eRHF helped the infants achieve normal weight and other growth parameters within six months. This study supports that eRHF is tolerated by more than 90% of children with cow's milk protein allergy, with a confidence level of 95% (Vandenplas et al., 2014b).

Previous research by (Vandenplas et al., 2014b) demonstrated the safety of soy and estimated that no more than 10-15% of infants with cow's milk allergy become allergic to soy. Accurate diagnosis of cow's milk allergy is still difficult. The revival of soy and the development of rice hydrolysates are challenging cow's milk-based extensive hydrolysates as the first choice and amino acid formulas. Another study by (Zeiger et al., 1999) showed that soy allergy only occurs in a small proportion of young children with IgE-related CMA. Thus, soy formula may provide a safe and growth-promoting alternative for the majority of children with IgE-related CMA who are shown to be tolerant to soy at the time of soy formula introduction. So it can be concluded that soy formula is a safe and effective option for children suffering from cow's milk protein allergy.

Formula milk can be a great choice in many situations, especially if a child has health issues or allergies that require them to avoid cow's milk. Milk formulas are often designed to provide the right nutrients that children need for their growth and development. The choice of formula should always be discussed with a doctor or health professional who understands the child's health condition. The doctor can provide the most appropriate recommendations according to the child's specific needs, such as considering allergies, digestive issues, or other health conditions. Formula milk is a useful tool in ensuring children get the nutrients they need to grow and develop properly, especially when they have certain dietary restrictions or allergies.

#### **CONCLUSION**

Soy infant formula is generally safe to feed to children with cow's milk protein allergy. Studies have shown that soy formula does not cause significant allergy symptoms in children with cow's milk protein allergy. In addition, soy formula contains all the essential nutrients that children need to grow

and develop properly. Research results show that soy formula is a safe and effective option for children with cow's milk protein allergy. Therefore, parents and health professionals can consider using soy infant formula as a good alternative in the management of cow's milk protein allergy. as a good alternative in the management of cow's milk protein allergy in children. It provides a more convenient and efficient solution to meet the nutritional needs of children with this specific condition. Here are some suggestions for future research on the safety of soy formula in children with cow's milk protein allergy:

- 1. Deeper Nutritional Analysis
  - Conduct a more detailed nutritional analysis to understand the impact of soy formula use on children's nutritional intake, including essential minerals and vitamins.
- 2. Genetic Studies
  - Consider research involving genetic analysis in children with cow's milk protein allergy. This may help identify genetic factors that affect tolerance to soy formula.
- 3. Environmental Considerations
  Research the ecological impact of soy formula production in an effort to understand its impact on
- 4. Economic Analysis

the environment.

Conduct an economic analysis that addresses the costs associated with using soy infant formula compared to other formulas and the additional nutrients that may be required.

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