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Health Education to Improve Maternal Awareness on Soy-Based Infant Formula for Individuals with Cow's Milk Allergy in Indonesia

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Abstract

Background: Cow's milk allergy is relatively common among Indonesian infants who are not exclusively breastfed. Despite extensive hydrolyzed formula and amino acid-based formula are the recommended nutrition for infants with moderate-tosevere illness, not all parents could provide those specialized formulas, presumably due to the high cost, low availability and poor palatability. In that case, soy-based infant formula could be an alternative nutrition. However, it was unknown whether Indonesian mothers were aware on that alternative nutrition. Objective: We therefore assessed the knowledge levels of mothers who participated in an online platform of PrimaKu on the usefulness of soy-based infant formula to support growth and development of children with cow's milk allergy. Methods: The study subjects appeared to have sufficient levels of knowledge on the usefulness of soy-based infant formula for children with cow's milk allergy. Results: In addition, by increasing their knowledge on iron and fiber fortification in soy-based infant formula, e.g., through regular academic presentations, mothers could be more selective in choosing alternative nutrition for children with cow's milk allergy. Conclusion: Our study suggested that Indonesian mothers who were active in the online platform of Primaku had sufficient levels of knowledge on the usefulness of soy-based protein for managing children with cow's milk allergy.

INTRODUCTION

The primary source of nutrition for infants to adequately grow and develop is milk. Human breast milk is the best food for infants, at least until 6 months of age. Unfortunately, not all infants can be exclusively breastfed because of various conditions, e.g., the production of breastmilk is insufficient. Infant formula, which is commonly based on cow's milk, would be provided to those infants. An early introduction of cow's milk, par-

ticularly its proteinaceous component, however, could sensitize infant's immune system that might result in food allergy against cow's milk protein.

Food allergy occurs following loss of oral tolerance, resulting in allergic sensitization to certain food allergens. The cause of losing oral tolerance is elusive yet. Alterations in gut microflora's composition have been recently proposed as a possible cause (Maslowski & MacKay, 2011; Noverr & Huffnagle, 2005), because gut microbi-



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ota serves important roles in maintaining gut mucosal homeostasis through promotion of epithelial integrity and regulatory T-cell activity (Ahern et al., 2014; Atarashi et al., 2011; Faith et al., 2014; Geuking et al., 2011; Macia et al., 2012). Cow's milk allergy (CMA) is one of the first and most common food allergies among infants. The incidence of CMA peaks during early childhood (up to 3% of children's population) and tends to recede afterward (Coppola et al., 2023; Jo et al., 2014). With an estimated prevalence varies from 2% to 7.5%, CMA is the second most common food allergy among Indonesian children after egg allergy (Sumadiono et al., 2014).

Extensively hydrolyzed formula (eHF) and amino acid-based formula are recommended by the Indonesian Pediatric Society for infants with mild-to-moderate and severe cow's milk allergy, respectively. However, the high cost, limited availability as well as poor palatability of eHF or amino acid-based formula prompted some parents to provide soy protein-based formula to their infants who could not tolerate cow's milk protein (Maslin et al., 2018; Paquete et al., 2022). This behavior is not unfounded because several studies, including ours, had demonstrated the safety and health benefits (e.g., normal pattern of growth) of administering soy-based infant formula to CMA infants (Setiabudiawan et al., 2021; Sunardi et al., 2021; Vandenplas et al., 2014, 2021). This was also aligned with the guideline by European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN), which consider the usage of soy-based formula after the age of 6 months if tolerance to soy protein has been established by clinical challenge (Agostoni et al., 2006). Similarly, the American Academy of Pediatrics (AAP) considers the usage of soybased formula for term infants with an indication of galacto-semia or hereditary lactase deficiency and if vegetarian diet is preferrable (Bhatia & Greer, 2008).

The soy-based infant formulas have been modernized to improve their protein digestibility and nutritional values (Verduci et al., 2020). During production, soy-based infant formulas are heated to eliminate up to 90% of protease inhibitors present in soy. This increases the digestibility of soy protein in those formulas. Similarly, the nutritional values of soy-based infant formulas have been improved due to addition of omega-3 and omega-6 polyunsaturated fatty acids as well as minerals (Verduci et al., 2020). Of note, soy naturally contains phytic acid that could bind to certain minerals, including iron, and inhibit their absorption. Modern soy-based infant formulas

are therefore fortified with iron to mitigate this issue. In addition, many soy-based infant formulas are supplemented with ascorbic acid as well to improve the iron absorption (Lynch & Stoltzfus, 2003). Certain soy-based infant formulas are also enriched with dietary fibers, because high-fiber feeding would rebalance the gastrointestinal microbiota and improve the oral tolerance (Tan et al., 2016).

An online event had been recently conducted to raise an awareness among women on the usefulness of improved soy-based infant formula to support growth and development of children with cow's milk allergy in Indonesia. To gauge the level of awareness, consented participants had been asked to complete the same questionnaire at the beginning and the end of the event. This study was written to report the analysis of collected responses.

METHOD Subjects

An online event to raise an awareness on the usefulness of improved soy-based infant formula to support growth and development of children with cow's milk allergy in Indonesia was conducted on September 20, 2023. Target participants were mothers with at least one child who were active in the online platform of PrimaKu, which provided updated information on growth, development and health status of children in Indonesia. The event was started with two educational presentations by a pediatric allergist (on role of soy-based protein for children with cow's milk allergy) and a clinical nutrition specialist (on nutritional challenges for children with cow's milk allergy) and concluded with a discussion between the attendants and both speakers. The same questionnaire, consisting of 6 multiple choice questions, was provided at the beginning (pre-test) and the end (post-test) of the event via Google Form. The questionnaire, which had been reviewed by both speakers, was prepared in Bahasa Indonesia. Each question had 4 alternative answers, in which only one answer was correct (Supplementary). Each participant was asked for consent prior to answering the questionnaire. While there were 734 attendants who completed the pre-test, there were 572 attendants who completed the post-test. Only answers from attendants who had completed both tests (n=542)were subsequently analyzed.

Statistical analyses

Data analysis and visualization were performed using the GraphPad Prism version 10.2.3

(GraphPad Software, San Diego, CA, USA). The paired categorical data of collected answers were analyzed with the McNemar's test.

RESULT AND DISCUSION

There were 542 participants who had completed both the pre- and post-tests. Their answers were analyzed to gauge subjects' level of knowledge on the usefulness of improved soybased infant formula to support growth and development of children with cow's milk allergy and to assess whether the educational presentations could improve their levels of knowledge. These analyzed subjects were from 23 provinces across the archipelago of Indonesia (Figure 1). Majority of participants were from the island of Java, in which the province of West Java had the most participants (n=182; 33.6%). There were 8 provinces that each only had 1 participant, i.e., Aceh, Riau Islands, North Kalimantan, East Kalimantan, Central Sulawesi, Southeast Sulawesi, East Nusa Tenggara and West Papua.



Figure 1. Distribution of the analyzed subjects.

There were 542 participants who completed both pre- and post-tests of the event, in which their answers were further analyzed. The map displays the origin of those subjects. Number below the name of each province indicates number of subjects originated from the respective province.

Six multiple choice questions were asked in both pre- and post-tests. Table 1 shows that prior to the educational presentations, there were 17.7% of 542 subjects who provided all incorrect answers. Immediately after the educational presentations, this number dropped to 0.7%. In addition, the proportion of subjects who answered

most questions correctly (i.e., with 4, 5 and 6 correct answers) increased from 66.5% to 80.5%. Taken together, it suggested that the educational presentations could improve short-term levels of knowledge on the usefulness of improved soybased protein to support growth and development of children with cow's milk allergy. The first question was which alternative nutrition suited to children with cow's milk allergy. Most subjects provided the right answer (i.e., soy-based protein), in which there was an increment from the pre- (n=388; 71.6%) to post-tests (n=471; 86.9%), as shown in Table 2. The statistical analysis on the paired answers from each subject subsequently supported the notion that the educational presentations were effective in improving the relevant level of knowledge (p<0.0001).

The second question was whether mothers knew gastrointestinal-related issues faced by children with cow's milk allergy. Majority of subjects provided the right answer for both tests (i.e., disturbance in the gastrointestinal tract and deficiency of important micronutrients, such as iron). An increase in correct answers was observed from the pre- (n=373; 68.8%) to post-tests (n=447; 82.5%). The statistical analysis on the paired answers from each subject further supported the notion that the educational presentations were effective in improving the relevant level of knowledge (p<0.0001). The third question was how to improve disturbance in the gastrointestinal tract of children with cow's milk allergy. More than half of the subjects provided the right answer (i.e., providing fiber), in which a slight improvement was observed from the pre-(n=307); 56.6%) to post-tests (n=336; 62.0%). Nonetheless, the statistical analysis on the paired answers from each subject supported the notion that the educational presentations were effective in improving the relevant level of knowledge (p=0.0395).

The fourth question was how to prevent the iron deficiency in children with cow's milk allergy. Majority of subjects provided the right answer for both tests (i.e., continuing to provide foods with high levels of iron and vitamin C). An increase in correct answers was observed from the pre- (n=378; 69.7%) to post-tests (n=477; 88.0%).

Table 1. Proportion of correct answer for each question.

| | Correct Answer | | | | | | | | |
|-----------|----------------|--------|--------|----------------|---------|------------------|---------|--|--|
| | 0 | 1 | 2 | 3 | 4 | 5 | 6 | | |
| Pre-Test | 96 | 6 | 31 | 49 | 87 | 121 | 152 | | |
| n (%) | (17.7%) | (1.1%) | (5.7%) | (9.0%) | (16.1%) | (<i>22.3%</i>) | (28.1%) | | |
| Post-Test | 4 | 13 | 24 | 65 | 116 | 175 | 145 | | |
| n (%) | (0.7%) | (2.4%) | (4.4%) | (12.0%) | (21.4%) | (<i>32.3%</i>) | (26.8%) | | |

The statistical analysis on the paired answers from each subject further supported the notion that the educational presentations were effective in improving the relevant level of knowledge (p<0.0001). The fifth question was whether mothers knew the role of fiber for child's growth and development. More than half of the subjects provided the right answer (i.e., supporting the intestinal colonization of beneficial microbes, improving the microbiota profile and assisting to attenuate allergic symptoms). A moderate improvement was observed from the pre- (n=321; 59.2%) to post-tests (n=382; 70.5%). The statistical analysis on the paired answers from each subject subsequently supported the notion that the educational presentations were effective in improving the relevant level of knowledge (p<0.0001).

The final question was whether mother knew the role of iron in a child's growth and development. More than half of the subjects provided the right answer (i.e., supporting the production of erythrocytes and child's intelligence), in which a slight improvement was observed from the pre- (n=313; 57.7%) to post-tests (n=352; 64.9%). Nonetheless, the statistical analysis on the paired answers from each subject supported the notion that the educational presentations were effective in improving the relevant level of

knowledge (p=0.0068).

Paired categorical data on answers for each question were displayed on a 2x2 contingency table. The marginal homogeneity was analyzed using the McNemar's test. A statistical significance was indicated in bold if p<0.05.

Four results could be extracted from this study. Firstly, as expected, the academic presentations were useful to improve the short-term knowledge levels of the subjects. The statistical analyses on paired categorical data of all answers indicated statistical improvement in the knowledge levels of all questions. Secondly, majority of the subjects were already aware that soy-based milk could be used as an alternative nutrition for children with cow's milk allergy (71.6% and 86.9% in pre- and post-test, respectively). This finding contrasted with the recent study on Canadian parents living in Toronto, which had reported 79% of their subjects were not aware of the usefulness of soy-based milk as an alternative nutrition for those with cow's milk allergy (Soczynska et al., 2023). This suggested that subjects within this study were more informed on this topic, presumably due to their active involvement in the online platform of PrimaKu that provided updated information on growth, development and health of Indonesian children (Skranes et

Table 2. Analysis of answers for each question by using the marginal homogeneity test.

| Table 2. Analysis of answers for each question by using the marginal nomogeneity test. | | | | | | | | | | |
|--|---------------------------|----------------|---------------------------------------|-----------|--------------------------|---------|--|--|--|--|
| | Marginal Homogeneity Test | | | | | | | | | |
| Question | | Post: Wrong | Post: Correct | Row total | Odds Ratio (95% CI) | p-value | | | | |
| | Pre: Wrong | 46 | 108 | 154 | | | | | | |
| 1 | Pre: Correct | 25 | 363 | 388 | 4.320 (2.776 - 6.969) | <0.0001 | | | | |
| | Column total | 71 | 471 | 542 | (2.770 - 0.707) | | | | | |
| 2 | Pre: Wrong | 61 | 108 | 169 | | <0.0001 | | | | |
| | Pre: Correct | 34 | 339 | 373 | 3.176 (2.143 - 4.818) | | | | | |
| | Column total | 95 | 447 | 542 | (2.110 1.010) | | | | | |
| | Pre: Wrong | 128 | 107 | 235 | | | | | | |
| 3 | Pre: Correct | 78 | 229 | 307 | 1.372 (1.015 - 1.861) | 0.0395 | | | | |
| | Column total | 206 | 336 | 542 | (1.010 1.001) | | | | | |
| | Pre: Wrong | 38 | 126 | 164 | | | | | | |
| 4 — | Pre: Correct | 27 | 351 | 378 | 4.667 (3.061 - 7.359) | <0.0001 | | | | |
| | Column total | 65 | 577 | 542 | (0.001 7.00) | | | | | |
| 5 | Pre: Wrong | 109 | 112 | 221 | 2.104 | <0.0001 | | | | |
| | Pre: Correct | 51 | 270 | 321 | 2.196 (1.564 - 3.121) | | | | | |
| | Column total | 160 | 382 | 542 | (1.501 5.121) | | | | | |
| | Pre: Wrong | 111 | 118 | 229 | | , | | | | |
| 6 — | Pre: Correct | 79 | 234 | 313 | 1.494 (1.114 - 2.012) | 0.0068 | | | | |
| | Column total | 190 | 352 | 542 | (1.114 - 2.012) | | | | | |
| · · · · · · · · · · · · · · · · · · · | · | | · · · · · · · · · · · · · · · · · · · | | · | | | | | |

al., 2014). It would be interesting in the future to compare the knowledge levels of mothers who are active in an online educational platform with the ones who are inactive.

Thirdly, the knowledge levels of subjects on the role of iron were varied. Many subjects acknowledged that provision of iron, supported with ascorbic acid, would minimize the iron deficiency in children with cow's milk allergy (69.7% and 88.0% in pre- and post-test, respectively). However, only half of the subjects knew the role of iron in children growth and development (57.7% and 64.9% in pre- and post-test, respectively). Optimum growth and development of children require adequate concentrations of iron in the body to support various physiological processes, including development of central nervous system, tissue growth, expansion of blood volume, as well as activation of immune system (Armitage A & Moretti D, 2019). Iron deficiency is one of the common nutrient deficiencies among children worldwide and iron deficiency was indeed observed in children with cow's milk allergy (Lai & Yang, 2018; Woźniak et al., 2022). Thus, supplementation of iron or iron-fortified food products (e.g., improved soy-based infant formula) would be crucial to prevent iron deficiency in Indonesian children, including the ones who suffered from cow's milk allergy (Sekartini et al., 2022; Sungkar et al., 2022). Taken together, these findings suggested that awareness programs on roles of dietary iron for the growth and development of a child should be more routinely conducted to educate mothers.

Finally, despite majority of mothers knew that cow's milk allergy would cause gastrointestinal disturbances (68.8% and 82.5% in pre- and post-test, respectively), only half of the subjects understood that provision of fiber could help to improve the gastro-intestinal disturbances (56.6% and 62.0% in pre- and post-test, respectively). Subsequently, only half of the tested mothers knew the usefulness of fiber in children growth and development (59.2% and 70.5% in pre- and post-test, respectively). It has been postulated that high intakes of fibers would support the growth of beneficial microbes within the gastrointestinal tract, in which the bacterial fermentation of the dietary fiber would also release beneficial shortchain fatty acids (SCFAs), including acetate, propionate and butyrate (Maslowski & MacKay, 2011). Certain dietary fibers indeed could act as prebiotics (i.e., a substrate that is selectively utilized by host microorganisms conferring a health benefit), including fructans (fructooligosaccharides and inulin) and galactans (galactooligosaccharides) (Gibson et al., 2017). It had been reported that a supplementation of infant formula with inulin-type prebiotics containing shorter and longer chains was well tolerated and modulated the infant gut microbiota towards higher levels of Bifidobacterium species (Neumer et al., 2021). SCFAs become the main energy source for the epithelial cells lining the gastrointestinal tract and help in maintaining barrier function, regulating cell proliferation and tumor suppression, reducing oxidative DNA damage as well as regulating cytokine production (Macia et al., 2012; Maslowski & MacKay, 2011). SCFAs will help to regulate immune responses within the gastrointestinal system, which influencing the whole body, and to resolve the inflammation presumably through increased activities of tolerogenic CD103+ dendritic cells and regulatory T cells (Macia et al., 2012; Maslowski & MacKay, 2011; Tan et al., 2016; Zhang et al., 2016). This suggested that mothers should be routinely educated on dietary fibers for them to appreciate the usefulness of fiber supplementation in food products, including soy-based infant formula.

This study had several limitations. First, majority of the subjects came from the Western side of Indonesia (n=525; 96.9%). The results of this study thus may not represent the knowledge levels of all mothers across Indonesia. Second, the assessment of knowledge was performed immediately after the educational presentations. This primarily reflects the short-term knowledge and whether the knowledge would remain is questionable. In addition, all subjects were active members of PrimaKu, hence the answers might only reflect answers from subjects who were active looking for health-related advice from various internet platforms. Third, this study did not verify whether the mothers im-plemented their knowledge in their daily behaviors in caring their children.

CONCLUSION

We observed that Indonesian mothers who were active in the online platform of Primaku had sufficient levels of knowledge on the usefulness of soy-based protein for managing children with cow's milk allergy. Most subjects had an awareness that soy-based milk could be used as an alternative nutrition for children with cow's milk allergy. However, their understanding on the usefulness of iron and fiber supplementations could be further improved. Therefore, improving their knowledge on iron and fiber fortification in soy-based infant formula, such as through regular academic presentations, we would expect that

mothers would be more selective in choosing improved soy-based infant formula as an alternative nutrition for children with cow's milk allergy.

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