

Correspondence

Reply

To the Editor:

We thank the authors of the correspondence for their interest and comments.¹

Cow's milk allergy (CMA) is one of the most common food allergies in infancy, and may result in anaphylaxis and/or impose substantial burdens through various other health issues.²⁻⁴ The Strategy for Prevention of Milk Allergy by Daily Ingestion of Infant Formula in Early Infancy (SPADE) study demonstrated that the early supplementation of a small amount of cow's milk formula (CMF) can serve as an effective strategy in the primary prevention of CMA.⁵

It should be noted that this study did not aim to assess the health-promoting effects of nonexclusive breast-feeding. In addition, we had considered CMF as a source of milk antigens rather than a nutritional alternative to breast milk.

We fully understand the benefits of breast-feeding, and therefore actively recommended its continuation to both the intervention and control groups. However, we did not force exclusive breast-feeding to either group for ethical reasons, but recommended the control group to use soy formula (which is relatively popular with Okinawan people) as needed. As a consequence, both groups continued breast-feeding at similar rates, which were equal to or surpassed the average rates of the general population in Okinawa Prefecture. This indicates that the introduction of small amounts of CMF from the first month of age did not interfere with continued breast-feeding after the intervention period.

The ingestion group in our study was instructed to consume greater than or equal to 10 mL of CMF, but in reality, a relatively large number of participants ingested nearly 200 mL of CMF per day. In the dose-response analysis, however, none of the participants who ingested greater than or equal to 70 mL of CMF per week developed CMA, indicating that a dose-response effect may exist in the prevention of this allergy. Nevertheless, downstream studies are still needed to ascertain the minimum dose of cow's milk protein that is effective in preventing CMA development without discouraging breast-feeding. Although CMF was used in our study for the ease of intervention, an extraction of cow's milk protein—similar to the approach of the Two-step Egg Introduction for preventing egg allergy in High-risk Infants with eczema (PETIT) study for the prevention of hen's egg allergy⁶—may be used to provide small controlled amounts of milk antigens to elicit a protective immune response without interrupting the continuation of exclusive breast-feeding.

The vast majority of infants in our study received CMF soon after birth. This might be in conflict with international recommendations and an issue that needs to be improved, but the SPADE study was conducted on the basis of real-world behavior of the participants at multiple institutions. Although the health risks due to the loss of exclusive breast-feeding were not evaluated, the highlight of this study was the demonstration of the preventative effect on CMA development through the early introduction of cow's milk protein. Further analyses are required to comparatively examine the CMA-preventative effects between exclusive breast-feeding after birth and the early introduction of CMF.

Tetsuhiro Sakihara, MD^a

Kenta Otsuji, MD^b

Yohei Arakaki, MD^c

Kazuya Hamada, MD^d

Shiro Sugiura, MD, MPH, PhD^e

Komei Ito, MD, PhD^e

From ^athe Department of Pediatrics, Heartlife Hospital, ^bthe Department of Pediatrics, Okinawa Kyodo Hospital, ^cthe Department of Pediatrics, Naha City Hospital, and ^dthe Department of Child Health and Welfare (Pediatrics), Graduate School of Medicine, University of the Ryukyus, Okinawa, and ^ethe Department of Allergy, Aichi Children's Health and Medical Center, Aichi, Japan. E-mail: odekorin2000@yahoo.co.jp. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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