

CORRESPONDENCE

Fish oil supplementation in pregnancy and childhood allergies

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I read the article by Palmer et al. with great interest (1). The authors did a randomized placebo-controlled trial on more than seven hundred pregnant women to see whether fish oil supplementation, a rich source of n-3 long-chain polyunsaturated fatty acid (LCPUFA), given from 21 weeks' gestation until delivery will alter the cumulative incidence of IgE-mediated childhood allergic diseases. The authors could not demonstrate any significant reduction in outcome measures including eczema, asthma, allergic rhinitis and food allergy at the age of 1 or 3. One explanation put forward by the authors was a possibly inadequate dosage of n-3 LCPUFA. However, what is more essential is the compliance to treatment in both arms of the trial, regarding which the authors did not provide.

As mentioned in the paper, owing to a cessation of supply of allergen extract, cow's milk was excluded from the outcome analysis. It is an unfortunate mishap, as cow's milk is a major source of nutrition and food allergen in childhood. In the absence of skin prick test for cow's milk, one simply cannot get a clear picture of the prevalence of food allergy in the offspring.

Furthermore, the authors have not controlled for important confounders. Firstly, there was no mention of breastfeeding

in the study. Although the role of breastfeeding in determining allergic outcome in childhood remains controversial (2–5), difference in the breastfeeding rate between both groups may confound the outcome. Secondly, it is strange that dog exposure and subsequent sensitization have not been included in the analysis. A recent review suggested that dog exposure during infancy may be associated with decreased risk of allergic sensitization (6). All in all, it will be inappropriate, from what the authors have found, to conclude a lack of difference in childhood allergic diseases between both groups.

Conflict of interest

I have no conflict of interest regarding the publication of this article.

Q. U. Lee

Department of Paediatrics & Adolescent Medicine, Princess Margaret Hospital, Lai Chi Kok, Hong Kong
E-mail: leequunui@gmail.com

References

- Palmer DJ, Sullivan T, Gold MS, Prescott SL, Heddle R, Gibson RA et al. Randomized controlled trial of fish oil supplementation in pregnancy on childhood allergies. *Allergy* 2013;**68**:1370–1376.
- Gdalevich M, Mimouni D, Mimouni M. Breast-feeding and the risk of bronchial asthma in childhood: a systematic review with meta-analysis of prospective studies. *J Pediatr* 2001;**139**:261–266.
- Snijders BE, Thijs C, Dagnelie PC, Stelma FF, Mommers M, Kummeling I et al. Breast-feeding duration and infant atopic manifestations, by maternal allergic status, in the first 2 years of life (KOALA study). *J Pediatr* 2007;**151**:347–351.
- Sears MR, Greene JM, Willan AR, Taylor DR, Flannery EM, Cowan JO et al. Long-term relation between breastfeeding and development of atopy and asthma in children and young adults: a longitudinal study. *Lancet* 2002;**360**:901–907.
- Kramer MS. Breastfeeding and allergy: the evidence. *Ann Nutr Metab* 2011;**59**(Suppl 1):20–26.
- Chen CM, Tischer C, Schnappinger M, Heinrich J. The role of cats and dogs in asthma and allergy—a systematic review. *Int J Hyg Environ Health* 2010;**213**:1–31.

REPLY

Lee has raised some questions that we are pleased to address regarding our randomized controlled trial (RCT) on the effect of n-3 long-chain polyunsaturated fatty acids (LCPUFA) supplementation, predominantly as docosahexaenoic acid (DHA), in pregnancy on the cumulative incidence of IgE-mediated allergic disease in the first 3 years of life (1). As reported in our study published in the *British Medical Journal* (BMJ) (2), which focussed on eczema and food allergy outcomes over the

first year of life, compliance with the trial products was good, with <2% of mothers in each group choosing not to take any capsules. At 28 weeks' gestation, 284/368 (77.2%) of mothers in the n-3 LCPUFA group and 280/338 (79.9%) of mothers in the control group reported that they had missed 0–3 capsules per week from a total of 21 capsules (2). The cord blood concentrations of total n-3 LCPUFA, DHA and eicosapentaenoic acid in the plasma phospholipids from women in the n-3

LCPUFA group were higher (median 8.8%, 7.5% and 0.54%) compared with the control group (median 7.2%, 6.2% and 0.27%, $P < 0.0001$ for all comparisons) (2). Hence, we do not consider that lack of compliance contributed to our finding that overall n-3 LCPUFA supplementation during pregnancy did not significantly reduce IgE-associated allergic disease in the first 3 years of life.

We specifically chose the panel of allergens to be tested at 3 years of age to reflect those found to be most commonly associated with allergen sensitization in Australian children. Another study found that the most common allergens to which children are sensitized at 4 years of age are house dust mite (11.9%), grass pollen (7.8%) and cat (5.8%) (3). Dog sensitization was only reported in 2.5% of children in this study and was not associated with the presence of a dog in the household (3). In our trial, 62.9% of families in the n-3 LCPUFA group had a dog as a pet in the first 3 years of life compared with 65.7% of families in the control group ($P = 0.44$), hence dog ownership was unlikely to have influenced our trial outcomes.

More infants (96.1%) in the n-3 LCPUFA group were initially breastfed than in the control group (91.0%) (2). As breastfeeding was a postrandomization variable, we did not adjust for this in statistical analyses; however, in exploratory analyses, we found no relationship between the initiation of breastfeeding and atopic eczema or egg sensitization (2). Although the cow's milk allergen extract became unavailable from the supplier for an extended period during the 3 year assessments, cow's milk skin prick testing was performed on 666/706 (94.3%) of infants at 1 year of age, by which age 99% of infants had been introduced to cow's milk (2). We did not find a difference between the groups for cow's milk sensitization at 1 year of age, with 1.7% of infants in the n-3 LCPUFA group having a positive skin prick test compared with 1.0% of infants in the control group ($P = 0.51$) (2). This was despite more infants in the control group (79.8%) consuming cow's milk protein formula in the first 6 months of life than the n-3 LCPUFA group (72.0%) (2). Collectively, these data suggest that the small imbalance between breast-

feeding and formula feeding in the first 6 months of life did not influence the outcomes of the trial.

In summary, we thank Lee for raising their questions; however, we do not believe that any of the issues raised influenced the allergy outcomes of the children in the trial.

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Conflicts of interest

MM serves on scientific advisory boards for the Nestle Nutrition Institute, Danone and Fonterra. All associated honoraria for MM are paid to her institutions for professional development of students and early career researchers. No other authors declare conflicts of interest.

D. J. Palmer^{1,2}, T. Sullivan³ and M. Makrides^{1,4,5}

¹Women's & Children's Health Research Institute, North Adelaide, SA;

²School of Paediatrics and Child Health, University of Western Australia, Subiaco, WA;

³Data Management and Analysis Centre, University of Adelaide, Adelaide, SA;

⁴School of Paediatrics and Reproductive Health, University of Adelaide, Children, Youth,

Women's Health Service, North Adelaide, SA;

⁵Healthy Mothers, Babies and Children, South Australian Health and Medical Research Centre, North Terrace, Adelaide, SA, Australia
E-mail: maria.makrides@health.sa.gov.au

References

1. Palmer DJ, Sullivan T, Gold MS, Prescott SL, Heddle R, Gibson RA et al. Randomized controlled trial of fish oil supplementation in pregnancy on childhood allergies. *Allergy* 2013;**68**:1370–1376.
2. Palmer DJ, Sullivan T, Gold MS, Prescott SL, Heddle R, Gibson RA et al. Effect of n-3 long chain polyunsaturated fatty acids (LCPUFA) supplementation in pregnancy on infant allergies in the first year of life: a randomised controlled trial. *BMJ* 2012;**344**:e184.
3. Arshad SH, Tariq SM, Matthews S, Hakim E. Sensitization to common allergens and its association with allergic disorders at age 4 years: a whole population birth cohort study. *Pediatrics* 2001;**108**:e33.