Investigation of the association of skin barrier structure and function and the development of sensitisation to food allergens: a prospective birth cohort study

Rhaglen ymchwil: Food allergy and intolerance research
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Background

A significant recent development in the science of food allergy has been recognition that food allergen sensitisation (the precursor to food allergy) could be acquired via routes of exposure other than dietary intake, notably through skin contact. However, whilst the importance of skin exposure in driving sensitisation to food allergens is suspected, and has been clearly demonstrated in animal models, it has not been established with certainty in humans.

The skin is constantly exposed to all types of allergens from the environment, and a protective outer layer known as the “skin barrier” prevents these from easily reaching the immune system. Loss-of-function mutations in the gene that produces the skin barrier maintenance protein, filaggrin (FLG), have been shown to be strongly associated with an increased risk of childhood eczema, and food allergy and eczema are known to be strongly associated in infants. The question is, therefore, whether a disrupted skin barrier, which may be genetically determined, facilitates the dermal exposure to food allergens during early life, and could thereby result in sensitisation and ultimately allergy to those foods developing. This study aimed to address this research question. The study aimed to test two specific hypotheses. The primary hypothesis was that abnormal skin barrier function (with or without eczema) predates and predicts food allergen sensitisation, independent of other post-natal dietary and environmental factors. The secondary hypothesis was that any relationship between skin barrier function and food allergen sensitisation is driven by loss-of-function mutations in the FLG protein.

Research Approach

The project built upon data obtained from two linked Irish studies: SCOPE and BASELINE. In SCOPE, 3000 first-time mothers were recruited in early pregnancy with the aim of establishing biomarkers to help predict pregnancy outcomes. The BASELINE Study aimed to provide a detailed follow-up of the babies born from SCOPE, including collection and storage of umbilical cord blood, assessment of growth and health, collection of data on breast-feeding and weaning practices, and assessment of eczema status.

This project used established clinical protocols to determine the status of 1903 SCOPE/BASELINE babies with regards to FLG mutation, skin barrier function, and food allergen sensitisation and food allergy in the first 2 years of life. FLG mutation status was determined by analysis of cord blood of those antenatally recruited and saliva samples of those postnatally recruited. Skin barrier function was determined at 2 days, 2 months and 6 months of age by

measuring the amount of water lost from the skin using a procedure known as Transepidermal Water Loss (TEWL). Food allergen sensitisation status was determined by Skin Prick Tests (SPTs) and blood tests for Specific Immunoglobulin E (SpIgE) antibodies at 2 years of age. Children whose parents reported adverse reactions to foods during the study underwent Double-Blind Placebo-Controlled Food Challenges (DBPCFCs) in order to determine their food allergic status.

The researchers anticipated that this prospective assessment would allow the genetic and functional status of skin barrier function to be determined and to identify whether these can be used as a means of categorising the children into groups according to their relative risk of developing food allergies.

Results

The study showed that of 1,259 infants who underwent skin prick tests at two years of age, 79 infants had positive results to at least one food (6.27%). The most prevalent food sensitisations were to hen's egg 3.82%, peanut 2.62% and cow's milk 0.95%

Of these infants, 52 (4.13%) were diagnosed as food allergic as a result of oral food challenges. The most prevalent food allergens were egg (2.87%), peanut (1.75%), milk (0.95%) and fish (0.16%). There were no cases of wheat or soya allergy in the cohort.

For the TEWL readings and food sensitisation, there was a statistically significant difference in mean TEWL values at two months between those who were sensitised and those who were not sensitised at two years. The two and six month values were higher in infants who had food sensitisation at two years compared to those who did not.

For the TEWL readings and food allergy, there was a statistically significant difference in mean TEWL values at two and six months between those with food allergy and those without. Again, as with the sensitisation results, mean TEWL was higher in those with food allergy compared to those without.

Results also showed that a higher proportion of those with food allergy were also diagnosed with atopic dermatitis at each of the different time points; 6 months (70%), 12 months (68.6%) and 24 months (63.5%).

There was a significant difference in association between FLG and TEWL at two months. Those with an FLG mutation gene had a higher mean TEWL reading (13.6g/water/m2) compared with those without the FLG mutation gene (10.93g/water/m2). Results also showed that the change of TEWL value between birth and two months was higher in those with the FLG mutation gene compared to those without.

Overall the results indicated that those with FLG mutation had a higher proportion of atopic dermatitis (from two months onwards) compared with those without the mutation gene. FLG mutation was also significantly associated with food allergy at two years: 11.8% of those with the mutation gene had food allergy and 4.2% of those without the mutation gene had food allergy.

Published Papers

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4. Kelleher, M., Dunn-Galvin, A., Hourihane, J.O.B., Murray, D., Campbell, L.E., McLean, W.H.I., Irvine, A.D. (2015) Skin barrier dysfunction measured by transepidermal water loss at 2 days and 2 months predates and predicts atopic dermatitis at 1 year. Journal of Allergy and Clinical Immunology,135: 930-5.
5. Kelleher, M., Dunn-Galvin, A., Gray, C., Murray, D.M., Kiely, M., Kenny, L., McLean, W.H.I., Irvine, A.D., Hourihane, J.O. (2016). Skin barrier impairment at birth predicts food allergy at 2 years of age. Journal of Allergy and Clinical Immunology [Epub ahead of print] doi: 10.1016/j.jaci.2015.12.1312.

Research report

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