Proceedings of the Nutrition Society (2023), **82 (OCE4)**, E265 doi:10.1017/S0029665123003415

Irish Section Conference 2023, 14–16 June 2023, Understanding the role of sex and gender in nutrition research

Th17 response following *in vitro* exposure to mercury with and without n-3 long chain polyunsaturated fatty acids in peripheral blood mononuclear cells from systemic lupus erythematosus patients compared to healthy controls

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Mercury (Hg) is an environmental toxin which humans are primarily exposed to through fish consumption. Exposure to Hg has been associated with increased inflammation in autoimmune disease[1,2]. Fish is rich in n-3 polyunsaturated fatty acids (PUFAs) with known anti-inflammatory properties, including the regulation of T helper (Th)-17 cells[3,4]. Th17 cells and associated cytokines are implicated in systemic lupus erythematosus (SLE) disease severity.[5] The effect of exposure to Hg and n-3 PUFA on Th17-associated cytokine regulation in SLE is not known. Therefore, this study aims is to investigate mercury's role in Th17 response in SLE peripheral blood mononuclear cells (PBMCs) and whether n-3 PUFAs reduce the response.

PBMCs were isolated from SLE patients (N = 15), and healthy controls (N = 15) matched on sex, age, and BMI. The isolated PBMCs were stimulated with lipopolysaccharide (LPS) and subsequently exposed to Hg (200nM) for 24hr with or without pre-exposure (24hr) to the n-3 PUFA, eicosapentaenoic acid (EPA; C20:5) or docosahexaenoic acid (DHA; C22:6) at 100uM. Th17 associated cytokines (Interleukin (IL)-17A, -E, -F, IL-21, IL-22, IL-23, IL-27, IL- 31, and IL-33) were quantified in the PBMC supernatant at baseline and after 24hr for each treatment. Analysis of covariance (ANCOVA) was used to assess the treatment effects on cytokine concentrations and identify differences in responses between SLE and healthy controls.

At baseline, SLE patients had significantly lower IL-33 concentrations compared to healthy controls (0.46(0.18) pg/ml and 0.65(0.3) pg/ml, respectively; $p = 0.02$). Following Hg and LPS exposure, no significant differences were observed in mean concentrations of IL-17A, IL-23, IL-27, and IL-33 between SLE patients and healthy control cultured cells. Pre-exposure to EPA resulted in significantly lowered concentrations of IL-27 in the supernatants of LPS-Hg treated PBMCs of SLE patients (29.58 ± 22.62pg/ml) compared to healthy controls (51.63 ± 42.96pg/ml) ($p = 0.04$).

This *in-vitro* investigation reported Hg exposure had no significant effect on LPS-induced stimulation of Th17 cytokines in PBMCs. The effect of EPA appears to reduce the expression of IL-27 only in SLE-derived cells. Further research is required to determine the clinical relevance of this finding, owning to the pleiotropic nature of IL-27.

Acknowledgments

The first author is in receipt of the Northern Ireland Department of Economy (DfE) studentship.

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https://doi.org/10.1017/S0029665123003415 Published online by Cambridge University Press