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Serum Lipidomics and Disease Activity in Pediatric-Onset Multiple Sclerosis: a nation-wide prospective cohort study


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Introduction:

Alterations in lipid metabolism and their effects on immune cells have been reported in relapsing MS. However, only a few metabolic pathways have been investigated for their relationship with MS course.

Objectives/Aims:

To evaluate the association between plasma lipids and subsequent disease activity in a prospective cohort of pediatric-onset MS (POMS) patients.

Methods:

Plasma samples were collected from POMS cases within 4 years of disease onset from 16 sites in the US Network of Pediatric MS Centers. Lipids and lipid mediators were assessed using untargeted and targeted liquid chromatography mass spectrometry. The association between clinical (time to first relapse, time to sustained EDSS progression, relapse count) and radiological outcomes (count of MRIs ≥ 1 new T2 lesion; or Gd+ lesion) with each metabolite (median dichotomization) was estimated using negative binomial regression offset by follow-up time and cox proportional hazards models. Baseline MRI was ±6 months from sample collection. Adjustment by sex, age, race, biological mother’s highest degree, DMT usage, and number of MRIs (radiological outcomes) was performed. False discovery rate threshold was set at 0.2.

Results:

446 POMS patients (65% female, 67% White) were included. At sample collection, 68% were treatment-naïve,
median EDSS was 1.5 (IQR 1.0-2.0), and median follow-up time was 3.2 years (IQR 1.5-5.2) after sample collection. A total of 2,104 metabolites were measured. Among those, 489 were chemically characterized, 16 of which were associated with subsequent disease activity. Of note, w-3 polyunsaturated fatty acids (PUFA) and their derivatives (docosahexaenoic acid, eicosapentaenoic acid (EPA), and 12-HEPE) were consistently associated with protective effects on clinical and MRI outcomes. For example, high EPA levels were associated with a 36% decrease in the incidence of T2 lesions (IRR 0.64, 95%CI 0.55-0.76, q<0.001) and 42% decrease in the risk of relapse (HR 0.58, 95%CI 0.45-0.74, q=0.04). Interestingly, w-6 PUFAs derivatives were associated with an increased risk of MS activity (10-HODE, 12-HODE, 9,10-DiHOME, 9,12,13-TriHOME), except arachidonic acid, which showed consistent protective effects. WGCNA clustering results will be presented.

**Conclusion:**

Several PUFAs and their metabolites were associated with multiple clinical and MRI disease activity outcomes. Our results suggest that w-3 PUFAs and their derivatives, whose levels rely exclusively on dietary ingestion of a-linoleic acid, are associated with a lower risk of MS activity.

**Disclosures:**

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BWG served as a consultant for Biogen, EMD Serono, Novartis, Genentech, Celgene/Bristol Meyers Squibb, Sanofi Genzyme, Bayer, Janssen, Labcorp and Horizon. She served in speaker bureau for Biogen. BWG also has received grant/research support from the agencies listed in the previous sentence. She serves in the editorial board for BMJ Neurology, Children, CNS Drugs, MS International and Frontiers Epidemiology.

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