Randomized Controlled Trial

Neurotherapeutics

. 2016 Apr;13(2):428-38.

doi: 10.1007/s13311-016-0420-z.

Oral Palmitoylethanolamide Treatment Is Associated with Reduced Cutaneous Adverse Effects of Interferon-β1a and Circulating Proinflammatory Cytokines in Relapsing-Remitting Multiple Sclerosis

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- PMID: 26857391
- PMCID: PMC4824021
- DOI: 10.1007/s13311-016-0420-z

Abstract

Palmitoylethanolamide (PEA) is an endogenous lipid mediator known to reduce pain and inflammation. However, only limited clinical studies have evaluated the effects of PEA in neuroinflammatory and neurodegenerative diseases. Multiple sclerosis (MS) is a chronic autoimmune and inflammatory disease of the central nervous system. Although subcutaneous administration of interferon (IFN)-β1a is approved as first-line therapy for the treatment of relapsing-remitting MS (RR-MS), its commonly reported adverse events (AEs) such as pain, myalgia, and erythema at the injection site, deeply affect the quality of life (QoL) of patients with MS. In this randomized, double-blind, placebo-controlled study, we tested the effect of ultra-micronized PEA (um-PEA) added to IFN-β1a in the treatment of clinically defined RR-MS. The primary objectives were to estimate whether, with um-PEA treatment, patients with MS perceived an improvement in pain and a decrease of the erythema width at the IFN-β1a injection site in addition to an improvement in their QoL. The secondary objectives were to evaluate the effects of um-PEA on circulating interferon-γ, tumor necrosis factor-α, and interleukin-17 serum levels, N-acylethanolamine plasma levels, Expanded Disability Status Scale (EDSS) progression, and safety and tolerability after 1 year of treatment. Patients with MS receiving um-PEA perceived an improvement in pain sensation without a reduction of the erythema at the injection site. A significant improvement in QoL was observed. No significant difference was reported in EDSS score,

and um-PEA was well tolerated. We found a significant increase of palmitoylethanolamide, anandamide and oleoylethanolamide plasma levels, and a significant reduction of interferon-γ, tumor necrosis factor-α, and interleukin-17 serum profile compared with the placebo group. Our results suggest that um-PEA may be considered as an appropriate add-on therapy for the treatment of IFN-β1a-related adverse effects in RR-MS.

Keywords: Anandamide; FAAH; N-acylethanolamines; NAAA; Neuroinflammation; Oleoylethanolamide; Pain.