Effects of Palmitoylethanolamide on Proinflammatory Markers in Adults Recently Diagnosed With COVID-19

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Objectives: Inflammation is at the core of many chronic conditions and exacerbates infectious conditions, including the severity of COVID-19 infections. The aim of this study was to examine the effects of a novel food supplement, palmitoylethanolamide, specifically Levagen+^{TM} (LEV), versus placebo (CON) on proinflammatory biomarkers in an adult population recently diagnosed with COVID-19 who were non-hospitalized.

Methods: This study was a double-blind randomized placebo-controlled trial conducted October 2020-March 2021. Participants ($n = 30$/group) were unvaccinated and recently infected with COVID-19 as indicated by a positive test per RT-PCR or antigen test (antigen tests accepted upon symptomatic infection consistent with COVID-19 symptoms per the CDC) and reported to the test site following diagnosis as allowed by the CDC's return to work policy. Participants were stratified by age, sex, and BMI and randomized by coin toss to receive LEV (600 mg BID) or CON tablets twice daily for four weeks. Participants completed health histories, 24-hour dietary recalls, anthropometrics, and non-fasting blood sampling at baseline and week four. Blood samples were analyzed for inflammatory biomarkers.

Results: There were no baseline differences by group for age, sex, weight, BMI, type or total number of COVID symptoms reported, nutritional profiles, or interval between date of COVID-19 diagnosis and study enrollment. Following the 4-week trial, change in serum concentration did not differ between groups for IL-6, TNFα, or CRP. However, IL-1β, IL-2, and P-selectin showed reductions in the LEV group after four weeks compared to the CON group which saw increases in these markers ($p < .05$), though only P-selectin remained significant after Bonferroni correction for multiple comparisons ($p < .05$).

Conclusions: Though inflammatory mechanisms are crucial to an optimal immune response, unchecked secretion of cytokines and thrombo-inflammatory markers can promote the development of the inflammatory response in unresolved disease states and are implicated in COVID-19 complications. Therefore, the reduction in inflammatory markers noted herein suggests that PEA may exert anti-inflammatory actions, and possibly reduce the severity of COVID-19 disease.