補充 n-3 不飽和脂肪酸對阿茲海默症病患其延緩智能退化之效果評估

Effect of n-3 Polyunsaturated Fatty Acids Supplementation on Improving Cognitive Degeneration in Patients with Alzheimer''s Disease

中文摘要

本試驗主要目地在探討台灣輕度認知功能缺損(MCI)及輕至中度的阿茲海默症患者以 n-3 不飽和脂肪酸介入，以評估其對認知功能及記憶力改善之效果。本試驗第一部份共募集 38 位從未用藥之 MCI 及輕至中度的阿茲海默症患者，同時募集性別相仿之 20 位認知功能正常老人作爲控制組，進行血液生化、飲食調查、心智評估(CDR、ADAS-cog、CASI 及 MMSE)、血液脂肪酸分析以及血液流變分析。第二部份將失智組隨機分爲魚油組(n=15)及安慰劑(n=15)組進行雙盲安慰劑控制試驗。魚油組給予 1.8 g 之魚油膠囊(EPA 1.08 g/day 及 DHA 0.72 g/day)；安慰劑組給予等量之橄欖油膠囊，二組於第 0、6、12 及 18 週進行心智評估(CDR、ADAS-cog 及 CIBIC-Plus)，於介入之第 0、12、18 週進行飲食記錄，並抽空腹血液進行一般血液生化、血液脂肪酸測定以及血液流變測定。第一部份結果顯示，飲食記錄，血液生化檢查，血液流變二組間無顯著差異；而血液脂肪酸分析，失智組之血漿及紅血球之 C18:2 n-6 皆顯著高於控制組以及失智組之紅血球總 n-6 脂肪酸顯著高於控制組($p < 0.05$)，失智組之紅血球 C18:1 n-9 顯著低於控制組($p = 0.002$)。第二部份結果表示，飲食評估二組間各時間點皆無差異；一般生化於介入之後前凝血酶原時間(prothrombin time)以及國際標準化比值(INR)顯著高於介入前($p < 0.05$)，然而皆在標準範圍內；魚油組血漿脂肪酸之 C18:3 n-3、EPA、DHA、總 n-3 以及 n-3/n-6 比值於介入後顯著增高($p < 0.05$)，魚油組紅血球脂肪酸之 C18:3 n-3 及 n-3/n-6 比值顯著比介入前高($p < 0.05$)；安慰劑組血漿及紅血球之飽和脂肪酸及 C16:0 於介入後顯著減少($p < 0.05$)；魚油組介入後紅血球聚集度顯著減少($p = 0.03$)而紅血球變形度顯著增加($p = 0.04$)，安慰劑組則無顯著差異；魚油組之心智評估 CIBIC-Plus 於介入第 18 週後比安慰劑組有顯著改善($p = 0.017$)，而 CDR 及 ADAS-cog 無顯著改善效果。本試驗單純給予非常輕度(MCI)至中度阿茲海默症患者魚油，於介入第 18 週時 CIBIC-Plus 比安慰劑組有顯著改善，血漿 EPA、DHA 及血漿血球之 n-3/n-6 比值增加，代表體內 n-3 脂肪酸顯著升高，同時紅血球變形度增加及紅血球聚集度下降，這些血液流變參數的改變可能使血液黏滯性下降，使微循環流動較佳，因此保護了神經組織。因此本篇研究的結論是，在 MCI 及輕至中度的阿茲海默症患者血液中的 n-6 脂肪酸偏高是導致認知功能下降之危險因子，並且補充魚油膠囊(含 EPA 及 DHA) 1.8 g/day 共 18 週對於 MCI 及輕度至中度的阿茲海默型失智症患者具有顯著改善認知功能的效

果，因此魚油的補充對於 MCI 及輕至中度的阿茲海默症患者是一個有效的營養輔助療法。

英文摘要

The aim of this study is to investigate the effect of n-3 polyunsaturated fatty acids on patients with MCI and mild to moderate Alzheimer's Disease (AD). The study included dietary assessment, blood biochemical characteristics, blood fatty acid profiles, cognitive assessment (CDR, ADAS-cog, CASI and MMSE) and hemorheological status between drug naïve AD patients ($n = 38$) and gender-matched control subjects ($n = 20$). After first visiting, the AD groups were divided into fish oil group ($n = 15$) and placebo group ($n = 15$) for a randomized double-blinded placebo-controlled interventional study. Fish oil group received fish oil capsual (eicosapentaenic acid, EPA 1.08 g and docosahexaenic acid, DHA 0.72 g per day) as well as placebo group received olive oil capsual (oleic acid 1.8 g/day). The blood fatty acids profile, blood biochemical characteristics, and hemorheological measure at week 0, 12, 18 and cognitive assessment (CDR, ADAS-cog and CIBIC-Plus) were measured at week 0, 6, 12, 18 in two groups. In results, there were no statistical differences between groups (AD group vs. control group) on dietary assessment, blood biochemical characteristics and hemorheological test. Plasma and RBC linoleic acid (C18:2 n-6) and RBC total n-6 fatty acid in AD group were significant higher than control subjects ($p < 0.05$). The AD's RBC oleic acid (C18:1 n-9) was significantly lower than control ($p = 0.002$). During the intervention, the dietary record showed no different between groups at each time intervals. The prothrombin time and INR were significant longer in the fish oil group ($p < 0.05$). The percentage of plasma C18:3 n-3, EPA, DHA total n-3 fatty acid and n-3/n-6 ratio in fish oil group were significant higher before intervention ($p < 0.05$). The RBC linolenic acid (C18:3 n-3) and n-3/n-6 ratio in fish oil group were significant higher before intervention ($p < 0.05$). The percentage of plasma and RBC palmitic acid (C16:0) and total saturated fatty acids (SFA) in placebo group were significant reduced before intervention ($p < 0.05$). In Fish oil group, RBC aggregation was significant reduced ($p = 0.03$) and RBC deformability was significant increased after intenvention ($p = 0.04$). There was no change of aggregation and deformability of RBC in placebo group. In cognitive assessments, the CIBIC-Plus was significantly improved in fish oil group ($p = 0.017$) than placebo group at week 18. However, CDR and ADAS-cog did not change. In our study, the CIBIC-plus score were improved than the placebo group and EPA, DHA and n-3/n-6 ratio were significant higher in fish oil group in 18 weeks. The increases EPA and DHA were inversed to increased deformability and decreased aggregation of RBC. In conclusion, higher blood n-6 fatty acids may contribute to the risk factor of

AD development; the daily supplementation of 1.8 g fish oil (EPA 1.08 g and DHA 0.72 g) showed significant improvement in patients with MCI and mild to moderate AD. Thus, fish oil supplement could be considered as an alternative choice to prevent or improve MCI and mild to moderate AD.