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Original Article

Continual supplementation with *n*-3 fatty acids does not modify plasma lipid profile in spinal cord injury patients

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Study design: A prospective study during a diet modification.
Objective: To observe the evolution of the plasma lipid profile in a group of spinal cord injury (SCI) patients given a supplement of a mixture of docosahexanoic acid (DHA) and eicosapentaenoic acid (EPA).
Setting: Department of Physiological Sciences II, Medical School of the University of Barcelona and Guttmann Institut of Badalona, Barcelona, Spain.
Methods: A total of 19 adult males with SCI, 17 with paraplegia and two with tetraplegia, were given a daily supplement of 1.5 g of DHA and 0.75 g of EPA for 6 months. Determination of plasma values of DHA, EPA, total cholesterol, HDL-c, LDL-c, VLDL-c, triglycerides, and glucose was performed before supplementation and at 3 and 6 months of supplementation.
Results: A statistically significant increase in the plasma concentration of EPA ($F=30.556$, $P<0.05$) and DHA ($F=106.6$, $P<0.05$) was observed after 3 and 6 months of supplementation. However, there were no observable differences in the plasma concentration of total-cholesterol, HDL-c, LDL-c, VLDL-c, and triglycerides during the study.
Conclusion: DHA–EPA supplementation for 6 months does not modify the glycemic and lipid plasmatic levels in SCI patients. Despite its absence of effect on the serum lipid profile, *n*-3 fatty acids may induce beneficial cardiovascular effects in this population.
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Keywords: spinal cord injury; docosahexaenoic acid; eicosapentaenoic acid; plasma lipid profile; *n*-3 fatty acids

Introduction

People with spinal cord injury (SCI) face daily activities that involve more effort than able-bodied subjects as wheelchair transport is a highly inefficient and strenuous mode of transport.[1] SCI also involves risk factors that reduce life expectancy compared with similarly aged able-bodied subjects.[2] Moreover, as a consequence of the SCI, low degree of activity and deconditioning result in muscle atrophy, increased adiposity, and decreased cardiorespiratory fitness.[3] These factors mean that SCI people are prone to risk factors such as insulin resistance, glucose intolerance, increased serum cholesterol, triglyceride plasma concentrations and decreased HDL-c values.[4] The sum of all these factors represent an increased risk of morbidity and mortality due to cardiovascular diseases that constitute the principal cause of death in patients with SCI,[5,6] especially more than 30 years after injury (46% of all deaths) and among those older than 60 years of age (35% of all deaths).[7] Important findings about the beneficial effects of polyunsaturated fatty acids (PUFAs) on cardiovascular disease have also become apparent over the years.[8,9]

The objective of this study was to observe the evolution of the plasma lipid profile in a group of SCI patients given a continual supplementation of a mixture of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) or six months.

Materials and methods

Subjects

19 adult males with SCI, 17 with paraplegia and two with tetraplegia, participated in the study, after informed consent. The study was approved by the Ethical

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Committee of Guttmann Institute. According to the ASIA neurological classification, 64% of the patients were ASIA A, 21% ASIA B, 10% ASIA C and 5% ASIA D. The time elapsed since the injury was greater than 12 months. Lifestyle (physical activity, diet, …) of the participants was fairly constant over the entire study period. Each subject lived normal lives and continued with their habitual diet. All subjects used a hand-propelled wheelchairs as the primary means of locomotion.

Protocol

The evaluations were carried out in basal conditions (control 1) at 3 months (control 2) and at 6 months (control 3) after the oral supplementation with the DHA + EPA mixture.

The total daily dosage was: 1.5 g of DHA and 0.75 g of EPA. These were supplied in the form of gelatin pearls (DHA + EPA®, Santiveri, Barcelona, Spain), six a day, taken with the three principal meals (two with breakfast, two with lunch, and two with supper).

Analysis of blood samples

Blood samples to evaluate the lipid profile were taken from the antecubital vein after an overnight fast. A part of the sample was used for the determination of total cholesterol, HDL-c, LDL-c, VLDL-c triglycerides, and glucose performed by means of an automatic analyser (model 717 Hitachi, Roche, Tokyo, Japan). The rest of the sample was centrifuged at 1815 rpm for 20 min to separate the blood plasma which was then used to determine the content and the proportion of the different fatty acids. These were determined by analyzing the methyl-esters of the corresponding compounds, obtained by a process of direct trans-sterification[10] and separated by means of gas–liquid chromatography, using a chromatograph (model HP 6890 serie GC, Hewlett-Packard, Wilminston, USA) equipped with a capillary column and a flame ionization detector.

Statistical analysis

A repeated measures ANOVA was used to determine the influence of *n*-3 supplementation for any of the variables, with adjustments with the Bonferroni test. The values are expressed as mean ± SEM. Significance was accepted at the $P<0.05$ level.

Results

A statistically significant increase in the concentration of EPA in plasma was observed as a response to the intake of the supplement. EPA levels increased 7.86 times between control 1 (basal conditions) and control 2 (3 months after beginning dietary supplementation), and 10.01 times between control 1 and 3 (6 months after beginning dietary supplementation) ($F=30.556$, $P<0.05$). The same happened in the percentages of DHA, that underwent a statistically significant increase between control 1 and 2 of the study, doubling the levels of the first control, and between control 1 and 3, increasing 125% ($F=106.6$, $P<0.05$). Plasma concentration of glucose, total-cholesterol, HDL-c, LDL-c, VLDL-c, triglycerides and glucose did not show differences between the different control days of the study (Table 1).

Discussion

At the beginning of the 1970s, various studies demonstrated differences between Greenland Inuit and the Danish population with respect to the plasma lipoprotein profile. The Inuit suffered fewer heart attacks, which was attributed to the beneficial effects of *n*-3 fatty acids that they consume in large quantities.[11–14] Changes in Western diets have been observed where the ratio of *n*-6 to *n*-3 fatty acids now ranges from 20 to 30:1 instead of the more traditional of 1 to 2:1. This imbalance may be responsible for the increase in blood viscosity, vasospasm and vasoconstriction and reduced bleeding time. *n*-3 Fatty acids also have anti-inflamatory, antithrombotic, hypolipemic, vasodilatory, and anti-arrhythmic effects and have a beneficial effect in primary and secondary prevention of ischemic heart disease.[11] Increased consumption of *n*-3 fatty acids reduces mortality from sudden cardiac death, even among men without evidence of prior cardiovascular disease,

Table 1 Mean ± standard error of the different blood parameters studied

Parameters	*Control 1*	*Control 2*	*Control 3*
EPA (%)	0.35 ± 0.22	3.67 ± 0.35	3.87 ± 0.49
DHA (%)	2.51 ± 0,2.8	5.54 ± 0.35	5.64 ± 0.54
Total-cholesterol (mmol/l)	4.04 ± 0.22	4.14 ± 0.18	4.44 ± 0.45
HDL-c (mmol/l)	1.06 ± 0.06	1.11 ± 0.07	1.04 ± 0.10
LDL-c (mmol/l)	2.46 ± 0.22	2.55 ± 0.19	2.88 ± 0.38
VLDL-c (mmol/l)	0.56 ± 0.09	0.42 ± 0.05	0.50 ± 0.04
Atherogenic index	0.27 ± 0.02	0.28 ± 0.02	0.24 ± 0.02
Triglycerides (mmol/l)	1.26 ± 0.34	0.96 ± 0.10	1.15 ± 0.05
Glucose (mmol/l)	4.49 ± 0.44	4.30 ± 0.34	4.21 ± 0.56

Control 1: before supplementation; control 2: at 3 months and control 3: at 6 months of supplementation with EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid)

indicating that such acids have antiarrhythmic effects.[8,9]

Other studies indicate that supplementation with fish oils might have beneficial effects on patients affected by rheumatoid arthritis and asthma, possibly because of the anti-inflammatory effects of *n*-3 PUFAs. A diet rich in *n*-3 PUFAs reduce the plasma concentration of VLDL-c.[15–17] Most of the research conducted on PUFAs has focused on EPA and DHA. These PUFAs are found in varying concentrations in fish products. The effects of EPA and DHA consumption in different pathologies and also in healthy individuals are well known, for example, in the secondary prevention after a heart attack with a reduction of 20% in mortality.

The important changes in patients with SCI after the lesion which decrease their life expectancy could be alleviated by supplementation with DHA + EPA.

Recent data suggest the beneficial effects of *n*-3 PUFAs on various cardiovascular disorders with more potent and beneficial effects attributed to DHA rather than to EPA.[18] Small supplement of *n*-3 fatty acids (120 mg/day of DHA and 73 mg/day of EPA) during 10 days change the LDL-c composition leading to less atherogenic LDL-c particles.[19] In our study, with a daily supplementation of 1.5 g DHA and 0.75 g EPA during 6 months, we did not observe changes in different blood variables analyzed despite a substantial increase in the concentration of these fatty acids in plasma.

In SCI patients different factors may modify the lipid profile with reduced serum HDL-c levels and increased cardiovascular risk, correlating with the severity and level of the neurological deficit.[20,21] In white and latin males immobilization from SCI appears to be associated with lower HDL-c[22] and different indicators of adiposity in SCI men (eg abdominal circumference) show an association with altered serum lipid profile (low HDL-c, higher triglycerides and higher total to HDL-c ratio).[23] Exercise resistance training[24] or early rehabilitation with interval training in SCI individuals[25] promote beneficial effects and healthier lipid profile in patients with chronic paraplegia.

In our study, SCI subjects show an important increase in DHA and EPA plasmatic levels while not affecting the lipid profile. Immobilization from SCI is, probably, a more important negative factor than the positive effect of the plasmatic increase in *n*-3 PUFAs. However, it is reasonable to assume that these type of fatty acids may have other beneficial effects in SCI patients. Future studies are needed with larger groups, including women, and with different doses and different periods of supplementation to assess the role of DHA and/or EPA in SCI and its potential beneficial health effects.

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