

DOUBLE-BLIND STUDY ON THE EFFECTS OF FISH OIL UPON DAYTIME SLEEPINESS AND SLEEP QUALITY IN PARKINSON PATIENTS

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ABSTRACT

Background and objective: Patients with Parkinson's disease (PD) often suffer from sleep disorders that impair their quality of life. The purpose of this study was to investigate how dietary supplementation with fish oil, which is rich in the omega-3 family fatty acids Docosahexaenoic acid (DHA) and Eicosapentaenoic (EPA), may affect sleep quality and excessive daytime sleepiness (EDS) in Parkinson patients lacking comorbidity or depression.

Methods: Thirty-seven patients from the Parana Association of Parkinson Carriers were divided into two groups; patients in one group (n=19, average age 66.6±11.6 years) were administered fish oil capsules while patients in the other group were given mineral oil (n=18, average age 62.1±13.3 years) for eight consecutive weeks. The two groups were evaluated using the Pittsburgh Sleep Quality Index (PSQI) and Epworth Sleepiness Scale (ES).

Results: We found that supplementation with fish did not affect daytime sleepiness in patients (F= 2.18; p = 0.15); both groups showed a reduction in daytime sleepiness (F= 4.26; p<0.05). We also did not observe an effect of supplementation on patients sleep quality (F=0, 27; p<0.61); both groups had an improvement in sleep quality (F= 5.46; p<0.05).

Conclusion: We found that polyunsaturated fatty acids, which ameliorate psychiatric disorders like depression, do not affect sleep alterations in Parkinson patients under the clinical conditions evaluated, although our conclusions are limited by a reduced sample size.

Keywords: Parkinson's Disease; fish oil, omega-3 fatty acids; daytime sleepiness.

INTRODUCTION

Parkinson's disease (PD) is a progressive neurodegenerative disease characterized by motor, behavioral and cognitive alterations. The etiology of the disease remains unknown (1). Included in these alterations are sleep pattern disturbances, with a reduction in nighttime sleep and excessive daytime sleepiness (EDS). Little attention has been paid to these disturbances in the last two decades (2). The large majority of Parkinson patients suffer from poor sleep quality, experiencing an increasing number of night awakenings and daytime naps, resulting in a reduction in

sleep efficiency and a poor quality of life (3,4). Insomnia and other sleep disorders can be associated with the presence of psychiatric diseases that are present concomitantly with Parkinson's disease (3,5,6). Such sleep alterations significantly affect the patient's psychological and cognitive aspects and may be associated with depression (6).

Polyunsaturated fatty acids (AGPs) are the major phospholipidic components of cell membranes. They can be divided into two families, omega-6 and omega-3, which are synthesized from two independent essential fatty acids, linoleic acid and α -linoleic acid, respectively. Docosahexaenoic acid (DHA) and Eicosapentaenoic

acid (EPA) are essential polyunsaturated fatty acids that can be isolated from fish and phytoplankton. The presence of AGPs in the cell membrane is important for a smooth functioning of the lipidic bilayer (7,8). Neuronal membranes are rich in AGPs, which can change the physical-chemical characteristics of the membrane. AGPs play an important role in both cell structure and function; they actively participate in cell signaling processes, the regulation of enzymatic activity, and apoptosis (8,9). Thus, changes in the AGPs composition affect the fluidity and permeability of neuronal membranes. Consequently, alterations in the dietary lipidic profile might be associated with different neurological conditions (7,10).

Recent studies have indicated that variations in the AGP composition of neuronal membranes can modify the structure and function of receptors, transporters, ion channels, and other signaling proteins. In addition, it has been suggested that eicosanoids participate in sleep induction (11,12). Eicosanoids are synthesized from arachidonic acid (omega-6 family), which is present in the phospholipids of cell membranes. They can also be EPA-synthesized, though to a lower extent (13).

Research conducted with elderly humans has demonstrated that the aging process is associated with a reduction in the capacity to convert α -linolenic acid (ALA) into DHA, compared with children, young people, and animals (14). The amount of DHA in the neuronal membranes of elderly people declines due to an increase in lipidic peroxidation products upon aging. In addition, the elderly patient with Parkinson's disease may have altered AGP concentrations in their neuronal membranes as a consequence of levodopa therapy (15).

A reduction in AGPs in erythrocyte membranes of patients with depression has been previously investigated (7,16). In a double-blind study conducted with Parkinson patients, the amount of DHA in the lipid profile of erythrocyte membranes was found to be three times higher after three months of dietary supplementation with fish oil, which is rich in DHA and EPA. Similarly, supplementation was also found to reduce the symptoms of depression in PD carriers (17).

The objective of the present study was to assess whether fish oil supplementation could affect sleep quality and daytime sleepiness in Parkinson patients.

MATERIALS/METHODS

This randomized double-blind study was conducted with patients cared for by professionals at the Parana Association of Parkinson Carriers. The project was approved by the Committee for Ethics in Research of UFPR Biological Sciences Department. Patients with a clinical diagnosis of depression associated with Parkinson's disease and/or using antidepressant medications were excluded from the study. In the initial screening, a total of 118 subjects were evaluated with the use of Beck Depression Inventory (BDI). From this total, 44 subjects were selected for the study, as their score was equal to or below 20 using the Beck's scale; a criterion that has been used in previous studies (18). The selected patients were subdivided into two groups: an experimental group

(E), which received capsules containing fish oil, and a control group (C), which received mineral oil. Patients signed an informed consent form prior to participating in the study and were evaluated with the use of the Pittsburgh Sleep Quality Index (PSQI) and Epworth Sleepiness Scale (ESS). The application of these two instruments was performed prior to and at the conclusion of the eight-week supplementation. Group E received 4g daily doses of a marine extract compound that is rich in family omega-3 fatty acids, containing 180mg of eicosapentaenoic acid (EPA), 120mg of docosahexaenoic acid (DHA), and tocopherol antioxidant; these doses were administered over 4 capsules/day. Group C received the same number of capsules of mineral oil. Of the 44 subjects that were initially recruited, seven were withdrawn from the study; four had to interrupt supplementation after experiencing gastrointestinal alterations; two gave up treatment because they had interrupted supplementation for more than one week, reporting forgetfulness; one subject chose to give up treatment because he/she had to be hospitalized. Thirty-seven (12 female and 25 male) patients completed the study. Group E was composed of 19 subjects (6 female and 13 male, age averaging 66.6 ± 11.6 years). Group C was composed of 18 subjects (6 female and 12 male, average age 62.1 ± 13.3 years). The average scores in the PSQI and ESS before and after fish oil supplementation are expressed as mean \pm standard error of the mean, and were submitted to two-way variance analysis (ANOVA), considering group and supplementation factors as dependent variables.

RESULTS

Figure 1 depicts the average scores and respective standard errors for daytime sleepiness, evaluated through ESS for both groups before and after supplementation. We observed no effect of supplementation on daytime sleepiness ($F = 2.18$; $p = 0.15$), as both groups showed a reduction in daytime sleepiness ($F = 4.26$; $p < 0.05$).

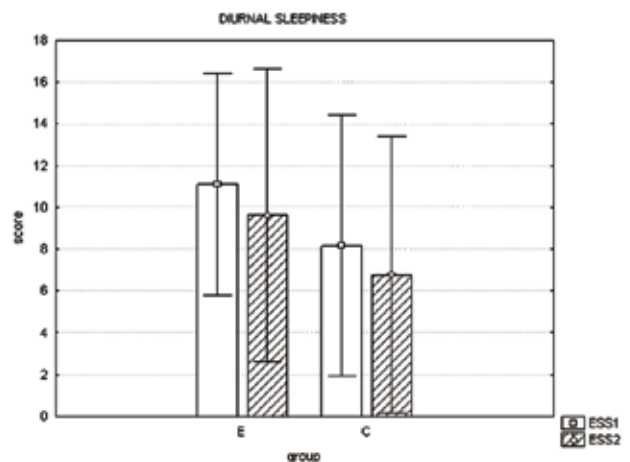


Figure 1: Effect of a two-month supplementation with fish oil upon daily sleepiness evaluated under the Epworth Sleepiness Scale (ESS) before and after supplementation carried out for both groups: E (experimental group) and C (control group). Values were expressed as average \pm average standard error.

Figure 2 depicts the average scores and standard errors for sleep quality evaluated through PSQI for both groups before and after supplementation. No effect of supplementation on patient sleep quality was observed ($F = 0.27$; $p < 0.61$), as both groups showed an improvement in sleep quality ($F = 5.46$; $p < 0.05$).

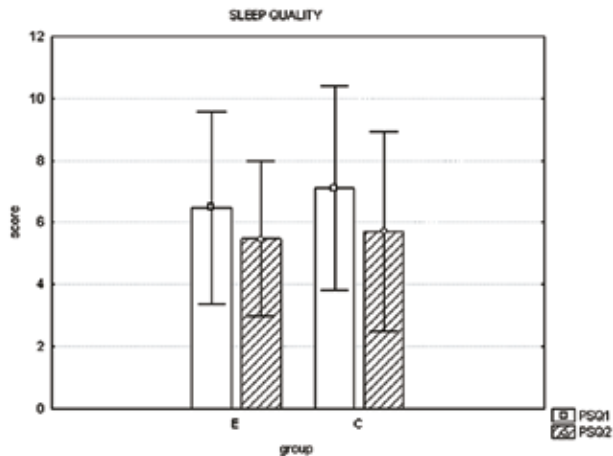


Figure 2. Effect of a two-month supplementation with fish oil upon daily sleep quality evaluated under Pittsburgh Sleep Quality Index (PSQI) before and after supplementation carried out for both groups: E (experimental group) and C (control group). Values were expressed as average \pm average standard error.

DISCUSSION

The objective of this study was to evaluate whether fish oil supplementation could affect daytime sleepiness and sleep quality in patients with Parkinson's Disease. We found no significant differences between the two treatments that we studied; both groups exhibited an improvement in sleep quality as evaluated by PSQI, as well as a reduction in daytime sleepiness evaluated by ESS, suggesting that there was a placebo effect with both treatments.

The placebo effect is highly prevalent in Parkinson's disease carriers (19), as this disease involves the brain's reward circuitry. (20,21,22). Damico and collaborators (19) have demonstrated that in Parkinson patients, the placebo effect may be related to the expectation of clinical improvement and might be mediated by a release of dopamine into the nigrostriatal pathways and into the nucleus accumbens. Thus, any improvement in patient sleep quality may have been masked by a placebo effect, considering the reduced size of our trial groups.

The daily dose of fish oil administered in this study was equivalent to, or higher than, supplementation doses that have been used in other studies with patients carrying neurodegenerative diseases (17,23). Still, two months may not have been a sufficient length of time to observe the desired effects; previous studies have used longer periods of supplementation (17,23).

To our knowledge, ours is the first study that has investigated the potential effects of the above-mentioned fatty acids on sleep quality and daytime sleepiness in Parkinson patients. It is unknown whether the sleep alterations in these patients are a primary manifestation of dopaminergic alterations, or a secondary

dysfunction related to disorders present in Parkinson's disease (24). We found that AGPs, which ameliorate psychiatric disorders like depression, do not affect sleep alterations in Parkinson patients under the clinical conditions evaluated, although our conclusions are limited by a reduced sample size.

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