Evaluation of Omega-3 Polyunsaturated Fatty Acids Plus Low-dose Aspirin Daily Supplementation in Non-Surgical Therapy to Treat Generalized Aggressive Periodontitis: Randomized Controlled Clinical Trial

NCT03093246

March 22, 2017

Abstract

Background: Periodontal destruction results mainly from the exacerbated host inflammatory response to the bacterial challenge. For this reason, research involving the modulation of host response has been developed aiming to facilitate the resolution of inflammation, as well as to promote tissue repair and periodontal stability. Recently, the use of omega-3 polyunsaturated fatty acids (Ω-3 PUFA) and low-dose acetylsalicylic acid (ASA) was related to the production of enhanced lipidic mediators and to better clinical outcomes in the treatment of chronic periodontitis.

Objective: The aim of the present randomized controlled clinical trial was to evaluate the use of 900 mg Ω-3PUFA and 100 mg ASA for 180 days as adjuvants to the non-surgical treatment (NST) of generalized aggressive periodontitis (GAgP).

Methods: Thirty-eight GAgP patients were submitted to subgingival debridement associated with Ω-3 PUFA and ASA (n=19) or placebo (n=19).

Results: Both groups showed a statistically significant decrease ($p<0.05$) in all clinical parameters, as well as a decrease in IL-1β, with no difference between treatments ($p>0.05$). The TIMP-2 level significantly decreased in the control group and remained stable in the test group.

Conclusion: The proposed new therapy did not bring clinical benefits in the non-surgical treatment (NST) of GAgP.

Study Protocol

This double-blind, placebo-controlled, randomized clinical trial was designed to evaluate the superiority of PUFA ω-3 + ASA vs. control. The study followed the CONSORT 2010 and the SPIRIT 2013 Statements. The trial was approved by the human subjects ethics board of Unesp (CAAE 66096817.3.0000.0077) and was conducted under the principles of the Helsinki Declaration of 1975, as revised in 2013. The study protocol was registered in ClinicalTrials.gov (NCT03093246).

Subjects with generalized grade C periodontitis were selected at the Division of Periodontics, Institute of Science and Technology, São Paulo State University (Unesp), Brazil. A complete dental exam was carried out and medical records were obtained. Subjects who fulfilled the inclusion criteria were invited to participate in the study. Each subject provided informed consent after a thorough explanation of the nature, risks, and benefits of the clinical investigations. The inclusion criteria were: 1) diagnosis of stages III/IV generalized grade C periodontitis (Papapanou et al, 2018); 2) presence of ≥20 teeth, excluding third molars and teeth indicated for extraction; 3) presence of ≥6 sites presenting PD ≥5 mm with bleeding on probing (BoP) and ≥2 sites with PD ≥7 mm (including incisors and first molars, in addition to three other non-contiguous teeth between them); 4) good general health; 5) at least 18 years old; and 6) agree to participate in the study and sign a written consent. Patients who 1) were pregnant or nursing; 2) were suffering from any other systemic disease (e.g., cardiovascular, diabetes, blood dyscrasias, immunodeficiency, etc.); 3) received antimicrobials or anti-inflammatory drugs in the previous 6 months; 4) received a course of periodontal treatment within the last 12 months; 5) smoked ≥10 cigarettes/day; 6) reported an allergy to ASA or seafood; 7) required antibiotic prophylaxis; 8) were currently using medication that could interfere with periodontal response; or 9) reported gastritis and/or gastric ulcers were excluded.

The randomization was done as follows: a researcher (NCCS) generated a random computer sequence to determine the order in which the treatments would occur (test/control) according to the stablished sample. This sequence was kept in a brown/opaque envelope and was followed as the subgingival debridement were performed . The treatment was revealed only after the

debridement session, when the patient received the pills. The professional responsible for patient recruitment (MPS), treatment (CFA), and the clinical measures (NMRBA) were distinct.

The sample size of the study was calculated based on the results obtained by a previous study that evaluated the effect of daily supplementation of Ω-3 PUFA and low-dose ASA in the treatment of chronic periodontitis (El-Sharkawy et al., 2010). Considering $\alpha = 5\%$ and $\beta = 20\%$ (80% power) to detect an intergroup difference of at least 1.2 mm in the PD of pockets > 5 mm, with a standard deviation of 0.8 mm, 16 patients would be needed in each group. To compensate possible attritions, 19 patients per group were included, obtaining a power > 80%.

All diseased sites were instrumented in a single session by a trained operator (CFA). The patients received local anesthesia and one-stage full-mouth ultrasonic debridement (FMUD) (Wennström et al., 2005) by an ultrasonic device with specific tips for subgingival scaling. The patients were assigned to the following groups according to the randomization:

- Test Group (TG) (n=19): FMUD associated with 900 mg PUFA Ω-3 + 100 mg ASA daily for 180 days;
- Control Group (CG) (n=19): FMUD and placebo.

All clinical measures were performed by one calibrated and blinded researcher (NMRBA). Clinical measures were performed at baseline, 3 and 6 months after the treatment, in all teeth, except third molars. The following clinical parameters were evaluated: 1) Probing depth (PD): distance from the bottom of sulcus/pocket to gingival margin; 2) Clinical attachment level (CAL): distance from the bottom of sulcus/pocket to cement–enamel junction (CEJ); 3) gingival recession (GR): distance from gingival margin to CEJ; 4) full-mouth plaque index (FMPI); and 5) full-mouth bleeding on probing (BoP). The clinical measures were assessed using a manual probe (North Carolina, Hu-Friedy). In addition, PD, CAL and GR measurements were done at six sites per tooth (mesiobuccal, buccal, disto-buccal, distolingual, lingual, and mesiolingual).

Statistical Analysis Plan

Mean and standard deviation were calculated for each parameter. The normal distribution was analyzed using the Shapiro-Wilk test. Demographic data were analyzed using the t-test for independent variables. The differences between the full-mouth variables were analyzed using a Generalized Estimated Equations Model and the reductions were evaluated by Generalized Linear Models, adjusted to baseline when indicated. The post-hoc test applied for each peer comparison was Bonferroni. The data were analyzed using the concepts of per-protocol and intention-to-treat. The statistical analysis was performed using significance level of 5%, using IBM SPSS.