Nutrición Hospitalaria

SENPE

Efecto de la suplementación con fibra prebiótica sobre la microbiota intestinal de un grupo de personas mayores con enfermedad de Parkinson de la ciudad de Santiago de Chile. Un estudio piloto

The effect of supplementation with prebiotic fiber on the gut microbiota of a group of older people with Parkinson's disease from the city of Santiago de Chile. A pilot study

10.20960/nh.05272

02/25/2025

5272

The effect of supplementation with prebiotic fiber on the gut microbiota of a group of older people with Parkinson's disease from the city of Santiago de Chile. A pilot study

Efecto de la suplementación con fibra prebiótica sobre la microbiota intestinal de un grupo de personas mayores con enfermedad de Parkinson de la ciudad de Santiago de Chile. Un estudio piloto

Paula García-Milla[1,2], Gema Nieto[1], Mario Maulén[3], Carlos Tapia[1], Waldo Díaz-Vásquez[3]

[1]Department of Food Technology, Nutrition and Food Science. Veterinary Faculty. Universidad de Murcia. Regional Campus of International Excellence “Campus Mare Nostrum”. Campus de Espinardo. Espinardo, Murcia. [2]Nutrition and Dietetics. Health Sciences Faculty. Universidad Autónoma de Chile. Providencia, Chile. [3]Molecular Microbiology and Food Research Laboratory. School of Nutrition and Dietetics. Faculty of Sciences for Health Care. Universidad de San Sebastián. Carmen Sylva, Providencia Santiago. Chile

Received: 19/04/2024
Accepted: 21/02/2025
Correspondence: Gema Nieto. Department of Food Technology. Nutrition and Food Science. Veterinary Faculty. Universidad de Murcia. Regional Campus of International Excellence “Campus Mare Nostrum”. Campus de Espinardo, 30100 Espinardo. Murcia, Spain
e-mail: gnieto@um.es

Gema Nieto y Waldo Díaz-Vásquez are the correspondence authors of this article.

Acknowledgments: We want to thank the collaborators and institutions that participated in this project, particularly those who allowed us to request for the participation of patients for the study. Clinical Neurological Center of Chile, CENPAR.
Funding: This work was funded by FONDECYT 11170885, Main Researcher Dr. Waldo Diaz Vásquez.

Ethics approval and consent to participate: This project has the approval of the scientific ethics committee of the Murcia University of Spain ID 2202/2018.

Authors' contributions: P. G.: main idea, planning, implementation, analysis, nutritional assessment, and manuscript's writing; M. M.: biostatistical analysis, results; W. D.: director of the FONDECYT Project, funding acquisition, manuscript's review; G. N.: doctoral thesis director, planning study, manuscript's review; C. T.: microbiota analysis.

Conflict of interest: The authors declare no conflict of interest.

Artificial intelligence: The authors declare not to have used artificial intelligence (AI) or any AI-assisted technologies in the elaboration of the article.

ABSTRACT

Introduction: Parkinson's disease (PD) is the second most common neurodegenerative disorder worldwide. It has been demonstrated that there is a correlation between the increase in bacterial abundance and the severity of certain symptoms associated with PD.

Aim: the aim of this pilot study was to analyze the effect of supplementation with prebiotic fiber on the gut microbiota (GM) and nutritional status of elderly volunteers with Parkinson's disease.

Methodology: this is a pilot study of pre and post intervention with prebiotic fiber. All subjects involved were volunteers with PD, who were given nutritional counseling and gut microbiota measured on time cero and after 30 days of prebiotic fiber intervention. **Results:** a statistically significant difference was found in calf circumference (*p* 0.0422) after the intervention with prebiotic fiber. GM analyses show an initial difference in gut bacterial abundance of older people with PD and people without PD. Furthermore, our results showed a difference in bacterial families and genera after the supplementation with prebiotic fiber. in addition, we found a statistically significant difference in the value of circumference calf and a trend in the improvement of body weight, Body mass index (BMI), neck circumference, arm circumference, brachial area, and Diet Quality Questionnaire (DQQ) for older adults.
Conclusion: supplementation with 20 g of prebiotic fiber for 30 days could modify the intestinal microbiota, reducing bacterial genera and phylum that are abundant in Parkinson's disease, such as *Verrucomicrobia*. Therefore, the use of prebiotic fiber could represent an alternative to improve intestinal health and nutritional status of people with Parkinson's disease.

Keywords: Dietary fiber. Inulin. Gastrointestinal microbiome. Parkinson's disease.

RESUMEN

Introducción: la enfermedad de Parkinson (EP) es el segundo trastorno neurodegenerativo más común a nivel mundial. Se ha demostrado que existe una correlación entre el aumento de la

abundancia bacteriana y la gravedad de determinados síntomas asociados a la EP.

Objetivo: el objetivo de este estudio piloto fue analizar el efecto de la suplementación con fibra prebiótica sobre la microbiota intestinal (MI) y el estado nutricional de voluntarios ancianos con enfermedad de Parkinson.

Metodología: este es un estudio piloto de pre y post intervención con fibra prebiótica. Todos los sujetos involucrados fueron voluntarios con EP, a quienes se les brindó asesoramiento nutricional y se midió la microbiota intestinal en el tiempo cero y después de 30 días de intervención con fibra prebiótica.

Resultados: se encontró diferencia estadísticamente significativa en la circunferencia de la pantorrilla (p 0,0422) después de la intervención con fibra prebiótica. Los análisis de transgénicos muestran una diferencia inicial en la abundancia de bacterias intestinales entre personas mayores con EP y personas sin EP. Además, nuestros resultados mostraron una diferencia en las familias y géneros bacterianos después de la suplementación con fibra prebiótica. además, encontramos una diferencia estadísticamente significativa en el valor de la circunferencia de la pantorrilla y una tendencia en la mejora del peso corporal, índice de masa corporal (IMC), circunferencia del cuello, circunferencia del brazo, área braquial y el Cuestionario de Calidad de la Dieta (DQQ) para adultos mayores.

Conclusión: la suplementación con 20 g de fibra prebiótica durante 30 días podría modificar la microbiota intestinal, reduciendo géneros y filos bacterianos abundantes en la enfermedad de Parkinson, como la *Verrucomicrobia,* por lo que el uso de fibra prebiótica podría representar una alternativa para mejorar la fibra prebiótica. Estado de salud y nutrición de las personas con enfermedad de Parkinson.

Palabras clave: Fibra dietética. Inulina. Microbioma gastrointestinal. Enfermedad de Parkinson.

INTRODUCTION

Gut microbiota (GM) is an assemblage of microorganisms present in the intestine and constitutes the largest population of microorganisms inhabiting the human body, including more than 1,000 bacterial species, with *Firmicutes* and *Bacteroidetes* being the predominant phyla in the human gastrointestinal tract and representing 90 % of the microbial population (1); these phyla are mainly associated with the metabolism of carbohydrates and amino acids, respectively.

GM is regulated by several factors throughout a person's life, such as delivery mode, gestational age, exposure to antibiotics and metals, and diet (2), this latter factor directly and significantly influences gut microbial communities, even in short periods of time; GM may be positively or negatively modulated when it comes to the subject's health, and can ultimately accelerate the progression of chronic diseases such as chronic kidney disease or Parkinson's disease (PD) (3).

PD is the second most common neurodegenerative disorder worldwide, after Alzheimer’s disease and is characterized by the loss of dopaminergic neurons in the substantia nigra pars compacta due to the build-up of Lewy bodies in these cells, causing oxidative stress and the consequent neuronal death (4). These events lead to diverse motor symptoms, with the most classic being gait difficulty, postural instability and involuntary tremor, and non-motor complications such as chronic constipation, deterioration of nutritional status, sarcopenia, and cognitive impairment (5).

Studies conducted in mice have demonstrated that there is a correlation between the increase in bacterial abundance present in GM and the severity of certain symptoms associated with the disease (6), even the relationship that GM has in the synthesis of dopamine

given the intrinsic enzymatic activity that is highly involved in dopamine metabolism (7). Researchers have studied GM of people who suffer from this disease and have identified an alteration in the biodiversity and abundance of resident bacteria, confirming a bidirectional relationship between gut microbiota (GM) and the central nervous system, establishing the existence of the microbiota-gut-brain axis (8), which is thought to be a potential trigger for brain diseases. According to recent studies, the alteration of GM is related to motor disorders, chronic constipation, muscle mass loss; moreover, it has been hypothesized that intestinal dysbiosis would be an indicator to determine the stages of cognitive impairment (9).

Vegetable dietary fibers are food-sourced carbohydrates that are not digested or absorbed by human enzymes, passing intact into the intestine where bacteria (10), mainly *Firmicutes* such as *Bifidobacteria* and *Lactobacillus*, ferment them, producing components that provide benefits to human health (11). Studies have shown that the intake of this type of fibers leads to an increase in phylum level and in the production of short-chain fatty acids such as butyric acid (12). For this reason, the objective of this pilot study was to analyze the effect of supplementation with prebiotic fiber on the GM and nutritional status of elderly volunteers with Parkinson's disease.

MATERIALS AND METHODS

This is a pilot study of pre- and post-intervention with prebiotic fiber. Nine people were recruited, of whom five completed the treatment. The median age was 71 years, with a minimum age of 62 years and a maximum age of 75 years. All subjects involved were volunteers with Parkinson's disease (Parkinson group), who received nutritional counseling at the Clinical Neurological Center CENPAR, Chile. They are individuals over 60 years old, with Parkinson's disease, who donated their samples to be analyzed and compared in their basal state (without prebiotic fiber intervention) with a group of 4 people over 60

years old, volunteers in an ongoing study at the molecular microbiology and food research laboratory, who did not have serious illnesses, did not suffer from Parkinson's disease (PD), and were self-sufficient. This group of people without PD served as the control group for the microbiota analysis in fecal samples “at time zero” (without intervention). The control group for fecal samples did not receive intervention or evaluation of nutritional status, as the samples had been voluntarily donated to the laboratory months earlier for an ongoing study in which their baseline gut microbiota had already been analyzed.

This pilot study aims to identify issues and errors in the protocol to improve the design for the final intervention study, which intends to analyze 40 fecal samples from volunteers with PD (non-probabilistic sample based on published studies).

Nutritional assessment

The Parkinson group underwent a Nutritional Status Assessment (NSA) that included measurements of weight, height, Body mass index (BMI) for this, a professional SECA® brand scale and stadiometer was used, according to the protocol declared in the Krause diet therapy book (13). Dynamometry, a CAMRY® hand dynamometer is used, based on the protocol described by Paz TDSR et al 2022 (14). Calf circumference, brachial circumference, tricipital skinfold thickness, neck circumference was measured with a SECA brand medical tape according to the measurement protocol of Raymond & Morrow, 2021.

It was also measured the application of the SARC-F screening sarcopenia tool (SARC-F) (15), Mini Nutritional Assessment (MNA) (16), and Diet Quality Questionnaire (DQQ) for older adults (17).

The nutritional evaluation method was applied before the intervention and at the end of the study, using the same instruments and protocols declared.

The collection of anthropometric data was carried out in the nutritional office especially implemented for the study, with a maximum duration of 1 hour to prevent older people to get tired.

Intervention with prebiotic fiber

The nutritional intervention consisted of the supplementation of 20 grams of inulin or oligofructose per day in the form of prebiotics derived from polysaccharides, for a period of 30 days, without modifying the diet.

The fiber (inulin/oligofructose) was randomly selected using software (26), without mentioning the type of fiber the volunteers were consuming. According to this distribution, 3 people were supplemented with inulin and 2 with oligofructose (Fructooligosaccharides).

Participants were instructed to consume 20 g of a prebiotic with a glass of water in the mornings, avoiding simultaneous dairy intake due to its possible chelating effect.

The determination of the dose and intervention time is based on previous studies (18) and subsequent modification according to own test carried out in the Molecular Microbiology and Food Research laboratory, San Sebastian University.

Inclusion and exclusion criteria

Exclusion criteria were defined as follows: use of medication such as antibiotics and laxatives; history of serious or severe pathology, immunodeficiency, digestive and intestinal disease, or malabsorption; chemotherapy or radiotherapy treatment; history of alcohol and drug abuse; morbid obesity, defined with a BMI over 40 kg/m^2; completely immobile, hospitalized, or institutionalized patients. Additionally, if there was a modification in diet or exercise, or a change in medical treatment during the intervention, or probiotic consumption, the participation in the study was over.

Any person over 60 years of age with Parkinson's disease who was willing to participate and voluntarily signed the informed consent was included.

Analysis of the gut microbiota

Measurement of GM was performed for 3 times: at the beginning or time zero (without intervention), after one week (7 days), and when the 30 days of supplementation were completed. The determination of GM was conducted using a qPCR-based GUt Low Density Array (GULDA), high-throughput real-time quantitative PCR-based analysis platform.

DNA extraction

DNA was extracted from stool samples with high fiber content, according to the standardized method of the Molecular Microbiology and Food Research laboratory.

Samples were thawed at 4 °C and placed in aliquots of 200 mg of sample containing 200 mg of beads for mechanical disruption. TE buffer was added for resuspension, vortexed at 2500 rpm for 10 min, then the sample was centrifuged for 1 min at maximum speed and transferred to a clean tube. Proteinase K was added to a final concentration of 1 mg/ml and incubated at 50 °C for 10 min. Subsequent steps were performed according to the manufacturer's instructions (Qiagen Power Fecal Kit protocol) and finally, the eluted DNA was stored at -20 °C until use (19).

Subsequently, the integrity of the genetic material obtained was visualized through the method of 1 % agarose gel electrophoresis, and quantified using TECAN methods, establishing an adequate presence of the genetic matter in a value higher than 50 ng/µl. To identify the different groups of existing bacteria, the real-time PCR-based GUt Low-Density Array (GULDA) was used. This technique was validated by Bergström et al. (2012). was designed for simultaneous

analysis of the change in the abundance of 31 different microbial 16S rRNA gene targets in fecal samples obtained from individuals at various points in time (20), to screen human stool samples from the volunteers.

The sequencing of the V4 region of the 16S rRNA gene was performed by synthesis sequencing with a Miseq illumina equipment, using 50 ng of bacterial genomic DNA from each sample provided by our laboratory. The primers that will be used were those indicated by the Argonne laboratory: 515F (5′-GTGCCAGCMGCCGCGGTAA-3′) y 806R (5′-GGACTACHVGGGTWTCTAAT-3′) (21).

In order to determine the richness and abundance of bacterial genera present in stool samples of each subject, evaluating the increase or decrease of such genera, we did use the DESeq2 package was used (R version 4.1.2, DESeq2 version 3.14).

To determine significant changes in the genera found in each sample, the SILVA database (version 138.1) was employed to assign the taxonomy to operational taxonomic units, so that it is possible to characterize the alpha diversity of each genus found, by means of the Microbiome package (version 3.14). The alpha indexes used were Shannon and Simpson.

Sample collection

Nutritional status assessment was conducted in the first appointment, and it was explained how the stool sample must be obtained, providing the subject with an informative leaflet along with a sampling kit that consisted of: gloves; a tongue depressor or wooden spatula; a sterile vial; labels to indicate name, date, and hour; a toilet hat.

Regarding the delivery of the stool sample, this must be handed under specific conditions, such as: handing it at room temperature immediately after having been collected or within a maximum of 1 hour, or it could be delivered frozen in case of handing it days after the sample collection; in the latter case, participants were informed

Nutrición Hospitalaria

about the cold storage and transportation conditions before delivering the sample in our laboratory.

Supplementation with fiber was introduced in the second appointment; subjects were required to provide a stool sample 1 week after initiating the supplementation, in order to observe if there were short-term changes in GM.

Telephone follow-up was conducted during the study, and a final nutritional appointment was scheduled to perform the initial assessment again; a stool sample was required at the end of the intervention, with prebiotic fiber being discontinued after the collection of the stool sample.

Ethics committee

All the participants of the intervention were handed an informative leaflet about the study; all the topics related to the intervention were reinforced in an in-person explanatory interview, with the aim of complying with the standards on ethics and dissemination of information, before signing the informed consent form.

The preparation of the ethical report, as well as the development of the intervention, were based on the declaration of Helsinki, and the CIOMS Guidelines were consulted for conducting the research with human beings.

This study was approved by the ethics committee of the University of Murcia, Spain ID 2202/2018.

Sampling and data collection

A non-probabilistic convenience sample was conducted, incorporating all individuals who met inclusion or exclusion criteria and agreed to participate and signed the informed consent form; a deadline and a minimum number of volunteers were established, conditions that were disrupted by reasons not related to the study, that was closed with 9 patients, of whom only 5 completed the intervention. We

consider that nutritional studies in Parkinson's disease usually have small samples (between 8 and 30 people) (22).

Statistical analysis

Statistical analyses were conducted by means of a non-parametric test to compare the middle range of two related Wilcoxon samples for NSA and GM Analysis data between intervention periods (pre and post). For that we used Statistical software for data science (STATA).

RESULTS

In this study, 5 of 9 subjects complete the intervention, of the 5 participants with PD, 1 was female (20 %) and 4 were male (80 %).

The reasons why not all participants completed the study include: use of antibiotics due to an infectious condition, discontinuation of treatment with the prebiotic fiber (non-adherence), failure to attend the final evaluation, and failure to submit the final fecal sample for analysis within the required timeframe.

According to the descriptive analysis of the nutritional status assessment (NSA), the average body mass index (BMI) was 25 kg/m^2, which corresponds to a normal nutritional status which is in line with the national criteria established and mentioned by the Spanish Society of Geriatrics and Gerontology (SEGG, for its acronym in Spanish) and the Spanish Society of Clinical Nutrition and Metabolism (SENPE, for its acronym in Spanish) (23), with no presence of sarcopenia or alterations in muscle composition, based on the assessment of: calf circumference, brachial circumference or arm circumference, brachial perimeter, brachial area, dynamometry, and the SARC-F screening questionnaire (Table I).

According to the data, we can mention a statistically significant increase in calf circumference (p 0.0422) after the intervention with prebiotic fiber, and a trend in neck circumference (p 0.0568) which presented a decrease of 2.8 in their medians, as did the Diet Quality

Questionnaire (DQQ) for older adults, which increased in comparison after the intervention (p 0.0796) (Table I).

Also, after the treatment with prebiotic fiber, the subjects reported a slight improvement in the consistency of their depositions, indicated in the quality of their stools according to the Bristol Stool Form scale (Table II).

Microbiota baseline analysis

Microbiota analysis was performed at time zero (without intervention) on the 5 volunteers suffering from Parkinson's disease and compared with fecal samples from 4 volunteers without Parkinson's disease.

By performing of Observed (A), Shannon (B) and Simpson (C) alpha diversity analysis, we observed a trend showing a difference in alpha diversity between people suffering from PD and older people without the disease (healthy controls) (Fig. 1).

Time-zero analyses of bacterial phyla abundance showed significant differences between the subjects with PD and the controls, the main differences are related to the phyla *Bacteroidetes, Proteobacteria* and *Verrucomicrobia*, which are present in greater abundance in people of the Parkinson group. The most abundant phylum, both in the Parkinson group and in the control group, is *Firmicutes*, with slightly higher numbers in the controls. Another abundant Phylum corresponds to *Verrucomicrobia,* with significantly greater numbers in people living with the disease (Fig. 2).

The relative abundance analysis of the bacterial genera identified in stool samples of the study subjects shows a significant difference in *Bacteroidetes, Akkermansia, Escherichia, Shigella, Agathobacter*, being highly predominant in the Parkinson group. In addition, a greater presence of *Streptococcus* and *Catenibacterium* can be noted in the controls (Fig. 3).

Microbiota analysis according to the intervention performed

In graph 4 you can see the analysis of alpha diversity expressed in the means of each of the groups and intervention time.
In the analysis of Observed (A), Shannon (B) and Simpson (C), a trend towards increasing alpha diversity is observed in the group that underwent inulin intervention after 30 days of intervention, which is observed as a separation in their values from the average between both groups (Fig. 4).

Genus abundance according to time and type of intervention

It was possible to observe that the intervention with oligofructose caused a modulation of genera in the intervened patients, both at 7 days of consumption and at the end of the 30 days of intervention. According to the figure 5, genera related to dysbiosis in subjects with PD, such as *Enterorhabdus, Bacteroidetes, Euryarchaeota, Proteobacteria* and *Verrucomicrobia* showed a decrease in the presence of oligofructose, along with a proliferation of *Firmicutes* in each one of the samples of the subjects treated with this prebiotic. Similarly, GM in patients who received Inulin was evaluated; it is observed a decrease in *Bifidobacterium, Verrucomicrobia*, Agathobacter (Fig. 5).
A similar effect was found in the phyla, where the intervention with oligofructose resulted in a decline in the abundance of *Bacteroidetes, Euryarchaeota*, *Proteobacteria* and *Verrucomicrobia* at the end of the treatment period, nevertheless, it was noted a slight increase in *Firmicutes* after 30 days.
With respect to the intervention with Inulin, it is observed a decline in *Verrucomicrobia* and a slight decrease in *Firmicutes* (Fig. 6).
A Wilcoxon statistical analysis was applied to the GM at baseline in the Parkinson's disease volunteers, comparing it with the group of volunteers without the disease. The results show statistically significant differences in 10 bacterial genera, which are detailed in table III.

The genera *Alistipes* followed by *Ruminiclostridium 50* are present in 4 and 5 of the evaluated volunteers, respectively, compared to 0.5 in the volunteers without the disease. It is important to note that *P50* refers to a value located in the middle range in relation to the other evaluated species.

DISCUSSION

Nutritional status is fundamental for older people suffering from PD; it has been noted that the severity and duration of the disease, as well as its symptoms and L-Dopa intake are closely correlated with nutritional status (24). It is important to mention thar levodopa or L-Dopa (3,4-dihydroxyphenylalanine), it is a chiral amino acid generated via biosynthesis from l-tyrosine in plants and some animals (25). Dopamine (DA) supplementation therapy by L-dopa for Parkinson's disease (PD) was established around 1970 and has since become the gold standard medical therapy (26).

The importance of Levodopa in nutrition lies in the high pharmaco-nutrient interaction between the drug and the amino acids in the diet (27); In addition to the association that has been found between the use of L-dopa and malnutrition in people suffering from the disease. According to a study that evaluated nutritional status through mini nutritional assessment (MNA) and compared it with the use of dopaminergic drugs, it concluded that otal levodopa (L-dopa) equivalent daily dose was associated with worse MNA (B = -0.14, 95 % CI = -0.26--0.02; p = 0.019). Presenting a worse nutritional status and risk of malnutrition (28).

Recent studies have highlighted the role of GM in PD, indicating that intestinal dysbiosis could promote the development and progression of the disease (29) and intervene in the absorption of levodopa (30). There is a connection between gut bacteria and PD (31) that might be the key in the treatment of the disease. Moreover, according to recent studies, there are bacterial species present in gut microbiota, such as *Clostridium sporogenes* (10), *Enterococcus faecalis* (11) that have the

ability to metabolize L-DOPA, reducing the effectiveness of this treatment in subjects with PD.

In the first instance, constipation of the participants was assessed after completion of the treatment. In a double-blind randomized controlled trial conducted with PD patients, it was found that the consumption of fermented milk along with prebiotic fiber was superior to placebo in improving constipation. On the other hand, animal studies have showed an increase in fecal water content in mice treated with Lotus seed oligosaccharides (LSO), along with an enhancement in the concentration of short-chain fatty acids (SCFAs), concluding that LSO or the combination with resistant starch has a better effect on relieving constipation (32). Similar results were obtained in a rat model with Diphenoxylate-induced constipation. The rats were treated with inulin and isomalto-oligosaccharide (IMO), showing an increase in SCFAs and an improvement in the number, weight, and water content of fecal pellets (33).

In our study, after the treatment with prebiotic fiber, the subjects reported a slight improvement in the consistency of their depositions, indicated in the quality of their stools according to the Bristol Stool Form scale (34), with similar results being observed with inulin versus oligofructose; however, the frequency or number of depositions did not increase (Table III).

When establishing the relative abundance of each one of the phyla present in the samples of subjects with PD and controls in time zero, we were able to determine that there is a significant difference in the abundance of *Bacteroidetes, Proteobacteria* and *Verrucomicrobia*; this last phylum stands out for its richness, since GM of Chilean subjects generally contains a higher percentage of *Verrucomicrobia* due to the high consumption of wheat-based baked products, such as bread. These results are similar to those found in a study on the characterization of GM in the Chilean population, which showed that the most prevalent phylum was *Firmicutes*, followed by *Bacteroidetes*, *Verrucomicrobia*, *Proteobacteria*, *Actinobacteria* and *Euryarchaeota*,

with *Verrucomicrobia* being one of the most abundant phyla in subjects with PD, thus representing a window of opportunity to examine if this prevalence of *Verrucomicrobia* in GM of Chileans is related to the prevalence of Parkinson's disease in Chile (35).

GM population profiles of individuals with PD are correlated with those presented by a meta-analysis that analyzed the 16S ribosomal RNA gene sequencing analysis in samples obtained from 223 patients with PD and 137 controls; it was found that genera *Akkermansia* and *Catabacter*, as well as families *Akkermansiaceae* were increased, whereas genera *Roseburia*, *Faecalibacterium,* and *Lachnospiraceae* were decreased in people with PD (36). This supports the view that subjects with PD present a characteristic intestinal dysbiosis. This has an impact on the health of people with PD, since these genera are producers of short-chain fatty acids (37), on the other hand, it has been found that an increase in *Akkermansiaceae* might degrade the intestinal mucin layer and may be involved in the pathophysiological processes of PD (38). In our study, when performing the treatment with the selected prebiotics, it could be noted a decrease in *Akkermansiaceae*, *Bacteroidetes*, *Verrucomicrobia*, and *Actinobacteria* in the treated subjects, both when employing inulin and oligofructose, modulating GM profile so that it was similar to that of the control subjects.

A group of researchers analyzed GM of people with PD, comparing them with a control group, finding significant differences. When analyzing baseline GM, it was found a greater abundance of *Alistipes*, *Rikenellaceae_RC9_gut_group*, *Bifidobacterium*, *Parabacteroides*, with a decline in *Faecalibacterium*. These results greatly differ from those observed in our intervention group, with the only similarity found being *Bifidobacterium* (39).

Furthermore, it was found that PD, constipation, sex, age, and the intake of catechol-O-methyltransferase (COMT) inhibitors affected the overall composition of GM (37).

In our study, it was observed a significant difference between time zero and post-intervention time in the parameter of calf circumference, and a trend in the parameters of weight, BMI, neck circumference, calf circumference, brachial area.

These results are similar to those found in a longitudinal study where it was observed a decrease in BMI, overall body fat percentage, visceral fat, and subcutaneous fat in comparison to controls, concluding that the severity of motor impairment is associated with a decrease in total body fat (40). On the other hand, BMI is significantly correlated with the global scores of parts I, II and III of the Unified Parkinson's Disease Rating Scale (UPDRS).

It is certainly interesting to examine what the real impact of prebiotic fiber supplementation is with respect to parameters of muscle composition and nutritional status of older people with PD, and how is microbiota involved in these potentially favorable changes.

Most studies related to the consumption and benefits of dietary fiber are oriented towards a gastrointestinal system and health benefits perspective, particularly targeting GM, cardiovascular health, and some types of cancer. Nevertheless, our view is that there is a knowledge gap when we want to examine the relationship between dietary fiber and nutritional status, specifically the effect on body composition parameters.

Limitations of the study

It is important to mention that the main limitation of the study was the number of samples and, subsequently, those who were able to complete the intervention. On the other hand, using two types of fiber in a sample of only five individuals does not allow for robust observations.

In the future, we will include a larger sample size with a control group, to which all evaluations and interventions will be performed, assigning participants according to the laws of randomization for this type of study.

Finally, we would like to mention that this pilot study has allowed us to analyze and improve the protocols and quality of the intervention, which in the future may help guide decision-making and be applied in the final intervention study, thus reducing potential biases and complications that may arise.

CONCLUSION

The consumption of 20 g of prebiotic fiber for 30 days could favorably modify the intestinal microbiota in people with Parkinson's disease. Bacterial populations such as *Verrucomicrobia*, which are found in a higher percentage in the Chilean population than in the rest of the world, and which increase abundance in subjects with PD, are reduced when consuming prebiotic fiber.

Many studies support the benefits of consuming prebiotic fiber for the health and microbiota of those who consume it. Moreover, our results allow us to state that the incorporation of fiber into the diet could be a treatment alternative to improve the intestinal microbiota and the health of older people with Parkinson's disease.

It is necessary to deepen how these changes could be affecting the symptoms of the disease, however, diet and in this case the use of prebiotic fiber may represent an alternative to improve the intestinal health of people with Parkinson's disease.

REFERENCES

1. Fujio-Vejar S, Vasquez Y, Morales P, Magne F, Vera-Wolf P, Ugalde JA, et al. The gut microbiota of healthy Chilean subjects reveals a high abundance of the phylum Verrucomicrobia. Front Microbiol 2017;8:1221. DOI: 10.3389/fmicb.2017.01221
2. Adak A, Khan MR. An insight into gut microbiota and its functionalities. Cell Mol Life Sci 2019; 76(3):473-93. OI: 10.1007/s00018-018-2943-4

3. Álvarez-Calatayud G, Guarner F, Requena T, Marcos A. Dieta y microbiota. Impacto en la salud. Nutr Hosp 2018;35(Spec No6):11-5. DOI: 10.20960/nh.2280
4. Castillo-Álvarez F, Marzo-Sola ME. Papel de la microbiota intestinal en el desarrollo de diferentes enfermedades neurológicas. Neurología 2022;37(6):492-8. DOI: 10.1016/j.nrl.2019.03.017
5. Bhattarai Y, Kashyap PC. Parkinson's disease: Are gut microbes involved? Am J Physiol Gastrointest Liver Physiol 2020;319(5):G529-40. DOI: 10.1152/ajpgi.00058.2020
6. Sampson TR, Debelius JW, Thron T, Janssen S, Shastri GG, Ilhan ZE, et al. Gut Microbiota Regulate Motor Deficits and Neuroinflammation in a Model of Parkinson's Disease. Cell 2016;167(6):1469-80.e12. DOI: 10.1016/j.cell.2016.11.018
7. Hamamah S, Aghazarian A, Nazaryan A, Hajnal A, Covasa M. Role of Microbiota-Gut-Brain Axis in Regulating Dopaminergic Signaling. Biomedicines 2022;10(2):436. DOI: 10.3390/biomedicines10020436
8. Góralczyk-Bińkowska A, Szmajda-Krygier D, Kozłowska E. The Microbiota-Gut-Brain Axis in Psychiatric Disorders. Int J Mol Sci 2022;23(19):11245. DOI: 10.3390/ijms231911245
9. Arikan M, Yildiz Z, Kahraman Demir T, Yilmaz NH, Sen A, Hanoglu L, et al. Axillary Microbiota Is Associated with Cognitive Impairment in Parkinson's Disease Patients. Microbiol Spectr 2022 Feb 23 [cited 2022 Jun 7];10(1). Available from: https://pubmed.ncbi.nlm.nih.gov/35138147/
10. van Kessel SP, de Jong HR, Winkel SL, van Leeuwen SS, Nelemans SA, Permentier H, et al. Gut bacterial deamination of residual levodopa medication for Parkinson's disease. BMC Biol 2020;18(1):137. DOI: 10.1186/s12915-020-00876-3
11. Jameson KG, Hsiao EY. A novel pathway for microbial metabolism of Levodopa. Nat Med 2019;25(8):1195-7. DOI: 10.1038/s41591-019-0544-x
12. Tian R, Hong J, Zhao J, Zhou D, Liu Y, Jiao Z, et al. Overall Structural Alteration of Gut Microbiota and Relationships with Risk Factors in

Patients with Metabolic Syndrome Treated with Inulin Alone and with Other Agents: An Open-Label Pilot Study. Mediators Inflamm 2022;2022:1-9. DOI: 10.1155/2022/2078520

13. Raymond JL, Morrow K. Dietoterapia. 15°. Elsevier, editor. Barcelona, España: 2021; 2021.
14. Paz TDSR, De Britto VLS, Yamaguchi B, Israel VL, Swarowsky A, Lourenço Correa C. Hand Function as Predictor of Motor Symptom Severity in Individuals with Parkinson's Disease. Gerontology 2021;67(2):160-7. DOI: 10.1159/000511910
15. Malmstrom TK, Miller DK, Simonsick EM, Ferrucci L, Morley JE. SARC-F: a symptom score to predict persons with sarcopenia at risk for poor functional outcomes. J Cachexia Sarcopenia Muscle 2016;7(1):28-36. DOI: 10.1002/jcsm.12048
16. Rubenstein LZ, Harker JO, Salvà A, Guigoz Y, Vellas B. Screening for Undernutrition in Geriatric Practice Developing the Short-Form Mini-Nutritional Assessment (MNA-SF). J Gerontol A Biol Sci Med Sci 2001;56(6):M366-72. DOI: 10.1093/gerona/56.6.m366
17. Durán Agüero S, Candia P, Mena RP. Validación de contenido de la Encuesta de Calidad de Alimentación del Adulto Mayor (ECAAM). Nutr Hosp 2017;34(5):1311-8. DOI: 10.20960/nh.1081
18. Lai H, Li Y, He Y, Chen F, Mi B, Li J, et al. Effects of dietary fibers or probiotics on functional constipation symptoms and roles of gut microbiota: a double-blinded randomized placebo trial. Gut Microbes 2023;15(1):2197837. DOI: 10.1080/19490976.2023.2197837
19. Miranda MV, González FC, Paredes-Godoy OS, Maulén MA, Vásquez CC, Díaz-Vásquez WA. Characterization of metal(loid)s and antibiotic resistance in bacteria of human gut microbiota from chronic kidney disease subjects. Biol Res 2022;55(1):1-12. DOI: 10.1186/s40659-022-00389-z
20. Bergström A, Licht TR, Wilcks A, Andersen JB, Schmidt LR, Grønlund HA, et al. Introducing GUt Low-Density Array (GULDA)-a validated approach for qPCR-based intestinal microbial community analysis.

FEMS Microbiol Lett 2012;337(1):38-47. DOI: 10.1111/1574-6968.12004

21. Caporaso JG, Lauber CL, Walters WA, Berg-Lyons D, Lozupone CA, Turnbaugh PJ, et al. Global patterns of 16S rRNA diversity at a depth of millions of sequences per sample. Proc Natl Acad Sci U S A 2011;108 Suppl 1(Suppl 1):4516-22. DOI: 10.1073/pnas.1000080107
22. Zilli Canedo Silva M, Carol Fritzen N, de Oliveira M, Paes da Silva M, Rasmussen Petterle R, Teive HA, et al. Protein intake, nitrogen balance and nutritional status in patients with Parkinson's disease; time for a change? Nutr Hosp 2015;31(6):2764-70. DOI: 10.3305/nh.2015.31.6.8938
23. Sociedad Española de Nutrición Parenteral y Enteral (SENPE); Sociedad Española de Geriatría y Gerontología (SEGG). Valoración nutricional en el anciano [Internet]. [cited 2021 Jun 1]. Available from: https://www.segg.es/media/descargas/Acreditacion %20de %20Calidad %20SEGG/Residencias/valoracion_nutricional_anciano.pdf
24. Budrewicz S, Zmarzły A, Rączka D, Szczepańska A, Koziorowska-Gawron E, Słotwiński K, et al. Clinical and nutritional correlations in Parkinson's disease: Preliminary report. Adv Clin Exp Med 2019;28(2):193-8. DOI: 10.17219/acem/76375
25. Giuri D, Ravarino P, Tomasini C. L-Dopa in small peptides: an amazing functionality to form supramolecular materials. Org Biomol Chem 2021;19(21):4622-36. DOI: 10.1039/d1ob00378j
26. Nagatsu T, Sawada M. L-dopa therapy for Parkinson's disease: Past, present, and future. Parkinsonism Relat Disord 2009;15:S3-8. DOI: 10.1016/S1353-8020(09)70004-5
27. Leta V, Klingelhoefer L, Longardner K, Campagnolo M, Levent HÇ, Aureli F, et al. Gastrointestinal barriers to levodopa transport and absorption in Parkinson's disease. Eur J Neurol 2023;30(5):1465-80. DOI: 10.1111/ene.15734
28. Laudisio A, Vetrano DL, Meloni E, Ricciardi D, Franceschi F, Bentivoglio AR, et al. Dopaminergic agents and nutritional status in Parkinson's disease. Mov Disord 2014;29(12):1543-7. DOI: 10.1002/mds.25991

29. Sharma S, Awasthi A, Singh S. Altered gut microbiota and intestinal permeability in Parkinson's disease: Pathological highlight to management. Neurosci Lett 2019;712:134516. DOI: 10.1016/j.neulet.2019.134516
30. Rekdal VM, Bess EN, Bisanz JE, Turnbaugh PJ, Balskus EP. Discovery and inhibition of an interspecies gut bacterial pathway for Levodopa metabolism. Science 2019;364(6445):1055. DOI: 10.1126/science.aau6323
31. Huang Y, Liao J, Liu X, Zhong Y, Cai X, Long L. Review: The Role of Intestinal Dysbiosis in Parkinson's Disease. Front Cell Infect Microbiol 2021;11:615075. DOI: 10.3389/fcimb.2021.615075
32. Su H, Chen J, Miao S, Deng K, Liu J, Zeng S, et al. Lotus seed oligosaccharides at various dosages with prebiotic activity regulate gut microbiota and relieve constipation in mice. Food Chem Toxicol 2019;134:110838. DOI: 10.1016/j.fct.2019.110838
33. Lan J, Wang K, Chen G, Cao G, Yang C. Effects of inulin and isomalto-oligosaccharide on diphenoxylate-induced constipation, gastrointestinal motility-related hormones, short-chain fatty acids, and the intestinal flora in rats. Food Funct 2020;11(10):9216-25. DOI: 10.1039/d0fo00865f
34. Heaton KW, Radvan J, Cripps H, Mountford RA, Braddon FEM, Hughes AO. Defecation frequency and timing, and stool form in the general population: a prospective study. Gut 1992;33(6):818-24. DOI: 10.1136/gut.33.6.818
35. Leiva AM, Martínez-Sanguinetti MA, Troncoso-Pantoja C, Nazar G, Petermann-Rocha F, Celis-Morales C. Chile lidera el ranking latinoamericano de prevalencia de enfermedad de Parkinson. Rev Med Chil 2019;147(4):535-6. DOI: 10.4067/S0034-98872019000400535
36. Nishiwaki H, Ito M, Ishida T, Hamaguchi T, Maeda T, Kashihara K, et al. Meta-Analysis of Gut Dysbiosis in Parkinson's Disease. Mov Disord 2020;35(9):1626-35. DOI: 10.1002/mds.28119

37. Nishiwaki H, Hamaguchi T, Ito M, Ishida T, Maeda T, Kashihara K, et al. Short-Chain Fatty Acid-Producing Gut Microbiota Is Decreased in Parkinson's Disease but Not in Rapid-Eye-Movement Sleep Behavior Disorder. mSystems 2020;5(6):e00797-20. DOI: 10.1128/mSystems.00797-20
38. Fang X, Li F jun, Hong D jun. Potential Role of Akkermansia muciniphila in Parkinson's Disease and Other Neurological/Autoimmune Diseases. Curr Med Sci 2021;41(6):1172-7. DOI: 10.1007/s11596-021-2464-5
39. Yan Z, Yang F, Cao J, Ding W, Yan S, Shi W, et al. Alterations of gut microbiota and metabolome with Parkinson's disease. Microb Pathog 2021;160:105187. DOI: 10.1016/j.micpath.2021.105187
40. Pisciotta MS, Fusco D, Grande G, Brandi V, Lo Monaco MR, Laudisio A, et al. Untangling the relationship between fat distribution, nutritional status and Parkinson's disease severity. Aging Clin Exp Res 2020;32(1):77-84. DOI: 10.1007/s40520-019-01166-x

Table I. Descriptive analysis of the Nutritional Status Assessment pre- and post-intervention. Values expressed in median (p25-p75) ($n = 5$)

variable	**PRE**			**Post**			***p***
	Median	**(p25**	**p75)**	**Median**	**(p25**	**p75)**	**value**
Weight (kg)	68.2	65.1	73.9	68	66.6	75.5	0.0796
Height (mts)	1.66	1.65	1.67	1.66	1.65	1.67	1.0000
BMI (kg/mt^2)	25	23.6	27.8	24.9	24.1	28.4	0.0796
Calf circ. (cm)	35	34	37	36	36	39.8	0.0422
Neck circ.	39.2	37.5	40	42	37.5	43.3	0.056

(cm)							8
Arm circ. (cm)	30	28	30	30	28.5	31	0.0568
Tricipital skinfold thickness (mm)	12	11	15	14	10	16	0.1736
BMA	5092.2	4797.0	5478.6	5248.0	5219.5	5372.2	0.2249
BMP	252.9	245.5	262.3	256.7	256.0	259.8	0.2249
Brachial area	7165.6	6242.0	7165.6	7165.6	6467.0	7651.3	0.0568
BFA	1687.0	1445.0	2068.1	1946.1	1771.5	2279.0	0.1380
Dynamometry (kg)	32.6	26	33.2	28	28	32.9	0.5002
SARC-F (points)	2	0	2	2	0	2	0.3173
MNA (points)	26	25.5	27.5	28	26.5	28.5	0.2228
DQQ (points)	81	80	87	86	85	87	0.0796

BMA: brachial muscle area; BMP: brachial muscle perimeter; BFA: brachial fat area; circ: circumference; MNA: Mini nutritional assessment; DQQ: Diet Quality Questionnaire for older adults; BMI: Body mass index. *Sarc-f: screening sarcopenia tool.*

Table II. Self-registration of the volunteers involved in the evaluation of constipation according to the Bristol stool form scale

Nutrición Hospitalaria

Subject	Initial assessment (without intervention)		Final assessment (after the intervention)	
	Frequency of depositions declared	Bristol Scale declared	Frequency of depositions declared	Bristol Scale declared
PDS1	7/7	2	7/7	4
PDS2	2/7	3	3/7	4
PDS3	7/7	3	7/7	4
PDS4	2/7	2	2-3/7	4
PDS5	5/7	2	5/7	4

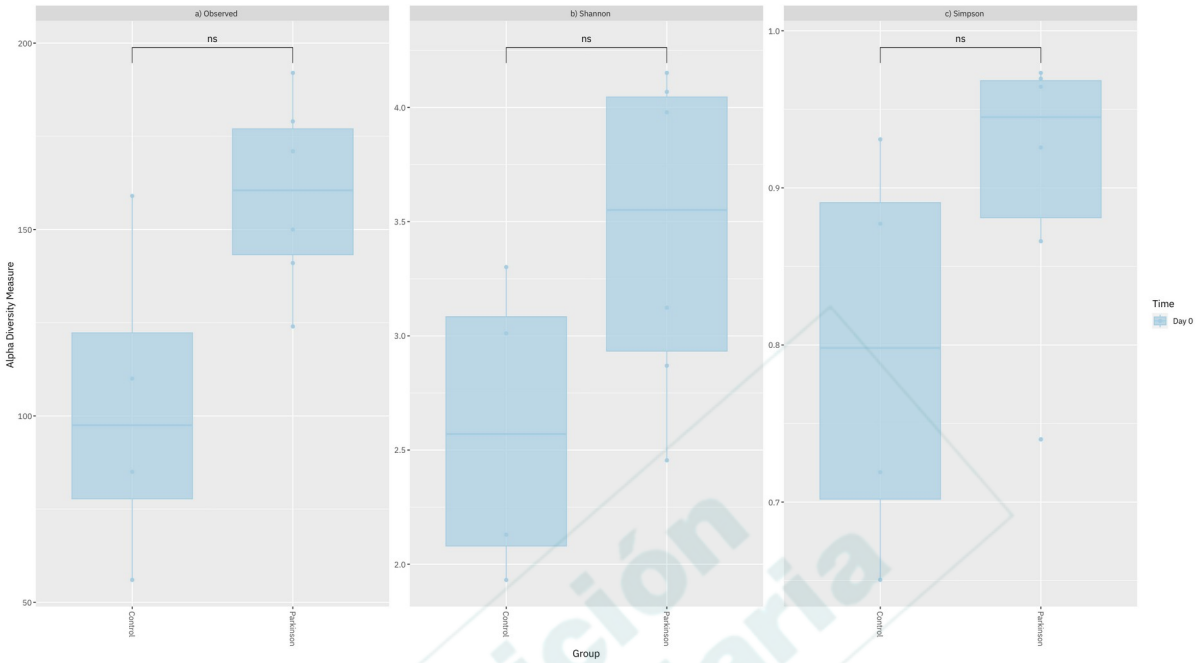
Subject: PDS corresponds to the coding of the intervened volunteers in accordance with data protection and confidentiality regulations.

Table III. Comparison of the microbiota at time zero between volunteers with Parkinson's disease and volunteers without Parkinson's disease ($n = 5$). The table shows the data in percentile values

Variable	Volunteers with Parkinson's disease		Volunteers without Parkinson's disease		*p* value
	n	p50 (p25-p75)	*n*	p50 (p25-	

						p75)	
Alistipes	5	5	(4-5)	4	0.5	(0-1)	0.0131
Butyricimonas	5	1	(1-1)	4	0	(0-0)	0.0237
Catenibacterium	5	0	(0-1)	4	1	(1-1)	0.0736
Desulfovibrio	5	1	(0-1)	4	0	(0-0)	0.0736
Flavonifractor	5	1	(1-1)	4	0	(0-0)	0.0285
Hungatella	5	1	(0-1)	4	0	(0-0)	0.0736
Intestinimonas	5	1	(1-1)	4	0	(0-0)	0.0237
Lachnospiraceae	5	0	(0-0)	4	0	(0-0)	0.079
Negativibacillus	5	1	(0-1)	4	0	(0-0)	0.0736
Odoribacter	5	1	(1-1)	4	0	(0-0)	0.0237
Oscillibacter	5	1	(1 -1)	4	0	(0-0)	0.0285
Parabacteroides	5	2	(2 -3)	4	0.5	(0-1.5)	0.0282
Paraprevotella	5	1	(0 -1)	4	0	(0-0)	0.0736
Parasutterella	5	1	(1 -1)	4	0	(0-0)	0.0237
Phascolarctobacterium	5	1	(1-1)	4	0	(0-0.5)	0.0253

Nutrición Hospitalaria



Prevotella	5	1	(0-1)	4	0	(0-0)	0.079
Prevotella 90	5	0	(0-0)	4	1.5	(1-2.5)	0.0528
Ruminiclostridium 50	5	4	(3-6)	4	0.5	(0-1.5)	0.0131

Figure 1. Comparison analysis of the alpha diversity of the microbiota without intervention (time zero) between volunteers with Parkinson's disease and volunteers without Parkinson's disease. The graph shows the mean values of each group evaluated for time zero (without intervention), evaluated in the indices a) observed b) Shannon and c) Simpson. ns: not significant for the Wilcoxon statistical test.

Nutrición Hospitalaria

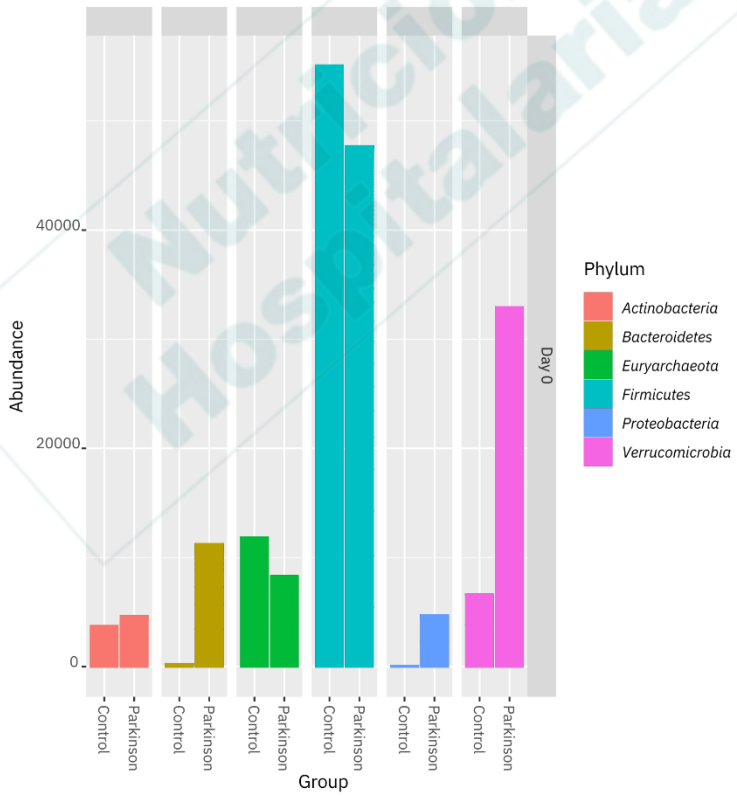


Figure 2. Analysis of microbiota phylum abundance without intervention (time zero) between volunteers with Parkinson's disease

and volunteers without Parkinson's disease. The graph shows an observation of the total abundance of phylum. Analysis of total abundance, the bacterial phylum is shown in colors, according to the volunteers; Control: Volunteers without Parkinson's disease; Parkinson's: Volunteers with Parkinson's disease. In colors you can see the bacterial phylum.

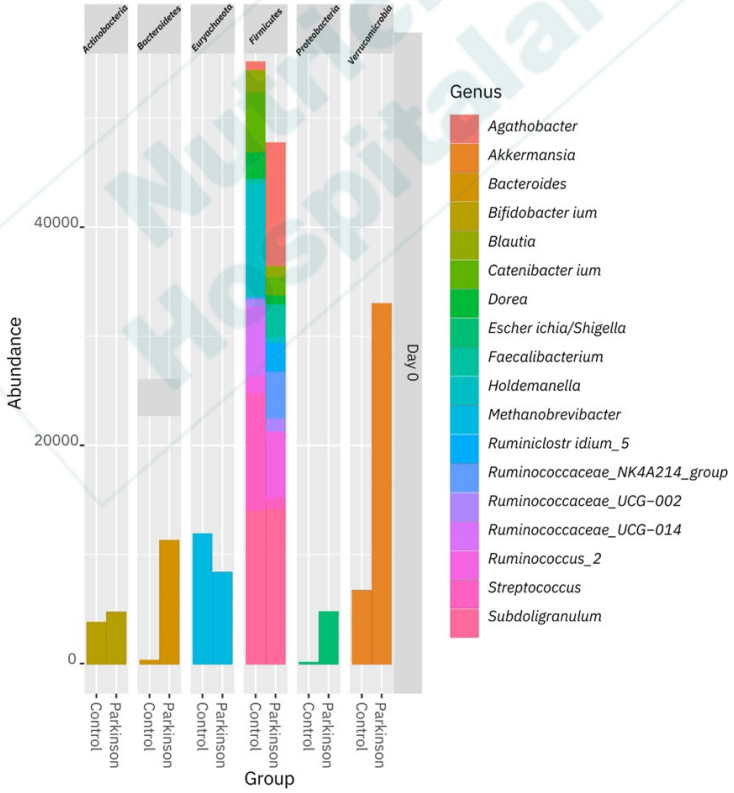
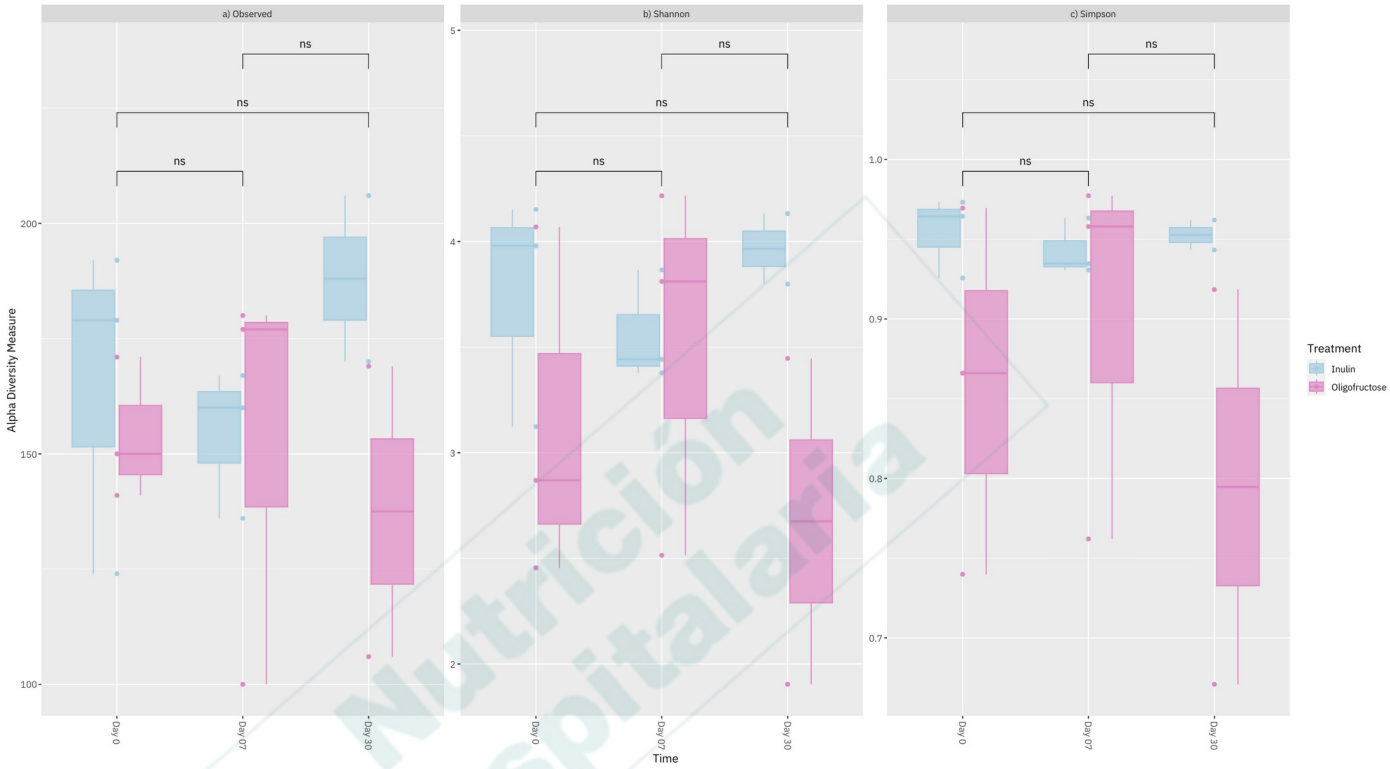


Figure 3. Analysis of microbiota genus abundance without intervention (time zero) between volunteers with Parkinson's disease and volunteers without Parkinson's disease. The graph shows an

observation of the total abundance of bacterial genus. Analysis of total abundance, bacterial genera are shown in colors, according to the volunteers; Control: Volunteers without Parkinson's disease; Parkinson's: Volunteers with Parkinson's disease. In colors you can



see the bacterial genera organized into phyla.

Figure 4. Analysis of the alpha diversity of the microbiota according to intervention time, in volunteers operated on with prebiotic fiber (inulin and oligofructose). The graph shows the standard deviation of the abundance measured in the Shannon and Simpson indices. Alpha

diversity analysis according to intervention time in volunteers with Parkinson's disease receiving prebiotic fiber. It is evaluated according to the indices a) observed b) Shannon and c) Simpson. In light blue, volunteers operated on with inulin and in pink, volunteers operated on

with oligofructose. ns: not significant after Wilcoxon test.

Figure 5. Analysis of the abundance of genera according to intervention time and type of prebiotic fiber. The graph shows the total sum of abundance of bacterial genera. Analysis of the

abundance of bacterial genera according to the type of prebiotic fiber used and intervention time. In colors the bacterial genus is observed.

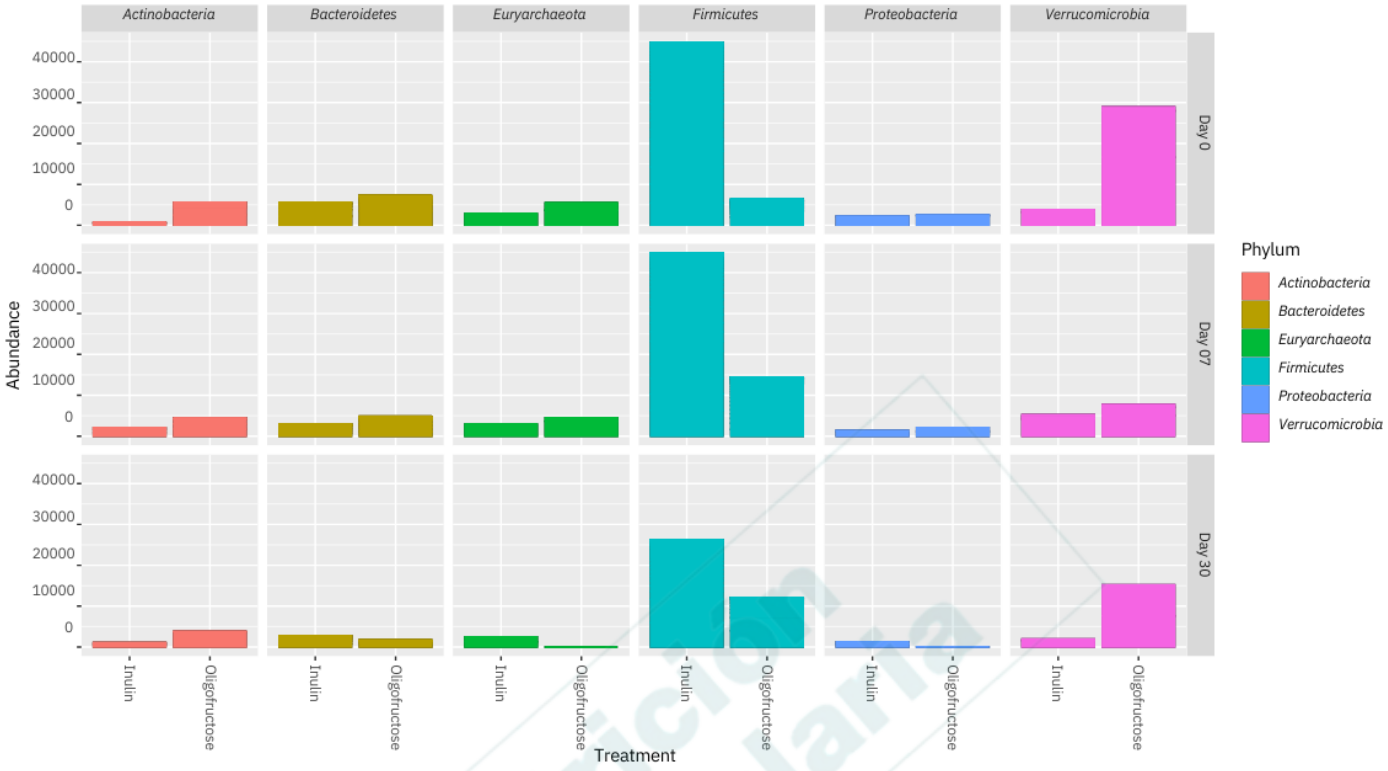


Figure 6. Analysis of the abundance of phylums according to intervention time and type of prebiotic fiber. The graph shows the sum of the abundance of bacterial phyla. Analysis of the abundance of bacterial phyla according to the type of prebiotic fiber and

intervention time. A particular color is assigned to each genus found among the 25 most abundant genera in the samples.

Nutrición Hospitalaria