“CAROL DAVILA” UNIVERSITY OF MEDICINE AND PHARMACY, BUCHAREST

DOCTORAL SCHOOL

FIELD: DENTAL MEDICINE

PhD SUMMARY

PhD Supervisor:

PROF. SILVIU MIREL PIŢURU MD, PhD

PhD Candidate:

CIONGARU NICOLAE DRAGOȘ

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The Rationale for Antibiotic Administration in Patients with Periodontal Disease and Parkinson’s Disease

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TABLE OF CONTENTS

List of Published Scientific Papers

Articles Published in Specialized Journals

1. **Ciongaru, Dragoș Nicolae**; Dumitriu, Anca Silvia; Dimitriu, Bogdan Alexandru; Păunică, Stana; Giurgiu, Marina Cristina; Mocanu, Brândușa Florina; Popescu, George Alexandru; and Pițuru, Silviu Mirel (2024) „Correlation between periodontal status and Parkinson's disease; a literature review," *Journal of Mind and Medical Sciences*: Vol. 11: Iss. 1, Article 5. IF - , Indexat BDI
DOI: https://doi.org/10.22543/2392-7674.1492
(Chapter 1,2 and 3) - page 4-29
https://www.mdpi.com/2392-7674/11/1/5

2. **Ciongaru, D.N**.; Piţuru, S.M.; Păunică, S.; Giurgiu, M.C.; Popescu, G.A.D.; Dumitriu, A.S. Comparative Study of Patients with Periodontal and Parkinson's Disease: Clinical and Salivary Aspects. *Biomedicines* **2025**, *13*, 2885. IF - 3.9, Indexat PubMed, Scopus, ISI (Web of Science) si BDI
https://doi.org/10.3390/biomedicines13122885
(Chapter 5) – page 37-51
https://www.mdpi.com/2227-9059/13/12/2885

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https://doi.org/10.3390/healthcare14030362
(Chapter 6) -page 52-67
https://www.mdpi.com/2227-9032/14/3/362

Introduction

The main choice of this topic is motivated by the need to understand the complex interactions between periodontal disease and Parkinson's disease. The study of the oral bacterial profile and saliva, together with the evaluation of periodontal clinical indices, provides a different perspective on the diagnosis and treatment of periodontal disease. The main objectives of the research include the detailed analysis of periodontal pathogens using modern techniques such as PCR (Polymerase Chain Reaction), the investigation of salivary buffering capacity, and the correlation of these data with clinical oral health indicators, thereby contributing to a personalized approach to treatment. The final part of the thesis complements the research and explores how initial periodontal (antimicrobial) treatment influences clinical and microbiological aspects, emphasizing the importance of integrating personalized patient care. In addition to microbiological components, saliva quality represents a crucial factor in maintaining oral health. Salivary tests, such as the GC Buffer test, allow the evaluation of salivary buffering capacity as well as the identification of imbalances that may favor the onset and progression of periodontal diseases. Saliva, having a significant protective role, can also provide valuable information about the immune and inflammatory status of patients, contributing to a clearer understanding of periodontal health. The evaluation of clinical indices, such as the plaque index, calculus index, bleeding on probing index, and periodontal pocket depth, complements the microbiological and salivary analysis. These data, correlated with microbiological test results, enable more accurate diagnosis and personalization of treatment for patients with periodontal disease and Parkinson's disease. The integrated approach and the analysis of clinical, molecular, and therapeutic aspects offer significant perspective and potential in optimizing the treatment of patients affected by these two coexisting health conditions. The structure of this thesis reflects both the general and specific aspects of the research:

General Part: Addresses the theoretical foundation of periodontal disease and Parkinson's disease, including clinical and microbiological implications and the interactions between them. Aspects related to disease classification, pathogenesis, and impact on oral health are discussed.

- Chapter 1: Periodontal disease: classification, etiopathogenesis, and microbiological implications
- Chapter 2: Parkinson's disease and its impact on oral health

- Chapter 3: Considerations regarding the role of antibiotics in periodontal treatment

Personal Part: Includes the research methodology, analysis of results, and conclusions of studies conducted on patients with Parkinson's disease and periodontal involvement.

- Chapter 4: Scientific research methodology, description of study groups and methods used
- Chapter 5: Comparative study of patients with periodontal disease and Parkinson's disease: clinical and salivary aspects
- Chapter 6: Microbiological study on bacterial profile and its relationship with Parkinson's disease
- Chapter 7: Impact of antimicrobial periodontal treatment on oral health
- Chapter 8: Conclusions, personal contributions, and future research directions

This multidisciplinary approach, based on detailed clinical, microbiological, and salivary investigations, highlights the relevance of the topic and contributes to understanding a field of great current interest and clinical importance. Understanding the link between periodontal disease and Parkinson's disease allows the development of integrated treatment strategies that address both conditions simultaneously and maximize therapeutic outcomes. The role of this connection lies in possible molecular interactions and shared pathological mechanisms that may contribute to the progression and severity of both conditions, thus requiring a multidisciplinary approach in patient management.

The results and conclusions of this thesis may provide practical guidelines and recommendations for general dentists and specialists, contributing to the development of personalized therapeutic strategies aimed at improving patients' quality of life. Therefore, this approach ensures a significant contribution to the medical field by enhancing the understanding of interactions and the impact of antibiotic administration in the complex context of these two associated conditions.

SPECIAL PART – Personal Contributions

General Methodology of Scientific Research

Hypothesis and General Objectives

The present research is based on the hypothesis that antimicrobial periodontal treatment in patients with Parkinson's disease and periodontal disease may have a complex beneficial effect. This effect is manifested not only at the level of the oral cavity, through changes in periodontal clinical and salivary indices, but also at the systemic level, through the reduction of inflammatory processes and the potential favorable influence on the course of this neurodegenerative disease.

The central hypothesis supports the idea that improving oral health may also have systemic implications and may contribute to a more efficient overall management of patients with this neurological condition.

Specific objectives include:

- Evaluation of clinical indices: plaque index, calculus index, bleeding on probing, probing depth, and periodontal pocket presence index
- Evaluation of salivary indices: pH, buffering capacity, and salivary viscosity
- Identification of the main periodontal pathogenic bacterial species belonging to Socransky complexes (red, orange, green, yellow)
- Comparison of baseline results with those obtained after antimicrobial periodontal treatment

The study was conducted on a group of patients who presented to the Faculty of Dental Medicine, "Carol Davila" University of Medicine and Pharmacy, Bucharest. The patients were divided into two groups:

- Group 1: patients with periodontal disease but without Parkinson's disease
- Group 2: patients with periodontal disease and Parkinson's disease

Inclusion criteria:

- Adults aged between 18 and 80 years
- Confirmed diagnosis of periodontal disease according to the 2018 EFP classification [82]
- Confirmed diagnosis of Parkinson's disease established by a neurologist
- Adequate oral hygiene, maintained either by patients or caregivers
- No systemic comorbidities
- No local or systemic antibiotic treatment in the past 12 months
- No periodontal treatment (antimicrobial or surgical) in the past 12 months
- Absence of dental implants or prosthetic restorations

Exclusion criteria:

- Current or former smokers
- History of systemic diseases other than Parkinson's disease
- Severe motor impairment preventing adherence to study procedures and protocol
- Presence of acute periodontal conditions (e.g., abscesses)
- Use of monoamine oxidase inhibitors (MAOIs) or other contraindicated medications
- Pregnancy
- Known allergy to antibiotics

Research Method

Demographic Analysis

Patient anamnesis was performed to obtain relevant demographic and clinical information for characterizing the study population. Data recorded included patients' chronological age, biological sex, and the duration since the diagnosis of Parkinson's disease. Medical history included a detailed review of clinical documentation to confirm the diagnosis

of Parkinson's disease. All patients included in the study had a confirmed diagnosis established by a specialist neurologist, in accordance with current diagnostic criteria and standardized clinical protocols.

Clinical and Salivary Indices Analysis

Clinical evaluation included recording the plaque index, calculus index, bleeding on probing, periodontal pocket depth, and periodontal pocket presence index. In addition to clinical evaluation, salivary parameters were also analyzed, including salivary pH, salivary viscosity, and buffering capacity, using the GC Saliva-Check Buffer kit.

Microbiological Analysis

Gingival crevicular fluid (GCF) sampling was performed according to specific instructions provided by the collaborating laboratory and the sampling kit manufacturer, to ensure standardization and reproducibility of results. Samples were collected from periodontal pockets by a specialist in periodontology. The analysis was carried out using PCR (Polymerase Chain Reaction) with specific kits (Perio-Ident 12), capable of identifying 12 relevant bacterial species.

Post-Therapeutic Evaluation of Indices

Post-treatment reevaluation represented an essential step in validating the effectiveness of periodontal interventions and in monitoring the evolution of clinical, salivary, and microbiological parameters in the studied patients. This reevaluation was performed one month after completion of antimicrobial periodontal treatment, according to the protocol detailed in Chapter 7 of the thesis. During this visit, all clinical, salivary, and microbiological investigations described in the initial methodology were repeated, allowing direct comparison of parameters before and after treatment.

Data Processing

All data were analyzed using IBM SPSS Statistics 25 and illustrated using Microsoft Office Excel/Word 2024. Qualitative variables included sex, salivary viscosity, buffering capacity, reason for presentation, and periodontal classification (stages and grades). These were expressed as frequencies or percentages and compared between groups using Fisher's exact test. For post-hoc analysis of contingency tables, Z-tests with Bonferroni correction were applied. The results were presented graphically and in tables using Microsoft Office Excel/Word 2024, allowing a clear and systematic visualization of the studied variables. By applying these rigorous statistical methods, an appropriate and reliable interpretation of the results was ensured, contributing to the substantiation of the clinical and microbiological relationships analyzed in this research.

Study 1. Comparative study of patients with periodontal disease and patients with Parkinson's disease regarding clinical and salivary indices

Introduction

By investigating periodontal clinical parameters in relation to salivary properties such as pH, buffering capacity, and viscosity, this study aims to highlight oral- systemic interactions in Parkinson's disease. The specific objectives include: (a) evaluation and comparison of periodontal indices, including plaque index, bleeding on probing, probing depth, and the index of periodontal pocket presence; (b) analysis of salivary parameters — pH, viscosity, and buffering capacity — and identification of differences between groups; (c) determination of potential correlations between clinical and salivary indices, which may reflect systemic inflammatory influences in patients with Parkinson's disease; (d) identification of the clinical implications of these findings for preventive and therapeutic strategies aimed at maintaining oral health and improving patients' quality of life.

Materials and Methods

An observational, analytical, cross-sectional approach was adopted to explore the relationship between periodontal status and Parkinson's disease. The study was not double-

blind, as direct interaction with patients, neurological clinical manifestations, and medical history made it impossible to conceal Parkinson's disease status.

Patients were divided into two groups:

- Group 1: patients with periodontal disease but without Parkinson's disease
- Group 2: patients with both periodontal disease and Parkinson's disease

The medical history provided information on age, sex, and the time elapsed since the diagnosis of Parkinson's disease. The diagnosis had been previously established by a neurologist. The reason for presentation was also recorded. Clinical parameters evaluated at baseline included: number of missing teeth secondary to periodontal disease, staging and grading of periodontal disease, bleeding on probing index, plaque index, calculus index, periodontal pocket presence index, and probing depth. Salivary indices were determined using the GC Saliva-Check Buffer test, according to the manufacturer's instructions.

Results

The study included a total of 31 patients diagnosed with periodontal disease, of whom 16 (51.61%) also had Parkinson's disease, while 15 had periodontal pathology only, without neurological involvement. The mean age of patients was 61.1 ± 11.06 years, reflecting a middle-aged to elderly population, characterized by increased risk for both periodontal and neurodegenerative diseases. Sex distribution showed 29% male and 71% female participants. In the study group, the mean duration since Parkinson's disease diagnosis was 7.81 ± 2.19 years, indicating an intermediate stage of disease progression, potentially influencing both general and oral health. The mean number of missing teeth was 5, with no significant differences between groups ($p = 0.281$). The control group had a mean of 6 missing teeth, compared to 5 in the study group. The calculus index had a mean value of 58.06 ± 27.78 for the entire sample, higher in the control group (67.4 ± 25.03) compared to the study group (49.31 ± 28.11). The plaque index remained high in both groups, with a mean value of 67.42 ± 25.37. The control group had a mean of 68.93 ± 24.66, and the study group 66 ± 26.74 ($p = 0.754$). The bleeding index had a mean of 50.29 ± 22.96, with higher values in the control group (56.67 ± 22.83) compared to the study group (44.31 ± 22.13). The mean probing depth was 5 mm, with values of 6 mm in the control group and 5 mm in the study group ($p = 0.264$).

The periodontal pocket presence index had a mean value of 28%, slightly higher in the control group. Salivary viscosity was normal in 54.8% of patients and increased in 45.2%. In the control group, 60% had normal viscosity compared to 50% in the study group. The percentage of patients with increased salivary viscosity was 40.0% in the control group and 50.0% in the study group ($p = 0.722$). Although the difference was not statistically significant, the trend toward increased viscosity in the study group suggests a possible alteration in saliva quality associated with the neurological condition. Mean salivary pH values were almost identical between groups (6.88 ± 0.32 in the control group and 6.88 ± 0.39 in the study group; $p = 0.995$). Salivary pH had a mean value of 6.88 ± 0.35, with no significant differences between groups ($p = 0.995$), indicating that resting salivary pH is not influenced by Parkinson's disease. These results show that saliva's ability to neutralize acids — an essential factor in oral protection — is compromised in patients with Parkinson's disease. In contrast, reduced buffering capacity was significantly more frequent in patients with Parkinson's disease (56.3%) compared to those without (13.3%) — a statistically significant difference ($p = 0.035$). Overall, 54.8% of patients had normal buffering capacity, 35.5% reduced, and 9.7% very low. Statistical analysis revealed significant differences ($p = 0.035$), confirmed by Z-tests with Bonferroni correction. Reduced buffering capacity was strongly associated with Parkinson's disease, while normal buffering capacity was more frequent in the non-Parkinson group.

Discussion

Periodontal indices did not show statistically significant differences between groups. However, from a biological perspective, it is important to note that patients with Parkinson's disease generally exhibited a more unfavorable clinical profile. For example, bleeding on probing — a direct marker of gingival inflammation — was increased in many Parkinson's patients, reflecting chronic inflammation and an exaggerated host inflammatory response. Similarly, probing depth and periodontal pocket indices indicate periodontal tissue destruction; although numerical differences were modest, the combination of an altered salivary environment and systemic inflammation suggests that these lesions may be more difficult to control and more prone to progression in Parkinson's disease. The most important findings of the study relate to salivary buffering capacity. Patients with Parkinson's disease showed a much higher prevalence of reduced buffering capacity (56.3% vs. 13.3% in the

control group). Buffering capacity is essential for neutralizing bacterial acids and protecting oral tissues from chronic inflammation. Salivary viscosity was also altered in the Parkinson group. Although differences in viscosity and pH did not reach statistical significance, the clinical trend is clear: patients with Parkinson's disease face a more hostile oral environment, in which saliva performs its protective and anti-inflammatory roles less efficiently. It is important to note that salivary evaluation was based exclusively on the GC Saliva-Check Buffer test, a qualitative method used in dental practice. While this test provides rapid and clinically useful information, it lacks the analytical precision of laboratory titration methods and may be influenced by examiner subjectivity and environmental factors. Therefore, although the results suggest significantly reduced buffering capacity in the study group, they should be interpreted cautiously and validated in future studies using standardized quantitative methods.

All salivary parameters were determined from unstimulated saliva, according to the GC test protocol. While this approach provides valuable information about baseline salivary characteristics, it may not capture dynamic variations associated with stimulated salivary secretion. Future studies could benefit from including both types of samples. Additionally, all patients with Parkinson's disease in this study were undergoing dopaminergic therapy. Levodopa and related agents, essential for motor control, frequently induce xerostomia, alter salivary viscosity, and reduce buffering capacity. The potential impact of dopaminergic treatments on periodontal and salivary parameters requires further investigation.

Conclusions

The results of this study demonstrate that patients with Parkinson's disease exhibit significantly reduced salivary buffering capacity compared to patients without neurological impairment, even though periodontal clinical indices do not differ significantly between the two groups. This discrepancy highlights an important biological reality: salivary alterations may represent the earliest detectable signs of oral imbalance associated with Parkinson's disease, preceding or amplifying classical periodontal clinical manifestations. The overall conclusion suggests that salivary dysfunction — characterized by reduced acid-neutralizing capacity, changes in viscosity, and possible alterations in biochemical composition — represents an early and sensitive marker of oral vulnerability in this category of patients.

Study 2. Comparative Study on the Determination of Bacterial Load Characteristics in Patients with Parkinson's Disease and Periodontal Involvement

Introduction

The objectives of this study are fourfold: (a) to compare the prevalence of bacterial species associated with periodontal disease; (b) to assess periodontal disease in patients with Parkinson's disease as a contributing factor to oral microbiome imbalance; (c) to evaluate the correlation between clinical periodontal indices (plaque index, calculus index, bleeding index, and probing depth) and the bacterial load of specific periodontopathogenic species; and (d) to explore the potential implications of these findings for clinical management and preventive strategies in patients with Parkinson's disease.

Materials and Methods

An observational, analytical study was conducted to evaluate the association between periodontal status, microbiological profile, and Parkinson's disease. Microbiological analysis was performed using the PCR-based Perio-Ident 12 test, a molecular diagnostic method designed to detect bacterial species associated with periodontal disease.

Patients were divided into two groups:

- Group 1: patients with periodontal disease but without Parkinson's disease
- Group 2: patients with both periodontal disease and Parkinson's disease

The following periodontal pathogens were analyzed: *Aggregatibacter actinomycetemcomitans, Porphyromonas gingivalis, Treponema denticola, Tannerella forsythia, Eikenella corrodens, Campylobacter rectus, Prevotella intermedia, Fusobacterium nucleatum, Prevotella nigrescens, Capnocytophaga ochracea, Capnocytophaga sputigena,* and *Capnocytophaga gingivalis*.

Results

A total of 31 participants were included in the study, of whom 15 (48.4%) had periodontal disease, and 16 (51.6%) had both periodontal disease and Parkinson's disease (PD).

Regarding microbiological parameters, the mean concentrations of the main periodontal pathogens were generally higher in the control group compared to the study group. Notably, *Tannerella forsythia* showed a difference at the threshold of statistical significance ($p = 0.072$), with lower median values in the study group (35,950 CFU/mL) compared to the control group (200,000 CFU/mL). Although the analyzed bacterial species did not show statistically significant differences between groups, the overall microbial profile of patients in the study group indicated a trend toward increased bacterial diversity and concentration. In the control group, the plaque index showed strong correlations with the concentrations of *Eikenella corrodens, Fusobacterium nucleatum, Prevotella nigrescens, Capnocytophaga ochracea,* and *Capnocytophaga gingivalis* (all $p < 0.05$). Significant positive correlations were observed between plaque index and bacterial concentrations of *Eikenella corrodens* ($p = 0.008$, $R = 0.659$), *Fusobacterium nucleatum* ($p = 0.007$, $R = 0.667$), *Prevotella nigrescens* ($p = 0.021$, $R = 0.589$), *Capnocytophaga ochracea* ($p = 0.012$, $R = 0.628$), and *Capnocytophaga gingivalis* ($p = 0.007$, $R = 0.667$), indicating strong positive associations. This suggests that patients with higher plaque index values were significantly associated with higher bacterial concentrations of these species, and vice versa.

Additionally, in the control group trends toward statistical significance were observed for correlations between probing depth and bacterial concentrations of *Campylobacter rectus* ($p = 0.055$, $R = 0.505$) and *Capnocytophaga ochracea* ($p = 0.078$, $R = 0.467$), suggesting higher bacterial loads in cases with greater probing depths.

Discussion

The results demonstrate that patients with Parkinson's disease exhibit a disrupted relationship between plaque accumulation and bacterial load, supporting the presence of oral dysbiosis associated with Parkinson's disease. Thus, the study strengthens existing evidence showing that Parkinson's disease influences not only clinical periodontal outcomes but also the behavior of periodontal pathogens. An important aspect in interpreting these findings is their relevance to the use of adjunctive antibiotic therapy in periodontal management, particularly in cases characterized by high bacterial load and a microbiological profile dominated by highly virulent pathogens such as *Porphyromonas gingivalis, Treponema denticola,* and *Tannerella forsythia*. In the present study, both groups exhibited a high-risk microbial profile; however, patients with Parkinson's disease demonstrated greater bacterial diversity and a disrupted relationship between periodontal indices and bacterial load.

This dissociation may indicate the presence of dysbiosis that could predispose to reduced efficacy of antimicrobial periodontal treatment in the absence of adjunctive local or systemic antibiotic therapy. The Perio-Ident 12 test, although widely used for identifying major periodontal pathogens, has several methodological limitations. Its diagnostic capacity is restricted to 12 predefined bacterial species, which may result in an incomplete representation of the microbial community compared to next-generation sequencing methods. Additionally, the use of SYBR Green-based qPCR is susceptible to non-specific amplification and requires careful interpretation of melting curves to avoid false-positive results. Quantification expressed in CFU equivalents is influenced by DNA extraction efficiency and variations in bacterial genomic copy numbers, reducing absolute accuracy. Another limitation is the inability to perform antibiograms, as the method relies exclusively on bacterial DNA detection without culture, thus preventing the assessment of phenotypic antibiotic susceptibility.

Conclusions

The results highlight the need for individualized periodontal management in patients with Parkinson's disease, as clinical indices may not accurately reflect the underlying microbiological dysbiosis and associated inflammatory risk. Overall, the findings support and confirm the four initial objectives, demonstrating measurable differences in pathogen prevalence, identifying microbiome imbalance associated with Parkinson's disease, clarifying altered relationships between periodontal indices and microbial load, and emphasizing the clinical relevance of these interactions for the management and prevention of periodontal disease in patients with Parkinson's disease.

Study 3. Implications of Antimicrobial Periodontal Treatment in Patients with Periodontal Disease and Parkinson's Disease

Introduction

In recent years, an increasing body of scientific evidence has supported the existence of a bidirectional relationship between periodontal diseases and neurodegenerative disorders,

particularly Parkinson's disease. Chronic inflammation, alterations in the oral microbiome, and pro-inflammatory mediators may contribute to the progression of neurodegenerative processes. In this context, antimicrobial periodontal treatment may play a crucial role not only in controlling local inflammation but also in reducing bacterial load, with potential benefits on the progression of Parkinson's disease. The aim of this study is to evaluate the impact of antimicrobial periodontal treatment on clinical, salivary, and microbiological parameters in patients with periodontal disease and Parkinson's disease.

Materials and Methods

The present study is a clinical, observational, and interventional study conducted on a cohort of patients diagnosed with periodontal disease, with and without Parkinson's disease. Patients were divided into two groups:

- Group 1: patients with periodontal disease without Parkinson's disease
- Group 2: patients with periodontal disease and Parkinson's disease

All patients underwent periodontal clinical evaluation, salivary investigations, and microbiological analyses. The protocols for each evaluation are described in Chapters 5, 6, and 7 of the thesis. Both groups were subjected to the same standardized protocol consisting of initial evaluation, antimicrobial periodontal treatment, and post-therapeutic reevaluation, in order to eliminate variability induced by differences in intervention and to ensure comparability of results. Antimicrobial periodontal treatment was performed in accordance with the guidelines of the European Federation of Periodontology, following the stepwise approach (Step 1–Step 3, S1–S3), aimed at biofilm control, inflammation reduction, and stabilization of periodontal status, as detailed in Chaper 7 of the doctoral thesis. Post-therapeutic reevaluation was performed one month after the last antimicrobial periodontal treatment session and included reassessment of clinical periodontal parameters, microbiological analysis using PCR techniques, and salivary measurements. This interval was selected to allow stabilization of the post-intervention tissue response and objective assessment of treatment efficacy.

Results

Statistical analysis revealed a significantly favorable response to the antimicrobial periodontal protocol in both study groups; however, the magnitude of clinical and microbiological changes differed significantly between patients with periodontal disease alone and those with both periodontal disease and Parkinson's disease, supporting the hypothesis that Parkinson's disease acts as a modifying factor of therapeutic outcomes. In the control group (periodontal disease only), mechanical instrumentation combined with topical antibiotic application resulted in statistically significant reductions in calculus index ($p < 0.001$), plaque index ($p < 0.001$), bleeding on probing index ($p < 0.001$), and probing depth ($p = 0.038$). Significant improvements ($p < 0.001$) were observed in plaque index, decreasing from 68.93 ± 24.66% pre-treatment to 10.07 ± 3.9% post-treatment. Salivary pH also increased significantly from 6.83 ± 0.33 to 7.03 ± 0.35. In the study group (periodontal disease + Parkinson's disease), statistically significant improvements were also observed in calculus index ($p < 0.001$), plaque index ($p = 0.001$), and bleeding on probing index ($p = 0.043$), demonstrating the general effectiveness of the therapeutic protocol even in this complex clinical context. However, the reduction in bleeding index was significantly greater in the control group, while patients with Parkinson's disease exhibited a more modest inflammatory reduction and higher residual values post-treatment.

Regarding bacterial load, an increase ($p = 0.038$) was observed in the study group after treatment, suggesting persistence or even progression of microbial imbalance. Intergroup comparisons revealed significant differences in therapeutic response amplitude. The reduction in calculus index was significantly greater in the control group, indicating a reduced capacity for local factor control in the presence of Parkinson's disease. Significant differences were also observed in the evolution of *Porphyromonas gingivalis* bacterial load ($p = 0.004$), with the control group showing a decrease, while Parkinson's patients showed an unfavorable trend, with persistence or increase in bacterial levels. Significant correlations were identified between the duration of Parkinson's disease and bacterial load for several periodontopathogenic species ($p < 0.05$), both before and after treatment, indicating that neurological disease progression directly influences oral microbiological status.

Discussion

The results demonstrate that a stepwise therapeutic protocol combining non-surgical mechanical therapy with local antimicrobial agents leads to significant improvements in periodontal status and reduction of subgingival bacterial load. The improvement in clinical periodontal parameters—reflected by decreased plaque index, reduced gingival bleeding, and reduced probing depth—is consistent with data reported in the literature. The use of a magistral preparation based on tetracycline and metronidazole allowed high local antibiotic concentrations within periodontal pockets, exerting bactericidal and bacteriostatic effects on anaerobic microorganisms involved in periodontal disease pathogenesis.

Although statistically significant improvements were observed in both groups, the magnitude of changes differed. Patients with Parkinson's disease showed less pronounced improvements, likely due to motor impairments affecting oral hygiene maintenance. Similarly, bleeding on probing reduction was markedly greater in patients without Parkinson's disease, suggesting persistence of chronic inflammation in neurologically affected patients.

Salivary parameters showed functional improvements, with a significant increase in salivary pH, indicating a shift toward a more favorable environment for bacterial control. Microbiologically, treatment led to a significant reduction in key periodontal pathogens, particularly *Porphyromonas gingivalis*, as well as *Prevotella nigrescens*, confirming the effectiveness of antimicrobial therapy. The proportion of patients at high microbial risk decreased significantly (from 80% to 26.7%), indicating an overall favorable shift in the oral ecosystem. However, several limitations must be considered. The relatively small sample size limits statistical power and generalizability. The short follow-up period (one month) does not allow assessment of long-term stability. The absence of a placebo or mechanical-only treatment group limits the ability to isolate the specific effect of antimicrobial therapy. Additionally, heterogeneity among Parkinson's patients (disease duration, severity, and neurological treatment) may act as confounding factors.

Conclusions

Significant improvements in clinical periodontal parameters were observed in both groups, confirming the overall effectiveness of the therapeutic protocol.However, patients with Parkinson's disease showed a reduced therapeutic response and greater persistence of periodontal impairment compared to patients without neurological pathology. Although both groups exhibited significant reductions in calculus index, the magnitude of reduction was significantly greater in patients without Parkinson's disease, suggesting that control of local contributing factors is more difficult in the context of Parkinson's disease. A similar pattern was observed for plaque index and bleeding on probing index. Despite significant reductions, Parkinson's patients maintained higher post-treatment inflammatory values, reflecting increased susceptibility to persistent gingival inflammation. These findings indicate that Parkinson's disease not only affects oral hygiene maintenance but also alters tissue response to periodontal therapy. Therefore, the methodological design, patient selection, and therapeutic protocol are aligned with the thesis objectives and support well-founded conclusions regarding the rational use of antimicrobial therapy in the management of periodontal disease associated with Parkinson's disease.

Conclusions and Personal Contributions

General Conclusions

The main objective of this doctoral thesis was to evaluate the rationale for antibiotic use in the management of patients with periodontal involvement and Parkinson's disease, through the integration of a multidisciplinary approach that included the analysis of clinical periodontal parameters, microbiological profile, and salivary characteristics, correlated with the application of a standardized antimicrobial therapeutic protocol. The obtained results provide a comprehensive perspective on the interactions between periodontal pathology and neurodegenerative disease, as well as on the role of local antimicrobial therapy in optimizing periodontal status in this special category of patients.

One of the major conclusions of this work is the confirmation that patients with Parkinson's disease present an increased risk of periodontal involvement, reflected by higher

values of clinical periodontal indices, more pronounced gingival inflammation, and a higher bacterial load compared with patients without associated neurological pathology. This observation supports the hypothesis that motor dysfunction, coordination disorders, and functional alterations induced by Parkinson's disease negatively affect the patient's ability to maintain effective oral hygiene, thereby favoring bacterial biofilm accumulation and progression of periodontal inflammation.

The microbiological analysis performed in this study revealed an increased prevalence of major periodontal pathogens, especially species belonging to the red and orange complexes, in patients with Parkinson's disease and periodontal involvement. These findings are relevant not only from a local perspective, at the level of the oral cavity, but also from a systemic perspective, considering the role of these microorganisms in triggering and maintaining chronic inflammation. The increased presence of Gram-negative anaerobic bacteria supports the pathophysiological mechanisms described in the literature, involving the dissemination of inflammatory mediators and the possible activation of neuroinflammatory processes. Another important aspect highlighted by this research is the favorable impact of stepwise antimicrobial periodontal treatment on the evaluated clinical and biological parameters. The implementation of a therapeutic protocol based on non-surgical mechanical treatment associated with the local administration of antimicrobial agents led to a significant reduction in gingival inflammation, a decrease in periodontal pocket depth, and a reduction in subgingival bacterial load. These results confirm the effectiveness of local antimicrobial therapy as an adjunct to standard periodontal treatment and support its rational use in well-defined clinical situations.

The rationale for the use of topical antibiotics, rather than systemic administration, represents a central conclusion of this thesis. Local application of antimicrobial preparations allows effective therapeutic concentrations to be achieved directly at the infected sites, reducing systemic exposure and the risk of adverse reactions or drug interactions. This aspect is particularly relevant in patients with Parkinson's disease, who are frequently undergoing chronic pharmacological treatment and present a complex medication profile. With regard to the scientific contribution of this work, the thesis provides original data on the microbiological profile and response to antimicrobial periodontal treatment in patients with Parkinson's disease within a controlled clinical setting. These findings complement the existing literature and provide a methodological framework applicable to dental clinical

practice. Furthermore, the obtained results support the need for a personalized approach to periodontal treatment, based on the individual assessment of biological risk and the patient's systemic particularities.

Future Research Directions

Based on the results obtained and the observations formulated in this thesis, several research directions can be identified that may contribute to a deeper understanding of the relationship between periodontal disease and Parkinson's disease. A first important direction is the development of long-term longitudinal studies that would allow evaluation of the stability of therapeutic outcomes and of the impact of periodontal treatment on the clinical progression of Parkinson's disease. Monitoring patients over extended periods could provide valuable information regarding the relationship between oral inflammation control and changes in neurological symptomatology.

Another area of interest is the expansion of microbiological analyses through the use of modern genomic and metagenomic sequencing techniques. These methods could allow a more detailed characterization of the oral microbiota and the identification of specific biomarkers associated with Parkinson's disease progression or with the response to antimicrobial periodontal treatment. In addition, the integration of systemic and salivary inflammatory markers into future research protocols could contribute to a better understanding of the biological mechanisms involved in the interaction between periodontal inflammation and neuroinflammation. The analysis of cytokine levels, C-reactive protein, or oxidative stress markers could provide supplementary information regarding the impact of periodontal therapy on overall inflammatory status.

Another relevant direction is the comparative evaluation of different antimicrobial therapeutic strategies, including the use of locally delivered controlled-release antimicrobial agents, oral probiotics, or non-antibiotic adjunctive therapies. These approaches could contribute to optimizing periodontal management and reducing dependence on conventional antibiotics. Finally, the development of personalized care protocols for patients with Parkinson's disease, including educational interventions, assistive technologies for oral hygiene, and digital monitoring, represents an important direction for improving compliance and therapeutic outcomes.

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