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ORIGINAL ARTICLE

Evaluation of Antimicrobial Photodynamic Therapy as an Adjuvant in Periodontal Treatment in Individual with Down Syndrome

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ABSTRACT

Objective: To evaluate the effectiveness of Antimicrobial Photodynamic Therapy (aPDT), associated with scaling and root planing in the non-surgical periodontal treatment of individuals with Down Syndrome. **Material and Methods:** A controlled, randomized, split-mouth study was conducted. A total of 8 participants diagnosed with Down Syndrome aged 17-38 years of both sexes with clinical periodontitis were included in the study. Participants were treated at least three times: at the baseline, Plaque Index (PI), Bleeding on Probing (BOP), and Probing Pocket Depth (PPD) were obtained. After one week, conventional scaling and root planing were performed, and two quadrants were randomly selected for aPDT application. The reassessment was obtained one month after the aPDT application. The significance level was set at 5%. Analyses were performed considering a 95% confidence interval. **Results:** In the intergroup evaluation, no statistically significant differences were observed ($p>0.05$). In the intragroup evaluation, no statistically significant variations were observed in relation to the PI ($p>0.05$) and PPD ($p>0.05$); however, a statistically significant reduction in the BOP was observed between the test group ($p=0.013$) and control group ($p=0.015$). **Conclusion:** The use of aPDT as adjuvant therapy did not promote additional benefits in decreasing PI and PPD after 1 month of treatment. However, a significant reduction in the BOP was observed in the intragroup evaluation.

Keywords: Down Syndrome; Lasers; Photochemotherapy; Periodontal Diseases.

Introduction

Down syndrome (DS) is an autosomal chromosomal abnormality associated with chromosome 21 trisomy [1]. Individuals with DS have intellectual impairment, in addition to certain phenotypic characteristics and medical conditions such as cardiovascular, hematological, neurological, respiratory, musculoskeletal, and immunological problems [2,3].

Periodontal disease in individuals with DS occurs due to abnormalities intrinsic to the immune system, which predisposes such individuals to infections [4]. In addition, some local disorders such as malocclusion, altered frenulum insertion, early mucogingival problems, and tongue positioning increase the occurrence of periodontal diseases. Therefore, they have a higher prevalence and severity of periodontal diseases than individuals without DS [1,4].

Conventional periodontal disease treatment reduces the pathogenic microbiota through oral hygiene guidance associated with scaling and root planning [5]. However, in some cases, such as the presence of deep periodontal pockets, involvement of furcation areas, and presence of anatomical variations, currently available manual instrumentation techniques are not sufficient for the complete elimination of pathogenic microorganisms and subgingival calculus [6,7].

Other therapeutic approaches such as scaling in open fields and antibiotics are used to reduce therapeutic failure. However, some adverse results such as postoperative discomfort and morbidity and the development of bacterial resistance have been reported [8-10]. Therefore, to reduce the therapeutic setback, some alternative therapies have been used, including antimicrobial phytochemicals and lasers [8].

The association of low-power Laser (Light Amplification by Stimulated Emission of Radiation - light amplification by stimulated emission of radiation) with photosensitizers - called Antimicrobial Photodynamic Therapy (aPDT). It is a therapy mediated by visible light, a photosensitizer (PS), and oxygen [11].

There are several photosensitizers available for aPDT, but disinfection related to periodontopathogens generally indicates the use of phenothiazine photosensitizers, such as toluidine blue and methylene blue (MB) [12]. The antibacterial action for most phenothiazine drugs appears to be located on the bacterial cell wall or on its cytoplasmic membrane, as they are related to the hydrophobic nature of these compounds [11].

In this context, the aim of the present study was to longitudinally evaluate the effectiveness of aPDT associated with scaling and root planing in the non-surgical periodontal treatment of individuals with Down Syndrome.

Material and Methods

Study Design and Ethical Clearance

This is a single-blind, controlled, randomized, split-mouth study. The research followed the main guidelines of the CONSORT initiative and was approved by the Ethics Research Committee (protocol number 2.578.911). All legal guardians, who agreed to patients' participation, signed the Free and Informed Consent Form.

Patient Selection and Inclusion and Exclusion Criteria

This is a non-probabilistic convenience sample consisting of individuals diagnosed with Down Syndrome duly enrolled in APAE-CG (Association of Parents and Friends of Exceptional Children, Campina Grande, Brazil) (Figure 1).

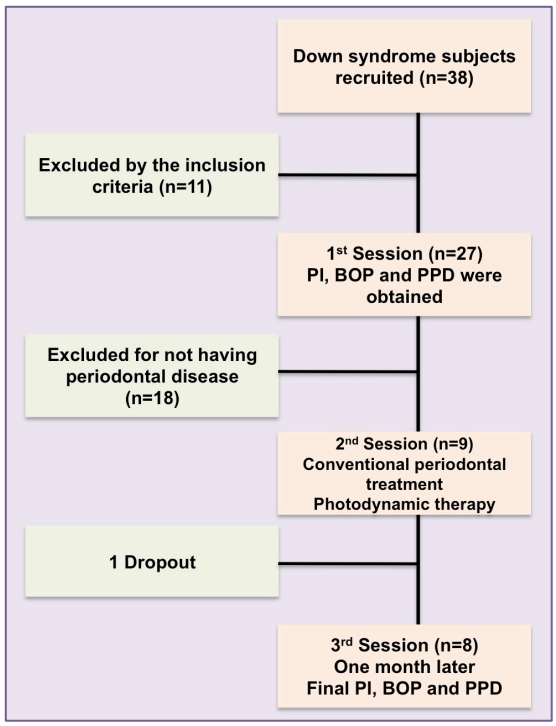

Figure 1. Study Flowchart.

Individuals were included in the study based on the following criteria: being over 12 years old; have at least 8 teeth in the mouth, 2 teeth for chosen quadrants; presenting clinical condition of periodontitis: Interdental Clinical Attachment Loss is detectable at ≥ 2 non-adjacent teeth or Buccal or oral Clinical Attachment Loss ≥ 3 mm with pocketing > 3 mm is detectable at ≥ 2 teeth [13]. Exclusion criteria were smokers; those who make chronic use of alcohol; illicit drug users; menopausal women; pregnant or lactating women; patients with diabetes mellitus or uncontrolled hyperthyroidism; unstable angina; hypertensive patients; patients with coagulopathies; patients requiring antibiotic prophylaxis for congenital heart diseases (according to American Heart Association guidelines); and patients with uncooperative behavior.

Data Collection and Clinical Protocol

A single calibrated examiner performed all clinical examinations and was blinded to treatments. Calibration consisted of two stages: theoretical-practical and clinical stages, which were performed by a dentist, and a gold standard, specialized in Periodontics. In the theoretical-practical stage, each index was discussed and visualized in a clinical examination. In the clinical stage, to assess the intra-examiner agreement for clinical parameters, a non-syndromic individual was assessed (k=0.77).

Before treatment, and after 1 month from the laser treatment, the examiner recorded the following clinical parameters for six sites of each tooth: Bleeding on Probing (BOP) and Probing Pocket Depth (PPD), and the Plaque Index (PI) for four sites of each tooth.

BOP and PPD were measured using a Willians millimeter probe (Trinity Ind. Com. Ltda, São Paulo, SP, Brazil) at six sites per tooth: mesiobuccal, midbuccal, distobuccal, mesiolingual, midlingual, and distolingual.

To measure PI, the disclosure of the bacterial biofilm was performed at four sites per tooth (buccal, lingual, mesial, and distal) using basic fuchsin solution (Eviplac - Biodinâmica, Ibiporã, PR, Brazil). Then, professional prophylaxis was performed with Robinson's brush and prophylactic paste (Herjos - Coltene, Rio de Janeiro, RJ, Brazil).

Treatment Protocol

During the first session, clinical parameters were assessed and periodontal charting has been done on all participants' teeth. In the second session, scaling and root planning was performed the whole mouth, in a single session, using manual instruments - Gracey curettes (Trinity Ind. Com. Ltda, São Paulo, SP, Brazil). In the third session, a week after the second session, two dentists qualified in laser therapy randomly chose two quadrants to receive aPDT. The protocol was applied only once. Oral hygiene instructions were reinforced at each session.

The individuals were included in the study are part of a group that regularly receives health promotion actions. Thus, oral hygiene guidelines are sporadically given to individuals and their caregivers. During the research, oral hygiene instructions were reinforced individually at each session. Oral hygiene kits (with toothbrushes, toothpaste and dental floss) were donated at the first session and were used to model the instructions.

Antimicrobial Photodynamic Therapy (aPDT)

All teeth included in the selected quadrants with periodontal pockets were irrigated with 0.01% methylene blue (Chimiolux®, Hypofarma, Ribeirão das Neves, MG, Brazil). Approximately 1 ml of the solution was inserted into the clinical gingival sulcus / periodontal pocket with the aid of a special syringe without bevel for 4 minutes of pre-irradiation time. After this period, a diode laser (InGAlP) (Therapy XT, DMC Equipamentos, São Carlos, SP, Brazil) was used with a wavelength of 658 nm. Irradiation was held in continuous emission mode via gingival sulcus (optical fiber) and area of the conductive tip of 0.000314 cm^2. Laser was applied with the aid of a light-curing fiber for aPDT (DMC Equipamentos, São Carlos, SP, Brazil), initially inserted in the mouth of the pocket or gingival sulcus with small apical-coronal movements to the bottom of the pocket/sulcus.

The total dose was 120 J/cm^2, which was divided into four points of 30 J/cm^2 (1 J per point). The application time was 10 s/point plus 10 seconds in sweeping movement (from mesial to distal directions) [3].

Statistical Analysis

Initially, descriptive statistical analysis was carried out to characterize the sample. Then, the assumption of normal data distribution of quantitative variables was investigated using the Shapiro-Wilk test. After confirmation, parametric statistical tests were selected. In the intergroup evaluation (test *vs.* control), the independent t-test compared plaque index, bleeding on probing index and probing depth values. In the intragroup evaluation (initial *vs.* final), the t-test for paired samples was used to compare values of the evaluated indices [14]. The significance level was set at 5%. Analyses were performed with IBM SPSS Statistics software version 20.0 (IBM Corp., Armonk, NY, USA) considering a 95% confidence interval.

Results

A total of 21 patients were initially evaluated and received basic therapy. Unfortunately, only nine patients met the inclusion criteria and one patient did not attend the treatment reassessment, totaling eight patients. The main reason for patient exclusion was the absence of clinical periodontitis condition and uncooperative behavior. After the beginning of the experiment, no adverse effects were observed or reported by patients. Infectious conditions, suppuration, or abscesses were also not observed.

Of the eight patients, 6 were female (75%) and 2 (25%) male. The age ranged from 17 to 38 years, with a mean age of 24.60 years.

Table 1 shows the results of comparative analysis of indexes evaluated in test and control areas according to the two evaluation moments. In the intergroup evaluation, no statistically significant differences were observed (p>0.05). In the intragroup evaluation, no statistically significant variations were observed in relation to the plaque index (p>0.05) and probing depth (p>0.05). However, a significant reduction in the bleeding index was observed for both test group (p=0.013) and control group (p=0.015).

Table 1. Comparative analysis of the clinical results observed in test and control areas according to evaluation moments (initial and final).

Variables	Evaluated Area										p-value[2]
	Test					Control					
	Mean	SD	Median	IIQ P25	IIQ P75	Mean	SD	Median	IIQ P25	IIQ P75	
Plaque index (PI)											
Initial	89.33^{Aa}	16.43	97.65	76.80	99.55	81.58^{Aa}	22.03	89.90	73.36	95.31	0.438
Final	92.68^{Aa}	4.17	93.12	89.06	96.85	92.14^{Aa}	6.94	93.54	88.75	96.35	0.855
p-value[1]	0.526					0.242					
Bleeding on Probing Index (BPI)											
Initial	48.21^{Aa}	30.82	41.80	19.40	74.52	48.35^{Aa}	30.19	51.58	18.74	67.19	0.993
Final	20.56^{Ab}	23.70	14.20	4.26	26.43	21.62^{Ab}	19.10	15.50	7.19	31.76	0.924
p-value[1]	0.013*					0.015*					
Probing depth (PD)											
Initial	2.67^{Aa}	0.64	2.78	2.15	3.08	2.68^{Aa}	0.64	2.66	2.24	3.14	0.975
Final	2.34^{Aa}	0.68	2.13	1.82	3.00	2.52^{Aa}	0.95	2.31	1.78	3.27	0.674
p-value[1]	0.140					0.463					

SD = Standard Deviation; IIQ = Interquartile Range (25th percentile - 75th percentile). Different letters denote significantly different results (p<0.05); [1]Capital letters compare values horizontally (intergroup evaluation, Test *vs.* Control); [2]Lowercase letters compare values vertically (intragroup evaluation, Initial *vs.* Final); *Statistically significant difference at 5% level (p<0.05).

Discussion

Periodontal disease is defined as an inflammation of teeth supporting tissues caused by specific microorganisms, which results in gingival bleeding, loss of periodontal tissue support, manifested through loss of clinical attachment, loss of alveolar bone, radiographically assessed, presence of periodontal pockets, gingival recession or both [15,16]. In individuals with DS, it is considered a serious, generalized, rapidly progressing and highly prevalent condition. It is estimated that in adolescents with DS, the prevalence of periodontal disease ranges from 30% to 40%, whereas in individuals aged 30 years, this percentage can reach 100% [17].

Some predisposing factors are related to the development of periodontal disease in individuals with DS, such as malocclusion, problems of insertion of the lingual frenum, mucogingival problems, and macroglossia, in addition to systemic conditions capable of interfering in the host's response to the disease. Thus, the etiological factor and the tissue reaction cannot be equated as a simple cause and effect reaction, nor can the local factors (with their intensity, frequency, and duration) be given full responsibility for the process because the tissues are governed by the patient's general health status [1,17].

This study sought to evaluate the effectiveness of aPDT associated with scaling and root planing in the non-surgical periodontal treatment of individuals with DS. After treatment was performed and reassessment after one month, no statistically significant differences between test and control groups were observed (p>0.05). However, a reduction in BOP was observed in both groups (p<0.05).

BOP is considered an important parameter for assessing the progression of periodontal disease [18,19]. The decrease in BOP incidence in the present study corroborates results obtained by Lang et al. [20], who found that a decrease in periodontal inflammation accompanies the reduction in this index. Although no statistically significant intergroup reduction was observed, results are similar to those presented by Balata et al. [21], who

observed intragroup differences but reported that the association between conventional treatment and aPDT does not present additional benefits to conventional therapy. Thus, as BOP has been considered the most consistent indicator of the current activity of periodontal disease, changes in mean Probing Depth values should not be emphasized, especially when evaluating limited sample sizes and short follow-up periods [18].

The lack of additional benefits of aPDT for people with DS was due to the limited sample size and the short follow-up period. However, the reduction in BOP demonstrates a remission of the inflammatory condition that, in the long follow-up period, would presumably indicate the reduction of PPD.

No statistically significant differences concerning the Plaque Index at both evaluation moments were observed, which differs from results found in research with HIV [17], smokers [18], and diabetic patients [22]. Although oral hygiene reinforcement was performed in each session, PI reduction was not observed, which may be hypothetically related to the fact that individuals with DS have a motor and neurological deficiencies that can lead to ineffective tooth brushing [2]. This result reinforces the importance of health promotion actions with parents and caregivers to stimulate oral hygiene performed by individuals with DS.

In the only clinical trial published that evaluates PPD in individuals with DS, a similar result was observed with a non-significant reduction in PPD after 1 month of treatment, compared to baseline3. Based on the clinical parameters analyzed in this study, it was observed that aPDT was not more effective than conventional periodontal treatment, which is in accordance with studies carried out with HIV, smokers, and diabetics patients [23-25].

Considering the sample size of studies and the positive results found, among other populations, for the association between aPDT and scaling and root planing, it is considered that, in larger samples and randomized controlled trials with at least 3-month follow-ups, the positive effects of this association should be better observed [25-28].

The aPDT is a therapy mediated by visible light, a photosensitizer (PS), and oxygen [11]. The mechanism of action of the aPDT consists of irradiation with light of an appropriate wavelength; the photosensitizer undergoes a transition from a low-energy-level "ground state" to a higher-energy "triplet state." This triplet-state sensitizer can react with biomolecules to produce free radicals or with molecular oxygen to produce singlet oxygen. This process can cause the oxidation of cellular constituents such as plasma membranes and DNA, resulting in cell death [29].

Although there are controversies in literature about the advantages of using aPDT as an adjunct treatment to conventional periodontal therapy, its effectiveness is related to its antimicrobial activity and its ability to reduce bleeding and inflammatory processes [22]. Comparison with other studies is difficult to be performed since there are divergences between clinical and methodological parameters and, considering the specific population included in this study, direct comparison with other populations - in the absence of additional previous clinical trials that contemplate them - conflicting results are obtained.

In this study, some limitations should be considered. Only periodontal clinical parameters were examined, and it is believed that the evaluation of radiographic and microbiological parameters could provide additional information important for further research in this field. In our study, the follow-up period was short and sample population was limited. Thus, further longer follow-up studies including more patients and evaluation of radiographic and microbiological parameters should be carried out to evaluate the effectiveness of aPDT in periodontal treatment of individuals with DS.

Conclusion

Considering the good acceptance by individuals with Down syndrome and their caregivers, in addition to the good results observed clinically, it was observed that the use of antimicrobial photodynamic therapy as adjuvant therapy did not promote additional benefits in decreasing plaque index and probing pocket depth after one month of treatment. However, a significant reduction in the bleeding on probing was observed in the intragroup evaluation.

Authors' Contributions

MGBS	https://orcid.org/0000-0001-9073-4611	Conceptualization, Methodology, Formal Analysis, Investigation, Resources, Data Curation, Writing - Original Draft and Writing - Review and Editing.
JAFN	https://orcid.org/0000-0003-3711-6966	Methodology, Formal Analysis and Writing - Review and Editing.
MHVC	https://orcid.org/0000-0001-7681-3225	Conceptualization, Methodology, Formal Analysis, and Writing - Review and Editing.

All authors declare that they contributed to critical review of intellectual content and approval of the final version to be published.

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None.

Conflict of Interest

The authors declare no conflicts of interest.

Data Availability

The data used to support the findings of this study can be made available upon request to the corresponding author.

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