ANTIMICROBIAL PHOTODYNAMIC THERAPY IN THE POST-OPERATIVE EXTRACTION OF LOWER THIRD MOLARS: A RANDOMIZED AND BLINDED CLINICAL TRIAL

Terapia Fotodinâmica Antimicrobiana na Extração Pós-Operatória de Terceiros Molares Inferiores: um ensaio clínico randomizado e cego

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Abstract

Objective: This study aimed to evaluate local antimicrobial reduction protocols in post operative inflammatory-infectious events of lower third molar extractions. **Methods** It was a clinical, crossover, randomized and blind study with a sample of 22 patients (36 teeth). The patients underwent two surgical moments at intervals. The allocation of teeth was in 3 experimental groups: Group 1: Antimicrobial photodynamic therapy (aPDT); Group 2: 0.12% Chlorhexidine (CLX); Group 3: Control - 0.9% Saline Solution (SS 0.9%). The groups received treatment immediately after tooth extraction, and the evaluated parameters were: pain, edema, maximum mouth opening, and infection. **Results:** The data showed a statistically significant difference with aPDT therapy in edema, intragroup evaluation, and the distance between the gonial-tragus points ($p = 0.022$). In measuring mouth opening, there was a statistical difference in the intragroup assessment of aPDT and CLX (aPDT with $p = 0.035$, CLX with $p = 0.038$). There was a statistical difference in the presence of postoperative infection, with the aPDT and CLX groups showing the lowest values ($p = 0.039$). Regarding the pain, there was a decrease in the analysis on the 7th day of the aPDT group ($P = 0.007$). **Conclusion:** In conclusion, treatment with aPDT favors a statistically significant reduction of infection, edema, pain, and trismus in the postoperative period of third molar extractions.

Keywords: Low-Intensity Light Therapy. Photodynamic therapy. Third molar. Chlorhexidine.

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Introduction

The prevalence of impacted third molars varies significantly between populations, with an average incidence of 44% (1). Although many asymptomatic third molars are detected during routine radiographic exams, literature suggests that failure to remove these teeth can lead to damage to adjacent teeth and even the development of pathological conditions such as infections, cysts, and tumors (2).

The removal of third molars often leads to pain, swelling, trismus, and infection, causing discomfort for the patient. To improve post-operative quality of life, systemic medications such as analgesics, anti-inflammatories, and antibiotics are commonly prescribed. However, for frequent surgeries like third molar extractions, rational use of medications—particularly antibiotics—is crucial. Uncontrolled antibiotic use can result in microbiota dysbiosis, leading to the excessive growth of resistant organisms, impaired drug absorption, altered metabolism of vitamins, diarrhea, and more severe conditions such as pseudomembranous colitis (3,4). Therefore, it is necessary to develop research to identify effective local antimicrobial strategies that reduce post-operative inflammatory and infectious events without causing systemic side effects.

Antimicrobial Photodynamic Therapy (aPDT) is a treatment widely used and studied in dentistry to reduce bacterial load. It is easy to perform, accessible, and free of side effects (5). This method involves a photosensitizer activated by a light source with a wavelength of 660±10 nm, generating highly cytotoxic reactive oxygen species capable of destroying pathogens (6). In their study, Chatzopoulos and Doufexi (7) demonstrated positive results using aPDT to treat periapical and periodontal lesions. However, they note that aPDT is still infrequently used in post-operative dental extractions.

Another method for reducing local microbial load is the use of chlorhexidine, developed in the 1940s as part of antiviral research. Chlorhexidine has a broad antimicrobial spectrum, effective against gram-positive and gram-negative organisms, bacterial spores, lipophilic viruses, yeasts, and dermatophytes (8,9). Chlorhexidine digluconate has been thoroughly studied and is widely used in dental practice for plaque control and as an antimicrobial agent for various oral disorders (10,11).

Several studies have evaluated the use of chlorhexidine to reduce the risk of post-extraction bacteremia, demonstrating its effectiveness in reducing post-operative pain, especially when used for local irrigation (10,11). The application of aPDT has also been studied as a post-operative treatment applied immediately after molar extraction. Although clinical studies in this area are rare, it has been observed that aPDT applied immediately after extraction reduces post-operative pain and swelling and improves oral health-related quality of life (6,12).

Given the lack of published studies comparing the effectiveness of aPDT and chlorhexidine, the present study aims to evaluate the effect of local antimicrobial protocols on post-operative inflammatory and infectious events following the extraction of impacted lower third molars.

Materials and methods

Study design

This research consisted of a unicentric, cross, randomized, and triple-blind clinical trial (blind blindness, surgeons, and statistics). The present study was duly submitted and approved by the Research Ethics Committee from the Federal University of Ceará, accredited by ConeP, obtaining the opinion number: 5.445.737. The confidentiality of all the information collected was guaranteed, ensuring the anonymity of the participants, according to the rules of Resolution No. 466/12 and Resolution 510/2016 of the Ministry of Health, which deals with guidelines and regulatory standards for research evolving human beings. Patients received treatment between June and November 2022, derived from spontaneous demand. The project was prepared according to the standards proposed by the Consort-Statement guide. The patients were subjected to two surgical moments, separated by a minimum interval of 15 days. Thus, each tooth was allocated among three experimental groups, according to postoperative treatment.

- Group 1: Treatment with antimicrobial photodynamic therapy (aPDT).
- Group 2: 0.12% chlorhexidine treatment (CLX).
- Group 3 (control): treatment with 0.9% saline solution (SS 0.9%) - placebo.

The treatment sequence applied to each tooth was randomly defined among the six generated combinations: aPDT and CLX; CLX and aPDT; aPDT and Placebo; Placebo and aPDT; CLX and Placebo; Placebo; and CLX. An external research collaborator performed the randomization through computer-generated randomization codes (Microsoft Excell®). Envelopes stored the randomization result, and the operator opened it only when applying the treatment.

The authors declare that they have no conflict of interest regarding the publication of this article.

Participants

The study population consisted of young individuals aged between 18 and 40 years, without severe chronic systemic diseases (according to the classification scale of the American Society of Anesthesiologists - ASA I), with the presence of impacted lower third molars, with good oral hygiene and who agreed to the terms of the study.

Volunteers who met at least one of the following criteria were excluded: (1) smokers, pregnant or lactating women; (2) presence of painful symptoms, pericoronitis, edema, hyperthermia, or limited mouth opening associated with third molars before the surgical procedure; (3) patients using medications that interfere with the research protocol or the drugs used in the study; (4) patients who used antibiotics in the last three months before the 1st surgery (in the case of antibiotic prescription after the 1st surgery, the patient was kept in the study and waited three months for the 2nd intervention); (5) presence of orthodontic bands on second molars.

Further exclusion criteria that were considered after inclusion in the study were: (1) patients who did not return for follow-up assessments; (2) patients who did not follow the postoperative recommendations and who had complications that interfered with the study evaluations.

Sample size

The sample calculation was obtained through the OpenEpi website, based on the results of the negative impact on oral health after extraction of 3rd molars found in the work of Batinjan et al [12]. There was a negative response of 26.5(±8.29) in the placebo group and 13(±3.84) in the group with local application of aPDT. Thus, considering a confidence interval and a power of 95%, a minimum sample of 24 teeth was estimated (20% added to the total due to the possibility of loss) for subsequent division among the six treatment combinations.

Interventions

The initial data collection was through a structured clinical form and applied by the researcher in charge. In the initial analysis, the value of maximum mouth opening was recorded (using a specific ruler (Therabite® - Range-of-motion Scales), and the distances between the facial points gonion X tragus, gonion X exocanthion, gonion X alare, gonion X X cheilium, X gnathion gonion, measured with the aid of dental floss attached to a flexible rod (Figure 1).

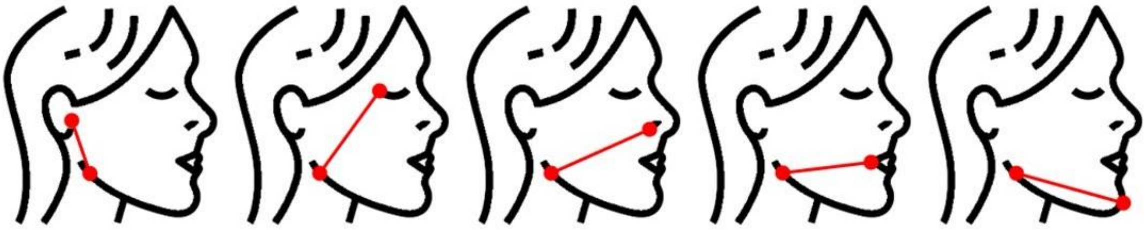

Figure 1: Facial measurements.

The Pernambuco index was used to measure the level of surgical difficulty (13). The technique of the surgical procedures was standardized and performed in an outpatient setting under local anesthesia. Students of the graduation course in Dentistry performed the surgeries, with the possibility of help from a researcher specializing in Oral and Maxillofacial Surgery and Traumatology with 5 years of experience in the respective specialty. All elaborated procedures were part of the environment of routine surgeries performed at the clinic. A strict biosecurity control followed. All surgeries were timed from the beginning of the incision (immediately after local anesthesia) and measured in minutes to allow an approximate standardization of surgical times.

After identifying the anesthetic effect, the lower third molar was removed, starting with the incision to access the tooth, using a #15 scalpel, followed by a detachment of the mucoperiosteal flap. When indicated, osteotomy and tooth sectioning were performed with #702 drills mounted at high speed with plenty of irrigation. Subsequently, the teeth were removed using appropriate levers or forceps. The cavity was curetted, when indicated, and irrigated with 0.9% saline solution, followed by the application of one of the study treatments, selected at random. The tissues were sutured with 4-0 silk thread, applying simple interrupted stitches.

For all patients, an anti-inflammatory medication was prescribed (Ibuprofen 600mg, every 8 hours for three days) and a rescue analgesic medication to be used only in case of pain (Dipyrone 1g every 6 hours). When there was evidence of an infectious process, antibiotic medication was prescribed. Postoperative recommendations were explained and delivered in writing.

Antimicrobial Photodynamic Therapy (aPDT) application protocol:

After tooth removal and debris removal, the alveolus was filled with 0.01% methylene blue solution (Chimiolux 10, Aptivalux Bioengineering LTDA and DMC Group, São Paulo, SP, Brazil) using a probe and syringe. This solution was left in the well for 5 min before irradiation. Irradiation was carried out with a diode LBP (Therapy EC DMC, São Carlos/SP, Brazil), with a wavelength of 660±10 nm, output power of 100 mW, spot of 0.028 cm2, output energy of 9 J, fluence of 300 J/cm², 90 s.

Protocol for applying chlorhexidine 0.12% (CLX) and control group (SS 0.9%):

After removing the tooth and debris, the socket was filled with 0.12% chlorhexidine solution using a probe and syringe. This solution was left in the alveolus for 5 min and then aspirated with a surgical suction cup. To maintain the patient's blindness to the treatment protocol, the laser device was inserted into the oral cavity without being activated, simulating its irradiation. The teeth in group 3 – Control (placebo) were treated by replacing 0.12% chlorhexidine with 0.9% saline solution (SS 0.9%).

Outcomes

Postoperative data collection was conducted by a calibrated external evaluator, who was blind to the treatment applied. Patients were clinically evaluated from the preoperative until the 14th day after the surgical procedure. When infection was identified during the clinical examination, an antibiotic was prescribed (Amoxicillin 500mg every 8 hours for seven days). The clinical criteria considered to reflect the presence of an active infection were intense erythema, pus, fever, intense pain, and severe trismus. The researcher provided patients with a means of communication, and as no patient sought care after 14 days of surgery, it is assumed that there was no development of late infection.

Postoperative edema was measured through a comparison of preoperative (T0), immediate postoperative (T1) and after 72 hours (T2), 5 (T3), 7 (T4) and 14 (T5) days.

of the surgical moment. Furthermore, the maximum mouth opening capacity was analyzed through the distance between the incisal edge of the upper and lower incisors and was measured in all evaluation periods, similar to the edema analysis times.

Patients received a form to record postoperative pain intensity. The measurement was through a 10-point visual analog scale (VAS), where 0 corresponded to no pain, and 10 reflected maximum pain. Patients were instructed to rate pain intensity preoperatively, immediately postoperatively, and at 8, 24, 72 hours, and 7 days after surgery.

Statistical methods

The data were tabulated in Microsoft Excel and exported for analysis in the SPSS software version 20.0 for Windows, adopting a confidence level of 95%. Means and standard deviations of all quantitative variables were calculated, which were subjected to the Shapiro-Wilk normality test and compared using the ANOVA tests for repeated measures, followed by the Bonferroni post-test (parametric data) or Friedman, followed by Dunn's post-test (non-parametric data). Categorical data were expressed as absolute and percentage frequencies and compared using Fisher's exact or Pearson's chi-square tests.

Results

The sample consisted of predominantly female individuals (63.6%) aged between 20 and 34 years, with an average of 24.41±3.75 years. In total, 23 patients entered the study, with 36 procedures performed. One patient was withdrawn from the study due to complications (severe trismus and transoperative dyspnea) in the 1st surgical intervention, and 08 patients did not return for the 2nd surgical intervention. It was observed that 9.1% of the patients were overweight, 13.6% had previous illnesses, 22.7% used medication (Table 1).

Table 1: Sample distribution

	n (%)
Gender	
Female	14(63.6%)
Male	8(36.4%)
Age (20-34)	24.41±3.75
Education	
2nd degree	18(81.8%)
Higher	4(18.2%)
Used Medicine	5(22.7%)
Allergy	1(4.5%)
Previous surgery	4(18.2%)
Alcoholic	0(0.0%)
Drugs	0(0.0%)
Previous illnesses	3(13.6%)
Overweight	2(9.1%)

Data expressed as absolute frequency and percentage or mean and standard deviation.

According to the analysis of tooth positioning (Table 2), it is observed that 86.1% of the teeth had their occlusal surface at the same height or a little below the line of occlusion of the second molar. Note that the vertical position was the most frequent, with 63.8% presenting this angle, 80.5% had more than one root, and 61.1% had torn roots. As for the relationship with the 2nd molar, most of the evaluated teeth had some contact (91.6%) with the crown (58.3%) or the root (33.3%), with only 8.3% without contact between the 3rd and 2nd molar. There was no statistically significant difference regarding the positioning of the included teeth between groups ($p > 0.05$).

Table 2: Surgical aspects and classification of the degree of surgical difficulty

	Group			
	aPDT	**CLX 0.12%**	**SS 0.9%**	**p-Value**
Osteotomy	8 (66.7%)	5 (41.7%)	8 (66.7%)	0,358
Tooth sectioning	8 (66.7%)	2 (16.7%)*	7 (58.3%)	***0,032***
Specialist assistance	8 (66.7%)	7 (58.3%)	10 (83.3%)	0,400
Occlusal_plan				
A	11 (91.7%)	11 (91.7%)	9 (75.0%)	0,395
B	1 (8.3%)	1 (8.3%)	3 (25.0%)	
C	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Retromolar space				
I	9 (75.0%)	10 (83.3%)	9 (75.0%)	0,852
II	3 (25.0%)	2 (16.7%)	3 (25.0%)	
III	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Angle				
Vertical	6 (50.0%)	10 (83.3%)	7 (58.3%)	0,478
Mesio	3 (25.0%)	1 (8.3%)	1 (8.3%)	
Horizontal	1 (8.3%)	1 (8.3%)	1 (8.3%)	
Disto	2 (16.7%)	0 (0.0%)	3 (25.0%)	
Root curvature				
Absent	5 (41.7%)	4 (33.3%)	5 (41.7%)	0,890
Present	7 (58.3%)	8 (66.7%)	7 (58.3%)	
Root number				
1 root	1 (8.3%)	2 (16.7%)	4 (33.3%)	0,289
>1 root	11 (91.7%)	10 (83.3%)	8 (66.7%)	
2nd_molar_relationship				
No contact	0 (0.0%)	1 (8.3%)	2 (16.7%)	0,594
crown contact	8 (66.7%)	6 (50.0%)	7 (58.3%)	
Root contact	4 (33.3%)	5 (41.7%)	3 (25.0%)	
Surgery Time(min)	101.92±23.80	81.50±29.99	100.42±29.12	0,149
Final score	12.58±1.51	11.67±1.67	12.08±2.35	0,496
BMI				
Normoweight	10 (83.3%)	12 (100.0%)	11 (91.7%)	0,336
Overweight	2 (16.7%)	0 (0.0%)	1 (8.3%)	

p<0.05, chi-square or Fisher's exact test (n, %) or Friedman/Dunn (mean±SD).

Table 2 describes that the duration of surgical procedures had equivalent average times between groups (p = 0.149) and presented an overall average of 94:61 minutes. During the surgical procedures, specialist assistance was required in 69.4% of the surgeries, osteotomy was performed in 58.3%, and tooth sectioning in 47.2% of the included teeth. As for the comparison between groups, a statistically significant difference (p = 0.032) was observed regarding the performance of tooth sectioning, which was less frequent in the group treated with chlorhexidine.

Regarding postoperative edema (Table 3), a statistically significant difference was observed between groups only in the distance between the gonio-tragus points. The group treated with aPDT had statistically higher values than the CLX and SS 0.9% groups in the gonio-tragus measure, but in the T2 and T3 analyses, CLX showed statistically lower values, differing both from the aPDT group and from the SS 0, 9%. However, in the intragroup analysis of the same distance, there was a statistically significant difference only in the group treated with aPDT, with statistically lower T4 and T5 values than the other analyzed times.

Table 3: Edema - mean values (cm) of facial distances between groups.

	Group			
	aPDT	**CLX 0.12%**	**SS 0.9%**	**p-Value**
Gonio_tragus				
T0	6.43±0.60^{Aa}	5.72±0.43^{Ba}	6.00±0.68^{Ba}	***0,016***
T1	6.57±0.55^{Aa}	5.82±0.48^{Ba}	6.04±0.69^{Ba}	***0,011***
T2	6.61±0.63^{Aa}	5.80±0.49^{Ba}	6.13±0.73^{Aa}	***0,012***
T3	6.59±0.62^{Aa}	5.75±0.51^{Ba}	6.06±0.69^{Aa}	***0,007***
T4	6.47±0.59^{Ab}	5.75±0.44^{Ba}	6.05±0.65^{Ba}	***0,015***
T5	6.45±0.58^{Ab}	5.74±0.43^{Ba}	6.03±0.66^{Ba}	***0,015***
p-Value	0,022	0,056	0,456	
Gonio_exocantio				
T0	10.47±1.01^{Aa}	9.91±0.63^{Aa}	10.09±0.51^{Aa}	0,194
T1	10.55±0.97^{Aa}	10.05±0.65^{Aa}	10.19±0.54^{Aa}	0,252
T2	10.62±1.02^{Aa}	9.97±0.70^{Aa}	10.38±0.77^{Aa}	0,175
T3	10.63±0.93^{Aa}	9.94±0.69^{Aa}	10.28±0.67^{Aa}	0,111
T4	10.53±0.92^{Aa}	9.89±0.67^{Aa}	10.13±0.52^{Aa}	0,107
T5	10.53±0.92^{Aa}	9.91±0.66^{Aa}	10.08±0.52^{Aa}	0,107

p-Value	0,114	0,264	0,196	
Gonio_alare				
T0	11.15±0.90^{Aa}	10.84±0.66^{Aa}	11.18±0.59^{Aa}	0,466
T1	11.27±0.83^{Aa}	11.06±0.63^{Aa}	11.33±0.56^{Aa}	0,607
T2	11.34±0.88^{Aa}	10.08±2.81^{Aa}	11.58±0.81^{Aa}	0,099
T3	11.26±0.81^{Aa}	10.05±2.80^{Aa}	11.33±0.60^{Aa}	0,139
T4	11.17±0.75^{Aa}	10.87±0.64^{Aa}	11.20±0.58^{Aa}	0,402
T5	11.17±0.73^{Aa}	10.86±0.63^{Aa}	11.17±0.53^{Aa}	0,402
p-Value	0,188	0,121	0,257	
Gonio_cheilio				
T0	8.91±0.68^{Aa}	8.92±0.56^{Aa}	9.03±0.65^{Aa}	0,881
T1	8.97±0.73^{Aa}	9.08±0.58^{Aa}	9.22±0.69^{Aa}	0,660
T2	9.18±0.89^{Aa}	9.09±0.52^{Aa}	9.30±0.73^{Aa}	0,781
T3	9.03±0.61^{Aa}	9.07±0.50^{Aa}	9.13±0.66^{Aa}	0,903
T4	8.92±0.60^{Aa}	8.99±0.65^{Aa}	9.16±0.63^{Aa}	0,632
T5	8.94±0.61^{Aa}	8.97±0.59^{Aa}	9.10±0.60^{Aa}	0,788
p-Value	0,145	0,082	0,209	
Gonio_gnatio				
T0	10.94±0.76^{Aa}	11.30±0.74^{Aa}	11.42±0.71^{Aa}	0,272
T1	11.18±0.72^{Aa}	11.48±0.77^{Aa}	11.48±0.67^{Aa}	0,498
T2	11.09±0.77^{Aa}	11.52±0.84^{Ab}	11.55±0.79^{Aa}	0,309
T3	11.08±0.70^{Aa}	11.38±0.68^{Aa}	11.38±0.74^{Aa}	0,492
T4	11.04±0.67^{Aa}	11.32±0.73^{Aa}	11.38±0.71^{Aa}	0,473
T5	11.03±0.68^{Aa}	11.31±0.72^{Aa}	11.39±0.69^{Aa}	0,411
p-Value	0,066	0,039	0,502	
Tragus_cheilio				
T0	11.45±0.72^{Aa}	11.23±0.62^{Aa}	11.39±0.68^{Aa}	0,699
T1	11.60±0.75^{Aa}	11.30±0.69^{Aa}	11.55±0.70^{Aa}	0,550
T2	11.69±0.78^{Aa}	11.38±0.57^{Ab}	11.61±0.67^{Aa}	0,502
T3	11.56±0.71^{Aa}	11.33±0.54^{Aa}	11.42±0.64^{Aa}	0,684
T4	11.48±0.65^{Aa}	11.27±0.61^{Aa}	11.44±0.65^{Aa}	0,700
T5	11.48±0.67^{Aa}	11.25±0.61^{Aa}	11.43±0.64^{Aa}	0,653
p-Value	0,151	***0,045***	0,065	

*p<0.05, Friedman/Dunn test (mean±SD). Letters with different symbols = significant difference between groups. Different lowercase letters = significant difference between periods.

In the mouth opening data, it was observed, in the intragroup evaluation of aPDT and CLX, that there was a significant difference, with the opening value in T0 statistically equal to T5, demonstrating that, at the end of the study (T5), there was a return to the initial standards (T0) mouth opening. In the SS 0.9% group, even 14 days after the operation, the mouth opening had still not returned to initial values (T0).

Regarding the data on postoperative infection (Table 4), there was a statistically significant difference between the groups when comparing all times (T0 to T5). The group treated with 0.9% saline solution was significantly more likely to develop postoperative infection compared to those treated with aPDT and CLX (p = 0.039). The analysis of the use of rescue medication did not show a statistically significant difference (Table 4). The results of the pain VAS showed that in the group treated with aPDT there was a significant reduction in pain in the 7-day analysis (p = 0.007) (table 4).

Table 4: Mouth opening (cm), rescue medication, VAS and infection.

	Grupo			
	aPDT	**CLX 0.12%**	**SS 0.9%**	**p-Valor**
Abertura Bucal *				
T0	52.33 ± 8.77^{Aa}	49.65 ± 8.77^{Aa}	51.36 ± 5.96^{Aa}	0,644
T1	47.56 ± 8.65^{Ab}	41.42 ± 9.52^{Ab}	42.99 ± 10.96^{Ab}	0,291
T2	39.80 ± 11.85^{Ab}	42.58 ± 9.41^{Ab}	39.64 ± 10.11^{Ac}	0,746
T3	41.41 ± 13.14^{Ab}	43.52 ± 11.13^{Ab}	40.18 ± 12.94^{Ac}	0,803
T4	44.18 ± 13.43^{Ab}	47.00 ± 9.86^{Ab}	44.15 ± 15.68^{Ab}	0,833
T5	47.40 ± 12.03^{Aa}	49.00 ± 8.57^{Aa}	47.58 ± 13.95^{Ab}	0,935
p-Value	***0,035***	***0,038***	***0,018***	
Rescue_medication*				
D1	1.08 ± 1.51^{Aa}	1.25 ± 1.29^{Aa}	0.50 ± 0.52^{Aa}	0,278
D2	1.17 ± 1.53^{Aa}	0.83 ± 1.27^{Aa}	0.58 ± 1.00^{Aa}	0,541
D3	0.75 ± 1.22^{Aa}	0.67 ± 0.89^{Aa}	0.42 ± 0.67^{Aa}	0,674
D4	0.75 ± 1.29^{Aa}	0.67 ± 0.98^{Aa}	0.17 ± 0.39^{Aa}	0,289
D5	0.33 ± 0.65^{Aa}	0.50 ± 0.90^{Aa}	0.17 ± 0.39^{Aa}	0,495
D6	0.42 ± 0.79^{Aa}	0.33 ± 0.89^{Aa}	0.17 ± 0.39^{Aa}	0,692
D7	0.42 ± 0.79^{Aa}	0.33 ± 0.89^{Aa}	0.08 ± 0.29^{Aa}	0,493
p-Value	0,350	0,069	0,483	
Total	4.92±5.87	4.58±5.21	2.08±2.47	0,293

VAS**				
inicial	0.75±1.48^{Aa}	1.42±2.11^{Aa}	0.75±1.06^{Aa}	0,785
immediate post	3.17±3.41^{Ab}	4.33±2.84^{Ab}	3.92±3.12^{Ab}	0,438
8h	3.58±3.09^{Ab}	3.58±2.23^{Ab}	3.75±2.70^{Ab}	0,957
24h	3.17±3.66^{Ab}	2.42±2.87^{Ab}	3.08±3.45^{Ab}	0,979
3d	3.08±3.12^{Ab}	3.17±3.13^{Ab}	2.92±2.94^{Ab}	0,990
7d	2.00±2.34^{Ac}	2.58±3.09^{Ab}	2.58±3.18^{Ab}	0,896
p-Value	***0,007***	***0,038***	***<0,001***	
Infection***				
T0	0 (0.0%)^{Aa}	0 (0.0%)^{Aa}	0 (0.0%)^{Aa}	1,000
T1	0 (0.0%)^{Aa}	1 (8.3%)^{Aa}	2 (16.7%)^{Aa}	0,336
T2	1 (8.3%)^{Aa}	1 (8.3%)^{Aa}	3 (25.0%)^{Aa}	0,395
T3	0 (0.0%)^{Aa}	0 (0.0%)^{Aa}	1 (8.3%)^{Aa}	0,358
T4	0 (0.0%)^{Aa}	0 (0.0%)^{Aa}	1 (8.3%)^{Aa}	0,358
T5	0 (0.0%)^{Aa}	0 (0.0%)^{Aa}	0 (0.0%)^{Aa}	1,000
p-Value	0,407	0,533	0,262	
T0-T5	1 (1.4%)^{A}	2 (2.8%)^{A}	7 (9.7%)^{B}	***0,039***

*p<0.05, ANOVA/Bonferroni test; **p<0.05, Friedman/Dunn (mean±SD); ***p<0.05 Fisher's exact test/chi-square (n, %). Different capital letters = significant difference between groups. Different lowercase letters = significant difference between periods.

Discussion

Edema, pain, and trismus are the most common causes of discomfort and morbidity during the postoperative period of impacted third molar removal surgeries (11, 15). These symptoms are associated with the patient's inflammatory response after surgery and significantly interfere with daily routines, impairing quality of life (12).

In the 1990s, research into the physiological effects and clinical applications of low-level laser therapy (LLLT) (16) gained momentum, leading to its increasing use in medical and dental treatments. Both the application of LLLT and the aPDT protocol offer several benefits: they are reliable, effective, fast, non-invasive therapies with good patient acceptance. These therapies present an alternative to reduce the prescription of systemic medications after surgery (6).

The current study aimed to evaluate the effect of local antimicrobial protocols during the postoperative period of impacted lower third molar extractions. The application of antimicrobial photodynamic therapy (aPDT) was compared to chlorhexidine and a control group using 0.9% saline, focusing on inflammatory/infectious events, including pain, infection, edema, and trismus. At present, no randomized clinical trials specifically addressing these evaluation conditions have been reported, prompting the investigation of the efficacy of this therapeutic protocol.

Regarding surgical procedure time, no significant difference was found between groups (general mean = 94.61 min). Most surgeries required specialist assistance to complete due to the complexity and prolonged operating time. A statistically significant difference ($p = 0.032$) was observed in the performance of tooth sectioning, with the chlorhexidine group having the lowest frequency of odontosection (16.7%, Table 2). Reduced tooth sectioning could have important clinical implications, as it minimizes inflammation and decreases the risk of postoperative infection. The aPDT group had the highest number of surgeries requiring odontosection.

Several studies have pointed out the benefits of laser therapy in preventing postoperative edema (12,17), showing reduced edema compared to control groups after lower third molar extractions. However, other researchers have found no statistically significant differences in facial edema reduction when comparing low-power laser (16), antimicrobial photodynamic therapy, and control groups. Fraga et al. (2020) suggest that variations in laser types and irradiation parameters may explain the discrepancies in study results (6).

It is well established that antimicrobial photodynamic therapy reduces local microbial load. Furthermore, the combination of aPDT and low-power laser decreases inflammatory mediators at the surgical site, thus reducing postoperative signs and symptoms like local edema [6]. In our study, a statistically significant difference in edema was observed only in the gonio-tragus distance. In intergroup comparisons, the aPDT group had statistically higher edema values than the CLX and SS 0.9 groups, likely because the aPDT group performed more dental sections, leading to longer surgical times. Additional factors such as procedure complexity and facial pattern variations may also have influenced the results. In the intragroup evaluation, only the aPDT group showed significant statistical values at T4 and T5 ($p = 0.022$).

Regarding mouth opening, in the intragroup evaluation of both the aPDT and CLX groups, T0 and T5 values were statistically equivalent, indicating a return to baseline mouth opening patterns by the 14th day (aPDT: $p = 0.035$; CLX: $p = 0.038$). In contrast, the 0.9% saline group did not regain baseline mouth opening by T0, demonstrating higher levels of trismus compared to the other groups. Other studies using LLLT (16,17) or chlorhexidine 0.12% [11] have reported trismus reduction between the 2nd and 7th postoperative days, although these reductions were not always clinically significant (11). No studies were found in the literature that used LLLT in conjunction with aPDT to assess trismus after extractions.

Infection rates were statistically different between the groups when postoperative evaluation times (T0 to T5) were compared. The groups treated with aPDT and CLX exhibited lower infection rates compared to the control group (SS 0.9%, $p = 0.039$). Infection signs such as erythema, pus, severe pain, marked trismus, and fever were standardized in the evaluations. This is especially relevant considering the aPDT group performed more dental sections, and surgical procedures were carried out by dental students in a routine clinical setting, leading to longer surgical times and higher infection risk.

In this study, methylene blue was used as the photosensitizer in the aPDT group. Some studies have reported that methylene blue combined with LLLT generates reactive oxygen species and reduces anaerobic bacteria by approximately 95.2% (6,18). Additionally, an in vitro study demonstrated that aPDT is effective against various bacteria and offers the advantage of not promoting antibiotic resistance compared to traditional antibiotics (5). Regarding chlorhexidine, studies have shown that the risk of post-extraction bacteremia is reduced by only 12%, with relatively low effectiveness (10,11).

The analgesic effect of low-power lasers has long been recognized by the scientific community. Several authors have reported a progressive decrease in pain after lower third molar removal over a 14-day postoperative period (12). One study found that the aPDT group had lower postoperative pain levels, with the group combining aPDT and an additional LLLT session showing the best pain reduction6. However, some studies have found little or no clinical pain relief (16,17). In our study, a statistically significant reduction in pain was observed on the 7th postoperative day only in the aPDT group ($p = 0.007$). The authors suggest that both the use of aPDT and LLLT as a light source may have contributed to a residual analgesic effect.

This study had some limitations. Variations in patients' facial patterns, as well as the subjective nature of the pain scale, may result in heterogeneous data. Additionally, operative times varied widely due to the fact that the procedures were performed by dental students, with specialist intervention only when tooth removal was unsuccessful.

Conclusion

Treatment with aPDT favors a significant statistical reduction in infection, edema, pain, and trismus in the postoperative extraction of lower third molars. Larger and more homogeneous samples can reproduce clearer and more consistent data in future research.

Resumo

Objetivo: Este estudo teve como objetivo avaliar protocolos locais de redução antimicrobiana em eventos inflamatórios-infecciosos pós-operatórios após exodontias de terceiros molares inferiores. **Métodos**: Este foi um estudo clínico randomizado, cego e cruzado com uma amostra de 22 pacientes (36 dentes). Os pacientes foram submetidos a dois momentos cirúrgicos com intervalos. Os dentes foram alocados em 3 grupos experimentais: Grupo 1: Terapia fotodinâmica antimicrobiana (TFD); Grupo 2: Clorexidina 0,12% (CLX); Grupo 3: Controle - Solução Salina 0,9% (SS 0,9%). Os grupos receberam tratamento imediatamente após a exodontia, e os parâmetros avaliados foram: dor, edema, abertura bucal máxima e infecção. **Resultados**: Os dados mostraram diferença estatisticamente significante com a terapia TFD no edema, na avaliação intragrupo e na distância entre os pontos goníaco-tragus (p = 0,022). Na mensuração da abertura bucal, houve diferença estatística na avaliação intragrupo de aPDT e CLX (aPDT com p = 0,035, CLX com p = 0,038). Houve diferença estatística na presença de infecção pós-operatória, com os grupos aPDT e CLX apresentando os menores valores (p = 0,039). Em relação à dor, houve diminuição na análise no 7º dia do grupo aPDT (p = 0,007). **Conclusão**: Conclui-se que o tratamento com aPDT favorece redução estatisticamente significativa de infecção, edema, dor e trismo no pós-operatório de extrações de terceiros molares.

Palavras-chave: Terapia de Luz de Baixa Intensidade. Terapia Fotodinâmica. Terceiro molar. Clorexidina.

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