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Immediate Effect of Photobiomodulation on pH and Salivary Flow and Its Preliminary Outcome

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Authors' contributions

This work was carried out in collaboration among all authors. Authors FJT, HACRT, SHRLR, SRF and MLJ did the conceptualization. Authors FJT, BACSM, SHRLR, LLMB, MSP, BSK, MLJ and SRF performed methodology. Authors BACSM, BSK and JAB did software analysis. Authors FJT, BACSM, ILMB, MSP, MLJ and SRF did data curation. Authors FJT, BACSM, MLJ and NS did formal analysis. Authors FJT, BACSM, SHRLR and HACRT wrote original draft. Authors JTF, BSK and MLJ wrote, reviewed and edited the manuscript. Authors SHRLR, HACRT and NS did data validation. Authors BSK and JAB searched for resources. Author MLJ supervised the study. All authors read and approved the final manuscript.

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ABSTRACT

Xerostomia, a common side effect of radiotherapy, can significantly impact patients' quality of life. This study aimed to compare the immediate effects of infrared light photobiomodulation on salivary flow and pH in individuals experiencing xerostomia. Twenty adults with xerostomia participated in the study, divided into two groups: Group 1 (G1) received extraoral photobiomodulation treatment, and Group 2 (G2) received both intra and extraoral treatment. Stimulated saliva was collected before and immediately after light application. In G1, the photobiomodulation was applied using a cluster (808 nm, 120 mW, 24J), while G2 received treatment with a pointer (808 nm, 100mW, 6J per point). The results confirmed our hypothesis, showing a statistically significant increase in immediate salivary flow stimulation with the headgear technique (G1) (p= 0.037). Analyzing the percentage of volume variation (ml) per minute, the average salivary flow increased from 0.86 ml/min to 1.2 ml/min after extraoral application with an infrared laser cluster, representing a 7% increase. In conclusion, the protocol involving only extraoral application was effective in stimulating salivary flow. Further research is needed to understand the specific mechanisms behind these differences and optimize photobiomodulation techniques for xerostomia management. This study found that using external infrared photobiomodulation can immediately increase salivary flow in xerostomia patients, potentially offering a comfortable and effective symptom management method. It emphasizes the need for refining these techniques and further research to understand long-term effectiveness.

Keywords: Salivary flow; photobiomodulation; hyposalivationon; low power laser; salivary pH; xerostomia.

1. INTRODUCTION

Xerostomia, also known as patient-reported subjective oral dryness, is a common side effect of cancer therapies, particularly radiation therapy in the head and neck region [1, 2]. It influences the quality of life, counting oral infection, caries, poor sleep quality [3–5].

Dry mouth is a prevalent symptom in the general population, estimated between 21% and 27%. In a study of 197 terminally ill cancer patients, it affected 77% of them. Research on dry mouth was mostly centered on healthy patients, those with Sjögren's syndrome, or those who had received head and neck radiotherapy, leading to it being considered an overlooked aspect of supportive care. In a study on advanced cancer patients, 78% of 120 participants reported dry mouth as the fourth most common and third most distressing symptom. Most patients experienced dry mouth frequently, and severity was often rated as moderate, severe, or very severe[1].

Saliva is a body fluid of complex composition that guarantees the health of the oral cavity. It originates from 3 pairs of major salivary glands: the parotid, submandibular and sublingual glands, and from numerous minor salivary glands located in the oral mucosa [2]

Saliva allows lubrication and humidification of the oral cavity and associated structures, due to its viscosity and elastic properties. Among some of its functions, we can mention: its importance in swallowing, through the formation of a cohesive food bolus and the unimpeded passage of the food bolus to the digestive tract; its performance in phonation, due to its lubricating property, and due to its buffering capacity, it acts in an important way in the modulation of remineralization and demineralization of the dental structure[2–4].

There is a high prevalence and/or incidence of caries among people with pathologically low salivary flow, compromised buffering capacity, and early colonization or high titer of *Streptococci mutans* in saliva[5]. Pyati et al (2018) found that the significant change in salivary flow rate, pH and total protein levels in active children with caries suggest that the levels of these physicochemical properties of saliva can act as strong indicators of caries status. in children[4].

Components such as sodium, calcium, magnesium ions, chlorine, bicarbonate, inorganic phosphate, ionic strength, and even pH, among others, may change due to increased salivary flow [2]

In addition to its physiological functions, saliva is a useful biological fluid in the diagnosis of diseases. Its composition includes enzymes, antibodies, bacteria, viruses, electrolytes, proteins, and other components, which is why saliva has been shown to be an excellent alternative for clinical analysis [3]
Phototherapy is a treatment with different modalities of light sources, such as laser, light emitting diode (LED) light, halogen light, or others[6]

To better understand the effects of photobiomodulation on cells, the theory that photobiomodulation reacts with target cells photochemically is cited. ((Freitas et al., 2016). This theory says that mitochondria contain chromophores that absorb photons from the PBM. The primary chromophore to absorb red light is the enzyme cytochrome c oxidase, which is located in unit IV of the mitochondrial respiratory chain, resulting in the activity of various molecules such as nitric oxide (NO), ATP, calcium ions, reactive oxygen species (ROS), and several other signaling molecules [7,8]. Glycolysis and ATP production are thought to be promoted due to the stimulation that PBM causes the electrons in the chromophores to move from higher energy orbits and, immediately, the electron carriers (such as the chromophore, cytochrome, and oxidase) deliver these electrons to their final electron acceptors while a proton gradient is made, in addition to creating a proton gradient which increases ATP production. In addition, several transcription factors are activated by PBM [7,9–11]

In dentistry photobiomodulation has been found to be effective in relieving the side effects of cancer treatment, relieving pain, alleviating the symptoms of Sjogren's Syndrome , reducing the amount of periodontal pathogenic bacteria, stimulating the salivary glands, increasing regeneration of undamaged glandular tissue after cancer irradiation, improving saliva properties, and acting on salivary rate in hyposalivation[11–13] Clique ou toque aqui para inserir o texto.

The literature shows the effects of low-level laser therapy on the salivary glands are not only stimulating but also regenerative to a certain degree, since the glandular response to the same amount of laser energy applied increased linearly with the time[14,15].

In the study by Nemeth et al. (2020), where the aim of the prospective randomized study was to verify how photobiomodulation of the major salivary glands, with polychromatic light or LED light, affects caries risk factors, in adult patients with high caries risk, where the risk factors caries were determined from saliva samples before therapy, two weeks after initiation, at the end of therapy and four weeks after the end of therapy; it was concluded that photobiomodulation of the major salivary glands in patients at high risk of caries can reduce cariogenic bacteria in saliva and improve some salivary parameters, thus reducing the risk of caries[16].

Studies show that there was an increase in salivary flow after the use of low-level laser [12,14], and an increase in salivary pH with the use of LED[16] but , studies such as the one by Louzeiro et al [17]where the effects of photobiomodulation on the salivary glands of patients undergoing head and neck radiotherapy were evaluated, and the study by Fidelix et al [13,18]which evaluated the action of low-intensity laser in Sjogren's Syndrome patients did not find improvements in salivary parameters. However, as in these two studies the salivary glands were compromised, the authors considered that this fact influenced the results.

Knowing the importance of salivary parameters being in balance for: maintenance of health in the oral cavity; adequate phonation and digestion. Considering that adequate salivary flow and pH are important in protecting teeth. Knowing that the use of photobiomodulation in salivary glands, are controversial in the measurement of flow and pH, in specific cases, where the salivary glands are not in its perfect functioning. And, considering the study of Bzark et al. [14] who concluded improvement in salivary parameters with the use of infrared laser compared to red laser.

The anlaysis of the saliva collection method is important because it provides a standardized and systematic approach to evaluating the effects of photobiomodulation on salivary flow and pH. Using sialogogues to stimulate salivation, followed by saliva collection at regular intervals, allows for a precise assessment of immediate changes in saliva production after laser application. Additionally, immediate measurement of salivary pH provides additional information about saliva composition and quality. By adhering to this detailed and rigorous protocol, researchers can ensure reliable and comparable results, which are crucial for evaluating the effectiveness of photobiomodulation therapy in managing xerostomia. The present study aims to evaluate and compare the immediate effect on pH and salivary flow with intraoral and extraoral photobiomodulation and only extraoral infrared laser on the salivary glands of adult subjects.

2. METHODOLOGY

2.1 Study Location and Sample Selection

The study was conducted with 20 participants experiencing xerostomia at Nove de Julho University and was carried out in compliance with regulatory norms governing research involving human subjects, with approval from the research ethics committee under opinion number 5,305,375. Participants expressed their agreement to participate by completing and signing the informed consent form, with clinical trial registration NCT05413993.

The sample size was determined based on the study by Marín et al. [18] using GPower software version 3.1 (Universitat Kiel, Germany), which recommended a total sample size of 15 participants per group, accounting for potential losses. However, 20 adults were recruited for the study using a convenience sampling method. Participants were recruited through face-to-face invitations at Universidade Nove de Julho and nearby locations. This study adhered to the CONSORT recommendations outlined by the EQUATOR network publication guidelines (http://www.equator-network.org).

2.2 Inclusion Criteria

Adults over 18 years of age with healthy dentition and xerostomia.

2.3 Exclusion Criteria

Participants with compromised health and those with teeth exhibiting caries, gingivitis, or other oral cavity alterations, as well as individuals who had used antibiotics or anti-inflammatory medication within the last 30 days.

2.4 Study Groups

Participants completed a questionnaire covering dental and medical history, as well as the Xerostomia Inventory - XID questionnaire, which utilizes a simplified format with three response options: never (1 point), occasionally (2 points), and always (3 points). Each participant's score was calculated by summing all points, resulting in a range from 11 to 33 points, with higher scores indicating greater xerostomia severity. All participants received both treatments—extraoral and intraoral—separated by a 7-day interval, serving as their own controls. Group 1 (n=20) underwent the extraoral application procedure, while Group 2 (n=20) underwent the intra and extraoral application for evaluation.

2.5 Conduct and Research Protocol

2.5.1 Saliva collection and analysis

Saliva collection took place at the Dental Clinic of Universidade Nove de Julho, with participants seated in the dental chair. Stimulated saliva was obtained through sialogogue chewing for 5 minutes, with collection performed by expectoration into graduated glass tubes every minute of chewing. Collection occurred before and immediately after laser application, following both extraoral and intra and extraoral application procedures. Subsequently, 3 drops of simethicone were added to eliminate gases and foam before measuring saliva volume. Saliva tubes were then placed on a bench for immediate pH measurement using colorimetric tape (MERCK Ⓡ Chemical, São Paulo, Brazil), featuring a pH scale ranging from 0 to 14.

2.6 Laser Application Protocol

2.6.1 Group 1 - Extraoral Application

Infrared laser application utilized the Ecco Reability equipment (Eccofibras, São Paulo, Brazil) with a cluster featuring 3 spots emitting at 808 nanometers and 120 mW power. A total energy of 24J was applied extraorally across the

Table 1. Dosimetric parameters used in applications in groups G1 and G2

Parameters	G1 infrared laser	G2 infrared laser
Wavelength [nm]	808	808
Operating mode	Continuous	Continuous
Power [mW]	120	100
Beam area [cm2]	21 cm2	0.0984 (with spacer)
Exposure time [s]	67 by region	60 per point
Fluence [J/cm2]	61	61
Energy [J]	24 by region	6 per point
Number of irradiated points	4	16
Application technique	Contact	Contact
Number of sessions	1	1
Treatment frequency	1 single application	1 single application
Total radiated energy [J]	96	96

bilateral parotid, submandibular, and sublingual gland regions, totaling 4 application regions.

2.6.2 Group 2 - Intra and Extraoral Application

Laser application lasted 60 seconds, with 2 intraoral and 2 extraoral points targeted at the bilateral parotid glands, as well as 1 intraoral and 1 extraoral point aimed at the submandibular and sublingual glands, totaling 16 points. Laser parameters included: central wavelength (nm) = 808 nm, continuous operating mode, 100 mW power, with a 0.354 cm opening diameter (using a spacer), and radiant energy of 6J (Table 1).

2.7 Statistical Analysis

Data were analyzed using Analysis of Variance (ANOVA) and Wilcoxon test ($\alpha = 0.05$). The Statistical Package for the Social Sciences (SPSS) (IBM Corp. launched in 2012. IBM SPSS Statistics for Windows, version 21.0. Armonk, NY: IBM Corp) version 15.0 was used for all analyses.

3. RESULTS

The sample consisted of 20 participants, 70% (n=14) of the female gender and 30% (n=6) of the male gender. The mean age was 30.25 years (sd=9.8). Table 2 presents the characteristics of the participants in relation to their dental and medical history. When evaluating the Xerostomia Inventory, the average score of the participants was 17.55 (sd= 3.4), considering that the maximum score is 33, with the highest 25 points and the lowest 14.

The volume of saliva of the participants during the 5 minutes was measured to calculate the salivary flow and the percentage of variation. After the initial collection of saliva, before the first application, it was found that the group that participated in this experiment presented an average of 0.86 ml/min of salivary flow rate. To verify if there was a difference in salivary flow between before and immediately after the application of photobiomodulation, the percentage of volume variation (ml) per minute was considered.

After extraoral application with an infrared laser cluster, the average salivary flow increased from 0.86 ml/min to 1.2 ml/min. This increase was 7% and was considered statistically significant compared to baseline on the same day ($p<0.05$). Fig 1 represents the volume and variation of salivary flow in G1.

After 7 days, when the participants returned, the pre-application measurement in G2 (intra and extraoral) of the infrared laser with a tip indicated a flow rate of 1.20 ml/min. It was observed that the rate remained unchanged in relation to the previous week. However, after applying the G2 procedures, the immediate flow variation was only 1% in relation to the pre-application measure on the same day (Fig 2), with a rate of 1.22 ml/min, as shown in Fig 3. The difference between before and after in G2 was not statistically significant ($p>0.05$).

Salivary pH analysis showed that there was no immediate change in either of the two application methods or in any of the participants. The initial average of the salivary pH at the first moment was 7.1 and immediately after the G1 application the average was 7.05. After seven days of the first application, the average pH of 7 went to 7.1 immediately after the G2 application (Fig 4). These subtle changes in pH were not statistically significant (p>0.05).

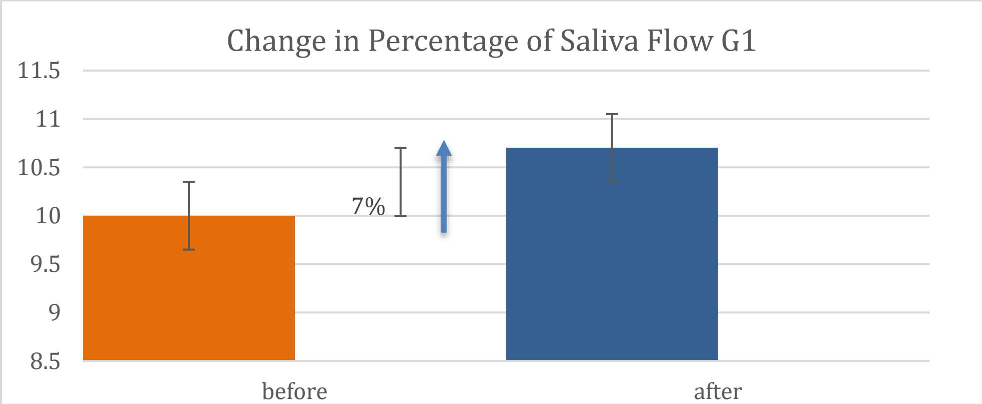

Fig. 1. Volume and variation of salivary flow after application of the extraoral infrared laser-G1
** statistically significant, p<0.05, Wilcoxon test*

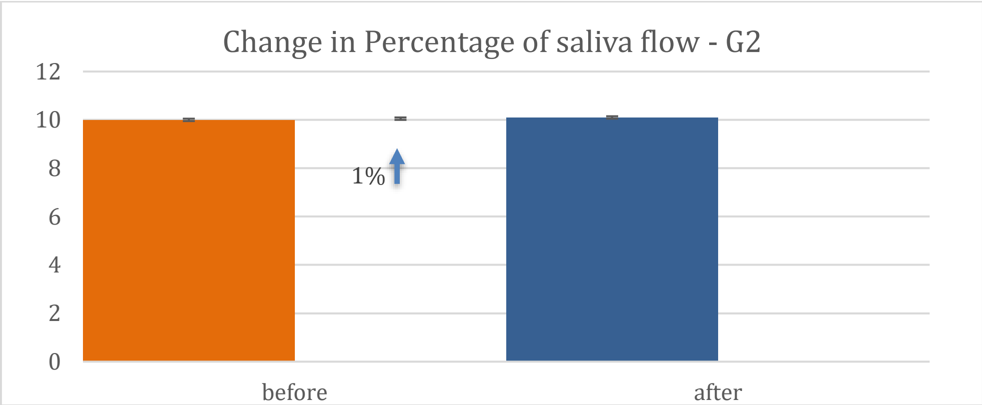

Fig. 2. Volume and variation of salivary flow after application of the extraoral and intraoral infrared laser-G2
statistically significant, p>0.05, Wilcoxon test

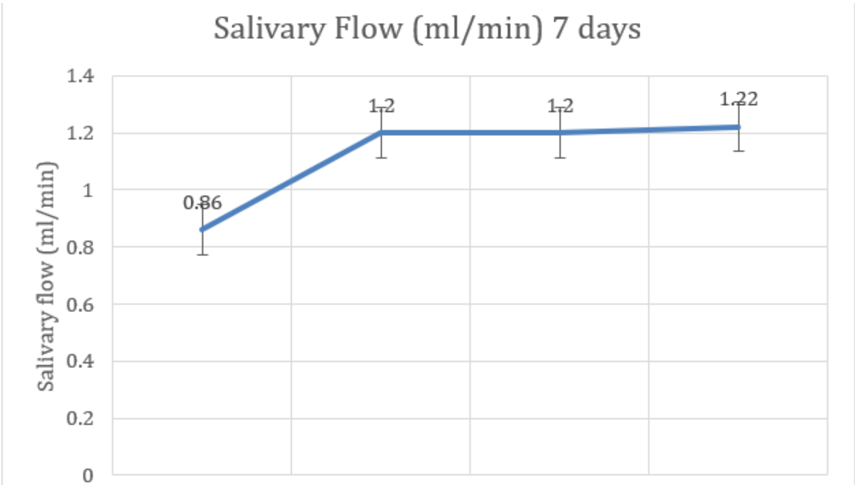

Fig. 3. Salivary flow (ml/min) in the four measurement moments

Table 2. Characteristics of the participants in relation to dental and medical history

When was your last visit to the dentist?	**6 months**	**1 year**	**More than a year**
	40% (n=8)	25% (n=5)	35% (n=7)
Do you regularly visit the dentist?	Yes 55% (n=11)	No 45% (n=9)	
Do you have any illness?	Yes 10% (n=2)	No 90% (n=18)	
Depression	Yes 10% (n=2)	No 90% (n=18)	
Are you undergoing radiotherapy or chemotherapy treatment?	Yes 0	No 100% (n=20)	
Do you have an eating disorder?	Yes 0	No 100% (n=20)	
Smoker?	Yes 30% (n=6)	No 70% (n=14)	

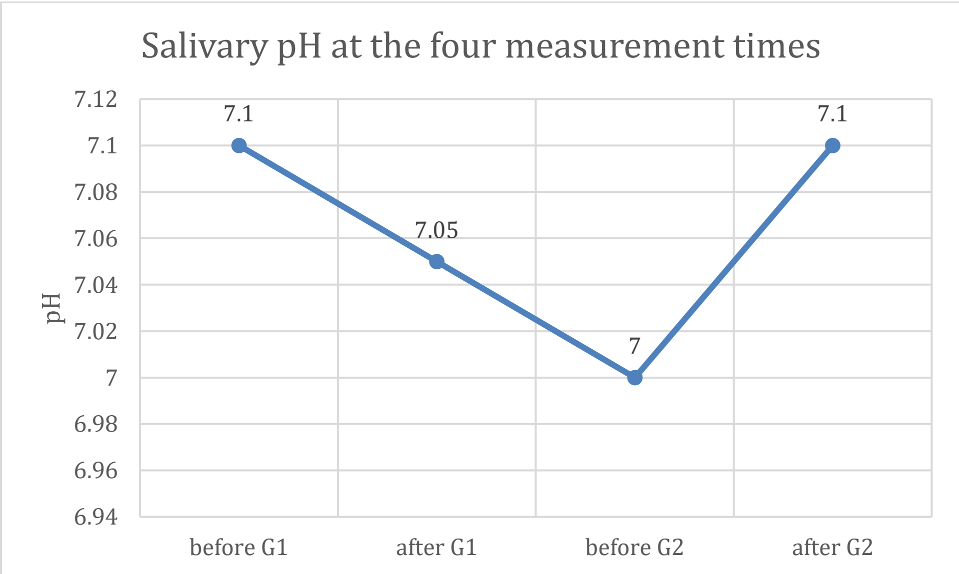

Fig. 4. Mean salivary pH at the four measurement times

4. DISCUSSION

Saliva is essential for oral health, serving critical functions in digestion, taste perception, speech, and tooth protection (Biology & [5]; Kim et al., [9] Louzeiro et al., [17], Wang et al., [19], Yoshizawa et al., [3]. Disruptions in salivary parameters, such as reduced flow and pH fluctuations, can result in various oral health issues, including dry mucosa, altered taste sensation, difficulty swallowing, and ulcerations [17].

Phototherapy, employing diverse light sources like lasers and LED lights, has been increasingly used in dentistry to mitigate adverse effects of cancer treatment, alleviate pain, and stimulate salivary glands. Nonetheless, the effectiveness of phototherapy in increasing salivary flow and pH remains contentious in scientific discourse (Carroll et al., [11], Fidelix et al., [13]. While some studies indicate a post-therapy rise in salivary flow, others suggest negligible improvement.

Studies by Louzeiro et al. [17] evaluating the effects of photobiomodulation on salivary glands in patients undergoing head and neck radiotherapy, and those investigating the action of low-level laser in individuals with Sjogren's Syndrome, did not observe improvements in salivary parameters. However, considering that the salivary glands were compromised in these studies, the authors suggested that this condition may have influenced the outcomes [13].

The most common approach for applying photobiomodulation to the salivary glands is through the combined use of intraoral and extraoral techniques (Abueva, [20], Brzak et al., [14], Campos et al., [21], el Mobadder et al., [12], Freitas et al., [13].

However, often, the patient in need of stimulation of the salivary glands can also suffer from other discomforts that make mouth opening difficult, such as ulcers, dryness of the labial commissure and others. Therefore, the possibility of a technique that deposits energy in the region of the salivary glands with an extraoral technique, exclusively, can bring more comfort during the procedure.

The present study aimed to compare and evaluate two types of light application techniques in the salivary glands, being Group 1, performed only the extraoral application and group 2 intra and extraoral applications, in order to evaluate and compare the immediate effect. in pH and salivary flow in these two techniques.

The satisfactory salivary flow of stimulated saliva is 1.0 to 3.0 ml/min (Tenuovo, 1997). In the present study, we observed an average flow rate of 0.86 ml/min for the stimulated saliva of the group of participants before any intervention. The literature points as a reference for hyposalivation rates below 0.7 ml/min.

The study aimed to compare two light application techniques in salivary glands: Group 1 received only extraoral application, while Group 2 received intra and extraoral applications, evaluating their immediate effects on pH and salivary flow. Prior to any intervention, the average flow rate of stimulated saliva was 0.86 ml/min, below the reference range of 1.0 to 3.0 ml/min (Tenuovo, 1997). Both techniques resulted in increased salivary flow, aligning with findings by el Mobadder et al. (2019) and Brzak et al. [14], although using different parameters. Group 1 showed significant immediate and sustained increase in salivary flow for 7 days, suggesting the effectiveness of the extraoral-only technique.

The study's novelty lies in assessing the extraoral technique exclusively, contrasting with the conventional intra and extraoral approach. Despite no immediate data available, the sustained increase in salivary flow aligns with literature findings, indicating the potential long-term effects of photobiomodulation. While Group 2 did not exhibit a significant increase, the methodology did not allow verification if this was due to the sustained effect of the initial application. Thus, it remains uncertain if the more commonly used intra and extraoral technique has a less significant effect than the extraoral-only approach.

Regarding salivary pH, no immediate effects were observed in either group, likely due to participants' neutral baseline pH. However, it's speculated that photobiomodulation may enhance buffering activity in compromised homeostasis, as observed in patients undergoing radiotherapy [17], despite not being evident in this study due to unaltered salivary gland conditions.

The infrared laser, applied extraorally with specific parameters, significantly activated salivary glands, surpassing the efficacy of conventional intrabuccal-associated application. However, due to variations in protocols, further clinical studies with larger samples and long-term follow-up are warranted to establish optimal photobiomodulation protocols. Immediate assessment studies across different groups may contribute to understanding long-term pH maintenance in both extraoral-only and conventional techniques. Overall, existing literature and this research support the positive effects of photobiomodulation on salivary parameters, advocating for the development of faster, more comfortable, and effective protocols through continued clinical research.

5. CONCLUSION

In this study, we compared two photobiomodulation application techniques to stimulate salivary glands and evaluated their effects on salivary flow and pH. One technique involved only extraoral application, while the other, a more conventional approach, included both intra and extraoral application, with identical parameters of wavelength and total energy.

Our findings indicate that both techniques effectively increased salivary flow, with the headgear-only technique yielding superior results. Interestingly, there were no significant changes observed in salivary pH for either group. Moreover, the extraoral technique demonstrated the ability to maintain satisfactory salivary flow for at least 7 days following treatment.

DISCLAIMER

This paper is an extended version of a preprint document of the same author.

The preprint document is available in this link: https://assets.researchsquare.com/files/rs-3253886/v1/62d564c4-da93-43cc-8830-3e31938b029f.pdf?c=1698167247 [As per journal policy, preprint article can be published as a journal article, provided it is not published in any other journal]

HIGHLIGHTS

- Salivary variations, such as decreased flow can lead to changes in oral health.
- Photobiomodulation as an adjuvant in salivary treatment.
- Extraoral application of laser light promotes salivary stimulation.

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CONSENT

As per international standards or university standards, Participants' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

This study was approved by the Ethics and Research Committee of our institution under protocol number 5.305.375.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Fleming M, Craigs CL, Bennett MI. Palliative care assessment of dry mouth: what matters most to patients with advanced disease? Supportive Care in Cancer 2020;28:1121–9. Available:https://doi.org/10.1007/S00520-019-04908-9.
2. Graphics Inc P. Saliva composition and functions: A comprehensive review. Oralpathol Dlearn Kmu Edu Tw; 2008.
3. Yoshizawa JM, Schafer CA, Schafer JJ, Farrell JJ, Paster BJ, Wong DTW. Salivary biomarkers: Toward future clinical and diagnostic utilities. Clin Microbiol Rev. 2013;26:781–91. Available:https://doi.org/10.1128/CMR.00021-13.
4. Pyati S, Kumar RN, … VK-J of C, 2018 undefined. Salivary flow rate, pH, buffering capacity, total protein, oxidative stress and antioxidant capacity in children with and without dental caries. MeridianAllenpressCom n.d.
5. Biology GP-A of O, 2018 undefined. Diurnal rhythm and salivary electrolyte. KclpureKclAcUk ;2018. Available:https://doi.org/10.1016/j.archoralbio.2018.05.001.
6. Freitas L de, in MH-IJ of selected topics, undefined. Proposed mechanisms of photobiomodulation or low-level light therapy. IeeexploreIeeeOrg n.d; 2016.
7. Huang YY, Chen ACH, Carroll JD, Hamblin MR. Biphasic dose response in low level lighttherapy. Dose-Response. 2009;7:358–83. Available:https://doi.org/10.2203/DOSE-RESPONSE.09-027.HAMBLIN.
8. Zecha JAEM, Raber-Durlacher JE, Nair RG, Epstein JB, Sonis ST, Elad S, et al. Low level laser therapy/photobiomodulation in the management of side effects of chemoradiation therapy in head and neck cancer: Part 1: mechanisms of action, dosimetric, and safety considerations. Supportive Care in Cancer. 2016;24:2781–92. Available:https://doi.org/10.1007/S00520-016-3152-Z.
9. Kim JE, Woo YJ, Sohn KM, Jeong KH, Kang H. Wnt/β-catenin and ERK pathway activation: A possible mechanism of photobiomodulation therapy with light-emitting diodes that regulate the proliferation of human outer root sheath cells. Lasers Surg Med. 2017;49:940–7. Available:https://doi.org/10.1002/LSM.22736.
10. Kalhori KAM, Vahdatinia F, Jamalpour MR, Vescovi P, Fornaini C, Merigo E, et al. Photobiomodulation in Oral Medicine. Photobiomodul Photomed Laser Surg. 2019;37:837–61. Available:https://doi.org/10.1089/PHOTOB.2019.4706.
11. Carroll JD, Milward MR, Cooper PR, Hadis M, Palin WM. Developments in low level light therapy (LLLT) for dentistry. Dental Materials. 2014;30:465–75. Available:https://doi.org/10.1016/J.DENTAL.2014.02.006.

12. el Mobadder M, Farhat F, el Mobadder W, Nammour S. Photobiomodulation therapy in the treatment of oral mucositis, dysphagia, oral dryness, taste alteration, and burning mouth sensation due to cancer therapy: A case series. Int J Environ Res Public Health. 2019;16. Available:https://doi.org/10.3390/IJERPH16224505.
13. Fidelix T, Czapkowski A, Azjen S, Andriolo A, Neto PH, Trevisani V. Low-level laser therapy for xerostomia in primary Sjögren's syndrome: A randomized trial. Clin Rheumatol. 2018;37:729–36. Available:https://doi.org/10.1007/S10067-017-3898-9.
14. Brzak BL, Cigić L, Baričević M, Sabol I, Mravak-Stipetić M, Risović D. Different Protocols of Photobiomodulation Therapy of Hyposalivation. Photomed Laser Surg. 2018;36:78–82. Available:https://doi.org/10.1089/PHO.2017.4325.
15. Mravak-Stipetić M, Baričević M, Lonč B, Stipetic´, MM, Stipetic´, S, Barič M, et al. The effect of low-level laser therapy on salivary glands in patients with xerostomia. Liebert pub Com 2011;29: 171–5. Available:https://doi.org/10.1089/pho.2010.2792.
16. Nemeth L, Groselj M, Golez A, Arhar A, Frangez I, Cankar K. The impact of photobiomodulation of major salivary glands on caries risk. Lasers Med Sci. 2020;35:193–203. Available:https://doi.org/10.1007/S10103-019-02845-X.
17. Louzeiro G, Cherubini K, de F M of P and, undefined. flow and composition, xerostomia and quality of life of patients during head and neck radiotherapy in short term follow-up: A randomized controlled clinical trial. Elsevier n.d; 2020.
18. Marín C, Díaz-de-Valdés L, … CC-J of C, undefined. Interventions for the treatment of xerostomia: A randomized controlled clinical trial. NcbiNlmNihGov n.d; 2021.
19. Wang K, Zhou X, Li W, Biology LZ-A of O, undefined. Human salivary proteins and their peptidomimetics: Values of function, early diagnosis, and therapeutic potential in combating dental caries. Elsevier n.d; 2019.
20. Abueva CDG. Photobiomodulation Therapy in the Treatment of Salivary Dysfunction. Medical Lasers. 2022;11:15–20. Available:https://doi.org/10.25289/ML.2022.11.1.15.
21. Campos L, Nesadal De Souza D, de Freitas PM, Simõ A, Campos L de, Alencar De Matos J, et al. Laser phototherapy as topical prophylaxis against radiation-induced xerostomia. Liebert pub Com. 2010;28:357–63. Available:https://doi.org/10.1089/pho.2009.2486.

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