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Evaluation of the Efficiency of Curcumin, Pomegranate Extract, and Photobiomodulation in the Management of Oral Lichen Planus

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Abstract:

Objective: This study evaluated the efficiency of pomegranate extract, curcumin medicaments, and photobiomodulation in the treatment of oral lichen planus (OLP).

Material and Methods: A total of 33 patients with OLP were arbitrarily divided into one of 3 treatment groups: Group I was given pomegranate extract, Group II was given curcumin (turmeric), and Group III was given photobiomodulation/ Photodynamic Therapy (PDT). For six months, all patients were instructed to apply the specific topical medication topically

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four times a day. After receiving the medication, patients were prohibited from eating or drinking for at least an hour. Clinical measurements of the health impact profile (patients' pain, lesion size, and oral health impact profile (OHIP)-14 score) were taken at baseline, three months, and six months. The data gathered were evaluated statistically.

Result: Between baseline and three to six months following therapy, there was a reduction in the sign score, pain score, OHIP-14 score, and lesion size in all the examined groups. There was improvement in symptoms for Group III, followed by Groups I and II, which was statistically significant. In all three groups, there was a statistically significant decrease in the Modified Oral Mucositis (MOMI) Index and Numerical Rating Scale (NRS) score from baseline to three and six months following treatment.

Conclusion: According to the current study, PDT and herbal remedies significantly reduce OLP symptoms, making them viable alternatives to corticosteroid treatment for OLP management.

Keywords: curcumin, efficacy, management, oral lichen planus, photobiomodulation, pomegranate extract

Introduction

Oral potentially malignant disorders (OPMDs) are caused by the consumption of tobacco-related products. OPMD has the risk of developing into a malignant transformation. Oral submucous fibrosis, oral leukoplakia, and oral lichen planus (OLP) are the three most common OPMDs[1]. OLP is a chronic mucocutaneous inflammatory, T cell-mediated illness that can affect the skin, mucous membranes, and oral mucosa[2]. It has been reported that between 0.1 and 4% of people globally suffer from OLP[3]. There is a disruption of the basal cell layer of the epithelium and the subepithelial invasion of T-cytotoxic and T-helper lymphocytes[4]. An antigen-specific cell-mediated immune reaction is the main cause of OLP[5].

OLP can present as either an asymptomatic or symptomatic type[5]. Atrophic ulcerative type, reticular, papular, bullous, erosive, and plaque-like lesions are among the six clinical forms of OLP lesions[6]. Since white keratotic forms are asymptomatic, they don't need to be treated. Conversely, red sores are painful, burning, and require medical attention. The WHO states that atrophic ulcerative (red sores) can progress to squamous cell carcinoma, a potentially malignant condition[7].

While OLP is usually found bilaterally and symmetrically on the buccal mucosa, it is less common on the tongue, gingival tissue, and lip mucosa[6]. Usually, patients complain of a burning pain that makes it difficult to eat, talk, and practise proper oral hygiene[8].

In order to treat OLP, clinicians employ a range of therapeutic approaches administered both topically and systemically. Reducing discomfort and mucosal ulceration is the main objective of current therapeutic strategies[3]. Corticosteroids are typically given intralesionally or systemically[9]. However, prolonged use of these medications has been related to a number of undesirable side effects, together with secondary candidiasis, elevated blood pressure, adrenal suppression, mucosal tissue atrophy associated with pain, and a high chance of recurrence[5,10]. The documented negative effects of corticosteroids have led to the suggestion of many natural plant extracts (aloe vera, chamomile, pomogranite, turmeric, and tulsi), as well as alternative techniques, such as photomodulation, lycopene usage, and alopethic medications[3,11,12].

Curcumin, an ingredient in turmeric, has anti-inflammatory, antioxidant, and antineoplastic effects[12]. Punica granatum L., a member of the Punicaceae family, is generally known as "pomegranate" and is used as a plant extract for a variety of medicinal ailments. It possesses immunomodulatory, antimicrobial, antifungal, anti-inflammatory, antioxidant, and anti-carcinogenic properties[3]. Pomegranate tannin complexes are frequently used to treat wounds and speed their healing because of their astringent qualities[13]. Miller, also known as Barbadensis aloe vera, is a cactus-like plant that is a member of the Liliaceae family. Aloe vera reduces inflammation. It aids in reducing OLP symptoms[14].

Photobiomodulation/Photodynamic Therapy (PDT) is a unique strategy in controlling OLP. This non-invasive method uses a photosensitizer (PS) to create photochemical and photobiological effects that promote cell destruction at the site of injury[15]. It is a simple and safe therapeutic method that causes damage to cells and tissue by exposing the photosensitizer to low-level visible light at the right wavelength[16,17].

The effects of PDT on oral lesions have not been well studied. Hence, in order to assess the topical effects of photobiomodulation, curcumin, and pomegranate extract in the treatment of OLP, this cross-sectional study was conducted.

Material and Methods

Aim and research questions

This research was conducted to assess the topical effects of photobiomodulation, curcumin, and pomegranate extract in the treatment of OLP.

Sample size calculation

Sample size was calculated using formula; $n=2(Z_{\alpha}+Z_{1-\beta})^2\sigma^2/\Delta^2$, where n is the sample size per group, Z_{α} and $Z_{1-\beta}$ Zα are constants from statistical tables (e.g., 1.96 for α=0.05 alpha equals 0.05 α=0.05 two-sided, 0.842 for 80% power), σ^2 sigma is the variance, Δ is the effect size (difference in means). Thus, for the 3 groups, a total of 30 samples was required, and we collected 33 samples.

Study design

This cross-sectional research was conducted in the Oral Medicine Department after attaining approval from the concerned authority with Ref No. KIIT/KIMS/IEC/716/2022 and written permission from the participants.

Inclusion and exclusion criteria

Both male and female patients (aged 18 to 55) diagnosed clinically and histopathologically as OLP cases were included in the study. Participants with systemic disorders, smokers, lactating mothers, patients on systemic or topical steroids, and those receiving systemic medicine were excluded from the study.

Data collection

A total of 33 patients with a diagnosis of OLP were included in the study from the Outpatient Department of Oral Medicine.

Methodology

A total of 33 participants were randomly assigned by computer-generated sheet into one of three therapy groups, each consisting of 11participants: Group I – pomegranate extract, Group II – curcumin, and Group III – photobiomodulation. For six months, all patients were instructed to apply the specific topical medication topically four times a day. After the medication was administered, patients were prohibited from eating or drinking for at least an hour. If any undesirable side effects developed, the participants were told to cease the medication immediately and get in touch with the researchers. The patients were

advised to utilize only the recommended treatment for their lesions. Patients were clinically evaluated and lesions were assessed and scored at baseline and after 1, 3 and 6 months, according to the Thongprasom score 5-0 (0: no lesion, normal mucosa; 1: mild white striae, no erythematous area; 2: white striae with atrophic area <1 cm^2; 3: white striae with atrophic area ≥1 cm^2; 4: white striae with erosive area <1 cm^2; 5: white striae with erosive area ≥1 cm^2)[18]. The study was done by a trained investigator.

Discomfort in each of the three groups was measured using a visual analogue scale (VAS) score ranging from 0 to 10, where 0 indicates no discomfort and 10 indicates excruciating pain. According to a study by Zakaria et al., Thongprasom et al., and Thomas et al.[3,12,8], the Modified Oral Mucositis (MOMI) Index, pain score, sign score, and oral health impact profile-14 (OHIP-14) score were assessed at baseline, and after three and six months. The MOMI and numerical rating score (NRS) were utilised to assess the signs (erythema and ulceration) and symptoms (burning).

Topical herbal medicament preparation

The seeds and peel of the pomegranate were separated. The peel and a little amount of water were combined in a mixer, filtered through Whamman no. 1 filter paper, and then evaporated in a distillation flask in a rotary evaporator set at 55.0 C to create a dry powder. After that, it was heated to a third of its original volume while the pressure was lowered until it ran out. For the seeds, the same process was used, but no water droplets were introduced. Both were individually made in gel form for topical treatment on the OLP lesions orally at a concentration of 4% after carboxymethylcellulose sodium salt was added[3].

The turmeric (Curcuma longa) was used as a commercial product, Snec G Self Nano Emulsifying Curcumin Oral Gel (10 gm) (Arbro Pharmaceuticals Pvt Ltd, India). Patients were asked to apply this gel 2 times daily for 6 months.

Photobiomodulation

A previously dried OLP mucosal lesion was treated with HELBO® Blue Photosensitizer* and allowed to sit for three minutes. Following a thorough rinse with sterile saline solution, a low-level laser (HELBO® TheraLite Laser, Bredent® Medical GmbH&Co.KG, Senden, Germany) was used to irradiate the lesion for 30 seconds per spot (active surface of the spot 19 mm^2) at an emission of 660 nm and an output power of 200 mW/cm^2.

Statistical evaluation

The recorded findings were statistically assessed with SPSS statistical software version 22.0 using the ANOVA test at p-value<0.05.

Results

The OHIP-14 score, sign score, and pain score decreased from baseline to three to six months following treatment. Group III showed improvement, which was statistically significant and followed by Group I and II (Table 1). From baseline to three and six months of follow-up, the lesion size decreased in all groups, although the variation among the groups was not statistically significant (Table 2). In all three groups, there was a statistically significant drop in the NRS score and MOMI Index from baseline to three and six months following treatment (Table 3).

Discussion

OLP is a chronic inflammatory condition of the mucous membranes that is very unpleasant and occurs frequently[16]. Ulcerative or erosive mucosa and desquamative gingivae with interlacing diffuse white striations are symptoms of OLP[18,19].

Table 1 Correlation of OHIP-14, sign score, and pain score among groups at various points in time

Groups	Sign score			Pain score (VAS)			OHIP-14		
	Baseline	3 months	6 months	Baseline (Mean±S.D.)	3 months	6 months (Mean±S.D.)	Baseline (Mean±S.D.)	3 months	6 months (Mean±S.D.)
Group I	2.61±0.31	2.10±0.24	1.30±0.28	5.73±1.27	2.53±1.45	0.71±0.61	14.42±1.11	7.35±1.14	2.62±0.32
Group II	2.69±0.27	2.32±0.22	1.42±0.25	5.81±1.28	3.67±1.38	1.53±0.57	14.52±1.12	10.64±1.17	4.70±0.54
Group III	2.65±0.30	2.12±0.28	1.17±0.30	5.51±0.23	2.61±0.27	0.41±0.41	14.21±1.12	6.89±1.16	2.43±0.30
p	0.857	0.854	0.001*	0.736	0.864	<0.001*	0.336	0.001	<0.001*

*significant

Table 2 Association for lesion size

Groups	Baseline	3 months	6 months	p-value
Group I	2.12	1.33	0.00	0.001*
Group II	2.16	1.72	0.00	0.001*
Group III	2.21	1.20	0.00	0.001*
p-value	0.757	0.357	0.759	

*Significant

Table 3 Comparison of the groups' MOMI Index and NRS scores

Groups	Group I	Group II	Group III
NRS score (Mean±S.D.)			
Baseline	5.11±0.51	5.12±0.31	5.13±0.70
3 months	2.17±0.54	4.18±0.36	2.18±0.75
6 months	1.36±1.11	2.25±1.21	1.12±1.30
% Change	62.3	51.3	74.2
p-value	<0.001	0.032	0.001
MOMI score (Mean±S.D.)			
Baseline	10.57	10.68	10.57
3 months	6.52	8.63	6.52
6 months	4.64	5.62	4.33
% Change	57.1	51.4	63.3
p-value	<0.001*	<0.001*	<0.001*

*Significant, NRS=Numeric Pain Rating Scale, MOMI score=Modified Oral Mucositis Index, S.D.=standard deviation

The VAS and NRS scores were used in this study to measure pain in OLP. The Modified Oral Mucositis (MOMI) Index and the Oral Health Impact Profile-14 (OHIP-14) score were used to evaluate the signs, symptoms, and burning sensation. Between baseline and three to six months following topical medication application and photobiomodulation, we observed improvements in sign score, pain score, and lesion size in all tested groups. In contrast to the other two groups, photobiomodulation was successful. There were no reported studies on the comparison of photobiomodulation with herbal medicaments

in the management of the symptoms of OLP. This research helps to choose the alternative treatment modalities for the management of OLP over corticosteroids. Atrophic ulcerative OPL is evaluated in the present study since this variety has a higher risk for malignant transformation.

Shivu et al. assessed the effectiveness of ashwagandha, turmeric, and aloe vera in treating OLP lesions. They claimed that for the treatment of OLP, aloe vera, ashwagandha, and turmeric can be beneficial substitutes for topical medications[5]. Aloe vera (AV) shows promising results, especially when compared to the many adverse effects of corticosteroids, according to a meta-analysis study by Ali et al.[20]. According to Choonhakarn et al., AV gel is statistically more successful than a placebo at improving OLP symptoms and clinical outcomes[21].

When Zakaria et al. compared the efficacy of topical pomegranate extract gel and topical steroid gel in treating atrophic OLP, they found that both groups significantly reduced their sign, pain scores, and OHIP-14 values[3]. Topical P. granatum extract gel can be used as an alternative treatment because Mahapatra et al. found that it is just as efficient at reducing OLP symptoms as topical corticosteroids[22].

Amirchaghmaghi et al. concluded that curcumin had no noticeable outcome in the treatment of OLP[14]. Moayeri et al. concluded in a systematic review that curcumin had no considerable benefit in the management of OLP symptoms compared to the control groups[23]. Similarly, we found lower benefits of curcumin compared to other groups in the treatment of OLP. While Khaitan et al. concluded that turmeric's active component, curcumin, is used commercially as a gel to treat various oral diseases and is quite successful in lessening the symptoms of OLP[24].

In their retrospective review, Nammour et al. found that PDT/PBM is useful for managing OLP and is substantially comparable to topical corticosteroids without the need for a prescription and without any known side effects[25]. PDT is a useful therapeutic approach for treating OLP, per the systematic study by He et al.[15]. In a systematic review and meta-analysis, Mahuli et al. discovered that PBM improved the clinical parameters of OLP when compared to topical corticosteroids[26]. As an alternate, easy, secure, and noninvasive treatment for OLP, Cosgarea et al. looked into the clinical and immunological effectiveness of PDT. According to the study, PDT is a special kind of treatment for OLP. After PDT treatment, the quantity of lesional T cells that produced IL-17a increased. In patients with OLP, PDT significantly reduces peripheral blood CD137+ and CD4+ T-cells[16].

The efficacy of a single laser photobiomodulation (PBM) session using a flat top handpiece in alleviating unpleasant symptoms in individuals with OLP was demonstrated by Roccon et al. They came to the conclusion that VAS pain considerably decreased over time with PBM (p-value<0.0001). For individuals with symptomatic OLP, a single laser PBM session may be both safe and successful in lowering pain[27].

Surgery to remove the lesion is not the main treatment option for lichen planus because it is an inflammatory disorder that may recur[28]. For erosive OLP that is unresponsive to previous treatment options, laser ablation with carbon dioxide and cryosurgery are being investigated. The size of OLP lesions was considerably reduced after PDT sessions. For the treatment of OLP, herbal medicine is regarded as an alternate monotherapy or as a supplement to first-line medications. We found a reduction of symptoms with herbal and photobiomodulation treatment. Therefore, using herbal medications to treat OLP can improve the effectiveness while lowering side effects.

Limitation of the study

Study limitations include a small sample size and restricted geographic area.

Future prospects

Early therapeutic intervention can prevent malignant transformation. Our findings support the use of complementary and alternative therapies, such as PDT and herbal remedies, for the successful treatment of OLP.

Conclusion

Numerous studies have demonstrated the effectiveness of several herbal extracts, including turmeric, pomegranate extract, ashwagandha, and aloe vera, in the treatment of OLP. According to the current study, photobiomodulation and herbal remedies significantly reduce the clinical symptoms of OLP, making them viable alternatives to corticosteroid treatment for OLP management.

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Conflict of interest

There are no conflicts of interest.

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