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Review Article

Current Treatment Options of Oral Lichen Planus: A Narrative Review

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Abstract

This review evaluates the main intervention used in managing Oral Lichen Planus (OLP) and the effectiveness of various treatment types. The search, conducted using electronic databases like PubMed, Embase, and DOAJ, aimed to identify articles on oral lichen planus, treatment, and randomized controlled trials from 2015 to 2021.

This review examines 45 randomized controlled trials, revealing steroids as the most commonly used drug for OLP treatment, along with calcineurin inhibitors and photo-dynamic therapy, showing efficacy and safety.

Topical steroids are the primary treatment for symptomatic OLP, but various pharmacological and non-pharmacological therapies are now under investigation for effective management.

Keywords: Calcineurin inhibitor, corticosteroids, curcumin, hyaluronic acid, oral lichen planus, treatment, triamcinolone, retinoids, photo-dynamic therapy, laser therapy

Introduction

Oral lichen planus (OLP) is an immune-mediated inflammatory chronic disease that involves the oral mucosal epithelium [1]. OLP is found in 0.2–2% of the population [2]. OLP can appear at any age, but is more common in females in their fourth to seventh decade and in males at an earlier age [3]. OLP is caused by the autoimmune activation of CD8+ T lymphocytes, which results in the death of epithelial basal cells [4].

The clinical manifestations of OLP have been widely characterized, with the following types of OLP being emphasized: papular, reticular, atrophic, blistering, erosive, and plaque [5]. The buccal mucosa and the dorsal aspect of the tongue are the most susceptible areas for OLP lesions [6]. A histopathology examination confirms the diagnosis, revealing sub-basal inflammatory infiltration, hydropic degeneration of the basal layer, and the absence of dysplasia [5]. These lesions can cause burning discomfort and compromise the patients' ability to speak, eat, and drink, lowering their living standard [7, 8].

Biopsy specimens should be assessed for early dysplasia or squamous cell carcinoma in the case of persistent lesions, regardless of treatment [3]. The goal of treating OLP is to reduce symptoms and the appearance of lesions, which are characterized by periods of aggravation and quiescence. Topical corticosteroids are the first-line medication,

but additional effective medications, such as photodynamic therapy (PDT) and the application of topical calcineurin inhibitors (TCI), have recently become effective [9].

The purpose of this review paper is to explore recent studies on treatment alternatives for OLP patients, which are intended to facilitate any practitioner involved in treating these modalities and their associated benefits and drawbacks.

Search methodology

The search was conducted utilizing electronic databases such as PubMed (Medline), Embase, and DOAJ. From January 1, 2015, to November 30, 2021, the initial search includes the terms "oral lichen planus", "treatment", and "randomized controlled trials". We included only articles that were based on prospective randomized controlled trials (RCTs). Topical interventions, oral medicines, herbal medications, biological products, laser therapy, photobiomodulation, ozone therapy, and photodynamic therapy (PDT) were all considered in this study. RCTs of surgical treatment, asymptomatic, and histologically unconfirmed patients were all excluded from this review. Non-randomized studies, observational studies, experimental studies, case series, case reports, review papers, and in-vitro studies were all omitted. We didn't also include articles that weren't written in English. To avoid duplication, articles were first sorted by title and author. The abstract was used to choose papers that were likely to be relevant. The papers that fulfilled the eligibility requirements were reviewed entirely after this final assessment was completed.

Results

Initially, the database scan yielded a total of 347 articles. The following is the number of papers from the various databases: 67 in PubMed (Medline), 86 in Embase, and 194 in DOAJ. After the removal of duplication, 288 articles remained. After reading the abstracts of these papers, 101 full-text articles were considered to be relevant. For this review, 78 full-text papers were found, with 45 RCTs being included [10–54]. For various reasons, the remaining 33 articles were omitted. The primary features of the studies included in this review are listed in Table 1.

These studies were conducted in different countries: India [13, 16, 20, 25, 27, 28, 40, 42, 50, 53], Turkey [43], Egypt [11, 15, 19, 36, 38, 44, 45], Iran [10, 14, 17, 18, 29, 35, 47-49, 51, 52], Italy [21, 22, 34, 46], Spain [54], Iraq [32], Sri Lanka [33], Saudi Arabia [37], Pakistan [24, 30], Croatia [41], France [26], Poland [39], Finland [31], and the USA [23]. All 45 studies were RCTs, with 43 being parallel group studies and two [14, 43] being split-mouth design trials.

Steroids were mostly employed as an active intervention in 31 RCTs. [10-12, 14-24, 26, 28-31, 35-43, 48, 50, 52] Triamcinolone was used in 21 studies [10-12, 14-20, 28-31, 36, 39, 40, 42, 45, 48, 50], clobetasol in four trials [20-22, 33], dexamethasone in three trials [23, 35, 37], prednisolone in four RCTs [24, 43, 52, 53], and betamethasone in two trials [26, 41].

In 10 RCTs, topical calcineurin inhibitors (TCI) were used. [20, 25, 27–34] Seven trials employed topical tacrolimus [20, 25, 27, 31–34], and four trials used topical pimecrolimus [27–30].

Other interventions included hyaluronic acid [12–14], curcuminoids [48–52], Bacillus Calmette-Guerin polysaccharide nucleic acid (BCG-PSN) [15], retinoic acid [18, 25], methotrexate [24], dapsone [25], rapamycin [26], selenium [19], hydroxyethyl cellulose gel [21], ozone therapy [45, 46], propolis [16], chamomile [54], PRP [42], and i-PRF [43]. Diode (either directly or photodynamically through the application of toluidine blue) and CO_2 lasers were employed in five RCTs. [35-39] Low-level laser therapy (LLLT) was used in two trials [37, 40].

Table 1: Features of included studies

Study (first author, year)	Intervention (n)	Additional treatment	Dose	Frequency of application	Clinical form of OLP	Recurrences (n)	Complete remission (n)	Treatment duration	Outcome variables
Azizi A, 2016 [10]	I, TA + nanoliposomal carriers (30); C, TA	Nystatin M/W (100,000 IU) once daily.	I, Topical orabase 0.1%; C, Topical orabase 0.1%	I, 3 times/day; C, 3 times/day	E	I, 0% (0); C, 0% (0)	I, 33.33% (20); C, 26.66% (16)	1m	Pain-burning sensation, and lesion size
Hesen R, 2017 [11]	I1, TA + GS (10); I2, TA + GS (10); C, TA (10).	No	Topical TA 0.1%, glucosamine sulfate oral capsule 500mg	I1, TA 4 times/day + GS 3 times/day; I2, TA 2 times/day + GS 3 times/day; C, TA 4times/day	AE	NR	NR	2m	Pain-burning sensation, Thongprasom clinical grading, and immunohistochemical analysis
Hashem A, 2018 [12]	I, HA (20); C, TA (20)	No	I, Oral gel 0.2%; C, Topical ointment 0.1%	I, 3 times/day; C, 3 times/day	AEM	I, 0% (0); C, 0% (0)	NR	4w	Pain, oral mucositis index, and size of erosive area
Shetty R, 2016 [13]	I, HA (25); C, Placebo (25)	No	I, Topical orabase 0.2%; C, Topical	I, 3 times/day; C, 3 times/day	AER	No	NR	2w	Pain, degree of erythema (modified oral mucositis index), and size of the lesions
Agha-Hosseini, 2021 [14]	I, HA + TA (17); C, TA (17)	No	1ml of itralesional injection/ $2cm^2$ surface area	NR	AER	I, 11.1% (2); C, 74.1% (13)	NR	NR	Pain, Thongprasom and Dhanuthai clinical grading
Metwalli M, 2018 [15]	I, TA (13); C, BCG-PSN (13)	No	I, Intralesional injections 0.2ml/1 cm intervals; C, Intralesional injections (0.5 ml)	I, Once□weekly; C, every other day	AER	I, 77.8% (7); C, 71.4% (5)	I, 38.5% (5); C, 38.5% (5)	2w	Pain and clinical assessment of OLP lesion.
Joshy A, 2018 [16]	I, Propolis (12); C, TA (15)	No	I, Topical paste 5%; C, Topical paste 0.1%	I, 3 times/ day; C, 3times/ day	A	NR	I, 91.67% (11); C, 100% (15)	15d	Pain, erythema and ulceration (modified oral mucositis index)
Sadeghian R, 2019 [17]	I, NT (20); C, TA (20)	No	I, Topical gel; C, Topical gel 0.1%	I, 4 times/day; C, 4 times/day	E	NR	I, 30% (6); C, 15.8% (3)	2w	Pain, Thongprasom clinical grading
Gholizadeh N, 2020 [18]	I, TA + retinoic acid (20); C, TA (20)	No	I, Oral paste (0.1% + 0. 05%); C, Oral paste 0.1%	I, 3 times/day; C, 3 times/day	AE	I, 10% (2); C, 15% (3)	I, 85% (17); C, 30% (6)	4w	Pain, Thongprasom clinical grading
Qataya P, 2020 [19]	I1, Selenium hydrogel (11); I2, Oral selenium (11); C, TA (11)	I1, No; I2, No; C, Miconazole oral gel 2% twice daily	I1, Oral gel; I2, Capsule 200 µg; C, Oral gel 0.1%	I1, 2 times/day;I 2, 2 times/day; C, 3-4 times/day	E	I1, 0% (0); I2, 9.09% (1); C, 9.09% (1)	NR	6w	Pain, Thongprasom clinical grading, and salivary MDA and TAC level
Sivaraman S, 2016 [20]	I1, TA (10); I2, Clobetasol propionate	No	I1, Topical orabase 0.1%; I2, Topical	I1, 4 times/day; I2, 4 times/day;	RE	NR	I1, 70% (7); I2, 100%	6w	Thongprasom clinical grading

	(10); I3, Tacrolimus (10)		orabase0.05 %; I3, Topical orabase 0.03%	I3, 4 times/day			(10); I3, 30% (3)		
Arduino, 2018 [21]	I, Clobetasol propionate + HCG (16); C, HCG 4% (16).	Miconazole gel once daily and chlorhexidine M/W (0.12%) twice daily	I, Topical gel 0.05%; C, Topical gel 4%	2 times/ day	AE	I, 37.5% (6); C, 50% (8)	I, 62.5% (10); C, 50% (8)	8w	Pain and burning sensation, Thongprasom clinical grading
Santonocito S, 2020 [22]	I1, Clobetasol propionate 0.05% (18); I2, Anti-inflammatory$^{\Omega}$ M/W (20)	No	I1, Oral gel 0.05%; I2, 20 mL oral M/W	I1, 2 times/day; I2, 3times/day for 5 min	AE	NR	I1, 72% (13); I2, 30% (6)	12w	Pain, Thongprasom clinical grading
Villa A, 2020 [23]	I, Dexamethasone + Mucolox (12); C, Dexamethasone (12)	Tablet fluconazole 200mg once a week or nystatin suspension 4 times daily	5 mL dexamethasone (0.1 mg/mL) solution	I, 3 times/day; C, 3 times/day	E	NR	NR	4w	Clinical assessment (REU score), subjective assessment of patients (COMDQ-26 items)
Saeed T, 2021 [24]	I, Methotrexate (30); C, Prednisolone (30)	I, Folic acid 1mg/day; C, Nystatin	I, Oral tablet 15 mg; C, Oral tablet 50 mg	I, Once daily; C, Once daily	AERP	NR	I, 73.3% (22); C, 60% (18)	8w	Assessment of frequency of complete resolution of mucosal lesions
Singh A, 2016 [25]	I1, Dapsone (10); I2, Tacrolimus (10); I3, Retinoid (10); C, TA (10)	I1, Iron with folic acid tablet.	I1, Oral tablet 100mg; I2, Topical paste 0.1%; I3, Topical; C, Topical paste 0.1%	I1, 2times/day; I2, 2times/day I3; 2times/day; C, 2times/day	AERP	I1, (0); I2, (3); I3, (1); C, (1)	I1, 50% (5); I2, 20% (2); I3, 0% (0); C, 20% (2)	3m	Pain, Thongprasom clinical grading, OLP severity score
Samimi M, 2020 [26]	I, Rapamycin (39); C, Betamethasone dipropionate (36)	No	I, Oral solution 1 mg/mL; C, Topical ointment 0.05%	I, 2 times/day; C, 2 times/day	E	I, 77.8% (7); C, 84.% (11)	I, 23.34% (7); C, 25% (8)	3m	Pain, clinical remission, adverse reaction,andhaematological assessment of rapamycin level
Vohra S, 2015 [27]	I1, Pimecrolimus (20); C, Tacrolimus (20)	No	I1, Topical cream 1%; I2, Topical ointment 0.1%	I1, 2times/day; I2, 2times/day	RE	NR	NR	8w	Clinical (net clinical score) and serological assessment (serum IL-6 and IL-8)
Arunkumar S, 2015 [28]	I, Pimecrolimus (15); C, TA (15)	No	I, Topical paste 1%; C, Topical cream 0.1%	I, 4 times/day; C, 4 times/day	NR	I, 6.7% (1); C, 33.3% (5)	I, 100% (15); C, 100% (15)	2m	Pain and burning sensation, Thongprasom clinical grading
Pakfetrat A, 2015 [29]	I, Pimecrolimus (14); C, TA (14)	30 drops of nystatin (100,000 units) M/W for 5 minutes in both groups.	I, Topical cream 1%; C, Topical paste 0.1%	I, 3 times/ day; C, 3 times/ day	AE	NR	I, 85.7% (10); C, 71.4% (12)	2m	Pain, Thongprasom clinical grading
Riaz H, 2017 [30]	I, Pimecrolimus (18); C, TA (18)	Chlorhexidine M/W used every nights before sleeping.	I, Topical cream 1%; C, Topical paste 0.1%	I, 4 times/day; C, 3 times/day	AER	NR	NR	2m	Pain, Thongprasom clinical grading, and oral health impact profile score

Siponen M, 2017 [31]	I1, Tacrolimus (11); I2, TA (7); C, Placebo (9)	No	I1, Topical ointment 0.1%; I2, Topical paste 0.1%; C, Topical paste	I1, 3times/day; I2, 3times/day; C, 3times/day	AERP	NR	NR	6w	Pain, lesion size
Mahdi K, 2019 [32]	I1, Tacrolimus (14); I2, Isotretinoin (14).	No	I1, Topical gel 1%; I2, Topical gel 0.1%	I1, 4 times/day; I2, 4 times/day	AE	NR	I1, 71.4% (10); I2, 35.7% (05)	8w	Pain, Thongprasom clinical grading
Hettiarachchi P, 2016 [33]	I, Tacrolimus (34); C, Clobetasol propionate (34)	Mouth rinse with 5 mL nystatin suspension (100 000 units/ mL) twice daily for 3weeks	I, Topical cream 0.1%; C, Topical cream 0.05%	I, 2 times/day; C, 2 times/day	NR	NR	I, 61.76% (21); C, 52.94% (18)	3w	Pain, Thongprasom clinical grading
Polizzi A, 2021 [34]	I1, Tacrolimus (19); I2, Anti-inflammatory Ω M/W (19)	No	I1, Topical ointment 0.1%; I2, 10-20 mL M/W	I1, 2 times/day; I2, 2 times/day for 5 min	AERP	NR	NR	12w	Pain, Thongprasom clinical grading, OLP severity score
Jajarm H, 2015 [35]	I, TB-PDT (11); C, Dexamethasone (14)	Control group took mouth rinse with 30 drops of nystatin (100,000 units) for 5 minutes 4 times daily.	C, 0.5mg/ 5 mL water M/W	I, TB (50 µl toluidine blue (1 mg/ml))-PDT (630-nm GaAlAs laser) 2session/week; C, 4 times/day	AE	I, 27.3% (3); C, 0% (0)	I, 100% (11); C, 100% (14)	1m	Pain, Thongprasom clinical grading, lesion size, severity of lesion and the efficacy indices of the improvement of lesions
Mostafa D, 2017 [36]	I, MB-PDT (10); C, TA (10)	I, Methylene blue 5% solution in water for 5 min	C, Topical orabase 0.1%	I, 1 time /week; C, 3 times/ day	E	NR	I, 37% (7); C, 21% (4)	2m	Pain, Thongprasom clinical grading
Mirza S, 2018 [37]	I1, TB-PDT (15); I2, LLLT (15); C, Dexamethasone M/W (15)	I1, Toluidine blue 50 µl (1 mg/ml); I2, no; C, 30 drops of nystatin (100,000 units) M/W for 5 min	I1, PDT; I2, LLLT; C, Dexamethasone (0.5 mg/5 ml water) M/W	I1, two sessions, two times/ week; I2, 10 sessions 2 times/ week; C, 5 minutes 4 times/ day	AE	No	I1, 81.4% (12); I2, 74.1% (11); C, 0% (0)	1m	Pain, Thongprasom clinical grading, and the efficacy indices of the improvement of lesions
Saleh W, 2020 [38]	I, MB-PDT (10); C, Betamethasone valerate (10)	No	I, Wavelength 660 nm, intensity 100−130 m W/cm^2; C, Topical ointment 100mg	I, 2times/week; C, 3times/day	E	NR	NR	4w	Pain, Thongprasom clinical grading, REU clinical score
Zborowski J, 2021 [39]	I, MB-PDT (30); C, TA (30)	No	I, Irradiated with diode laser; C, 0.05% cream	I, 4 session/2-3 days; C, once daily	E	NR	I, 54.2% (13); C, 62.% (17)	I, 4 session every 2-3 days; C, 9 days	Pain, Thongprasom clinical grading, treatment efficacy, oral health impact profile score, ABSIS score
Jain R, 2021 [40]	I, LLLT + TA (15); C, TA (15)	No	TA 0.1% orabase	I, 2 times/week for 9	AE	I, 11% (1); C, 66% (2)	I, 60% (9); C, 20% (3)	4w	Pain-burning sensation, size of the lesion, clinical

				session; C, 5 times/day					resolution and recurrence
Rogulj A, 2021 [41]	I, NAVS naphthalan (15); C, Betamethasone dipropionate (15)	No	I, Topical paste; C, Topical ointment 0.05%	I, 3 times/day; C, 3 times/day	AE	No	NR	4w	Pain, clinical improvement, and oral health impact profile score
Sethi Ahuja U, 2020 [42]	I, PRP (10); C, TA (10)	No	I, 0.5ml of itralesional injection/ 1cm^2 surface area; C, 0.5ml (10 mg/mL) of itralesional injection/ 1cm^2 surface area	Once weekly	E	I, 10% (1); C, 30% (3)	I, 90% (9); C, 70% (7)	2m	Pain-burning sensation, erythema, and lesion size
Saglam E, 2021 [43]	I, i-PRF (24); C, Methyl-prednisolone acetate (24)	No	I, Intralesional injection; C, Intralesional injection of 0.2 mL	I, 1 session/ 15 days; C, 1 injection / 15 days	E	NR	NR	45d	Pain, Thongprasom clinical grading, and oral health impact profile score
Fathy Samhan A, 2021 [44]	I, PBM + honey (23); C, PBM + Placebo (23)	Both groups used chlorhexidine M/W	PBM dose 4 J/cm2 for each spot area	Both groups received PBM 3session/week + topical substance 4 times/day	AE	NR	I, 52.2% (12); C, 0% (0)	4w	Pain, Thongprasom clinical grading, and oral function scores
Mostafa B, 2018 [45]	I1, Ozone (22); I2, Ozone + TA (22); C, TA (22)	No	I1, 60% gaseous ozone for 1 minute; I2, Topical gaseous ozone + topical ointment (TA) 0.1%; C, Topical ointment (TA) 0.1%	I1, 2 times/ week; I2, 2 times/ week C, 4 times/day	NR	NR	NR	4w	Pain, Thongprasom clinical grading
Veneri F, 2020 [46]	I, Ozonized water (26); C, Placebo (25)	Both groups received betamethasone 500mg soluble tablets as M/W, 2 times/day	I, Oral rinse; C, Oral rinse	I, 2 times/week ; C, 2 times/week	AE	I, 34.% (9); C, 40% (10)	I, 9.8% (5); C, 0 (0%)	4w	Pain, Thongprasom clinical grading, lesion size, and treatment efficacy
Amirchaghmaghi M, 2015 [47]	I, Quercetin hydrate (15); C, Placebo-lactose (15)	All patients received dexamethasone 0.5 mg M/W and nystatin suspension (100,000 unit) 4 times daily	I, Oral capsule 250 mg; C, Oral capsule	I, 2 times/ day; C, 2 times/ day	AE	NR	NR	4w	Pain, severity index, adverse reaction

Kia S, 2015 [48]	I, Curcumin (25); C, TA (25)	No	I, Topical paste 5%; C, Topical paste 0.1%	I, 3 times/day; C, 3 times/day	AE	NR	I, 36% (9); C, 32% (8)	4w	Pain, Thongprasom clinical grading
Amirchaghmaghi M, 2016 [49]	I, Curcuminoids 95% (12); C, Placebo (8).	Both groups received dexamethason M/W (0.5mg) + nystatin suspension (100,000 unit) thrice daily	I, Oral tablet 500mg	I, 2 times/ day; C, 2 times/day	AE	NR	I, 75% (9); C, 62.5% (5)	4w	Pain-burning sensation, Thongprasom clinical grading
Thomas A, 2017 [50]	I1, Curcuminoids (25); I2, Curcuminoids (25); C, TA (25)	No	I1, Oral gel 1%; I2, Oral gel 1%; C, Topical ointment 0.1%	I1, 3 times/day; I2, 6 times/day; C, 3 times/day	E	NR	NR	3m	Pain-burning sensation, modified oral mucositis index score
Bakhshi M, 2020 [51]	I, Nanocurcumin (14); C, placebo (17).	Triamcinolone 1% mouth rinse thrice daily	I, Topical gel 1%; C, Topical gel	I, 3 times/day; C, 3 times/day	E	NR	I, 0% (0); C, 0% (0)	1m	Clinical assessment lesion, and efficacy index
Kia S, 2020 [52]	I, Curcumin (29); C, Prednisolone (28)	No	I1, Capsule 80mg; C, Capsule e 10 mg	I, once daily; C, once daily	NR	NR	NR	1 m	Pain, Thongprasom clinical grading
Naik R, 2021 [53]	I, Curcumin (34); C, Curcumin + prednisone (34)	No	I, Oral gel; C, Oral paste consist of curcumin oral gel with crushed prednisone tablet	I, 3 times/day for 15 min; C, 3 times/day for 15 min	NR	NR	NR	20d	pain, clinical assessment of reticulation and erosion
Lopez Jornet, 2016 [54]	I, Chamaemelum nobile (26); C, Placebo (29)	No	I, 2% topical gel 0.5 mL; C, topical gel 0.5 mL	I, 3 times/day; C, 3 times/day	NR	NR	I, 19.2% (5); C, 0% (0)	4w	Pain and burning sensation, Thongprasom clinical grading, oral health impact profile, anxiety-depression, and treatment responses

A, atrophic; ABSIS, autoimmune bullous skin disorder intensity score; BCG-PSN, Bacillus Calmette-Guerin polysaccharide nucleic acid extract; C, control group; COMDQ, chronic oral mucosal diseases questionnaire; d, days; E, erosive; GS, glucosamine sulfate; HA, hyaluronic acid; HCG, hydroxyethyl cellulose gel; I, intervention group; IL-6, interleukin-6; IL-8, interleukin-8; i-PRF, injectable platelet-rich fibrin; K, keratosis; LLLT, low level laser therapy; M, mixed form of OLP; m, months; MB-PDT, photodynamic therapy mediated by methylene blue; MDA, malondialdehyde; mg, milligrams; M/W, mouth wash; n, number; NAVS, non-aromatic-very rich in steranes; NR, not reported; NT, nano-based triamcinolone acetonide gel; OLP, oral lichen planus; PBM, photobiomodulation; PDT, photodynamic therapy; Pl, plaque; PRP, platelet-rich plasma; R, reticular; REU, reticulation-erythema- ulceration/erosive scoring system; RCT, randomized clinical/controlled trial; TA, triamcinolone acetonide; TAC, salivary total antioxidant capacity; TB-PDT, toluidine blue-mediated photodynamic therapy; TGPC, total glucosides of paeony capsule; w, weeks.
Ω, Anti-inflammatory M/W consisted of calcium hydroxide (10%), hyaluronic acid (0.3%), umbelliferone and oligomeric pro-anthocyanidins (obtained from Pinus Pinaster).

Study outcomes

The key outcome in all of the trials considered in this review was pain and burning sensations. However, different pain metrics were employed in each of these trials. Pain was assessed as a primary outcome employing visual analogue scales (VAS) of various lengths in all studies, except seven RCTs [15, 16, 19, 22, 25, 32, 45]. A numerical rating scale (NRS) was utilized in five studies [15, 16, 19, 22, 32]. Singh *et al.* [25] assessed pain and burning sensations by employing the Raj *et al.*

[55] method. Raj *et al.* [55] described a five-point (0–5) point scale to assess the pain and burning sensation of OLP patients during taking their food. One study [45] measured pain according to the Garnick *et al.* grade of pain scale. Garnick *et al.* [56]used a five-point (0 = no symptoms, 1 = mild discomfort and capable of eating, 2 = moderate discomfort but still capable of eating, 3 = severe discomfort and unable to eat, 4 = tolerated pain and unable to eat) grading system to measure pain or discomfort during eating.

The Thongprasom scale was employed to evaluate the clinical recovery of the lesions (0 = no lesion, normal mucosa, 1 = mild white striae, no erythematous area, 2 = white striae with atrophic area less than 1cm², 3 = white striae with atrophic area more than 1cm², 4 = white striae with ulcerative or erosive area less than 1cm², 5 = white striae with ulcerative or erosive area more than 1cm²).

Almost all of the trials employed Carrozzo and Gandolfo [57] criteria for determining therapeutic efficiency, which split clinical effectiveness into three categories: complete remission, partial response, and no response.

A periodontal probe, a vernier caliper, or a calibrated tongue depressor was used in all of the trials to measure the size of the lesion.

Other study variables were the assessment of immunohistochemical markers [11] and the study of serum IL-6 and IL-8 levels [27]. The assessment of an enhancement in life quality following treatment utilizing the Oral Health Impact Profile (OHIP-14, a metric that measures the disease's impact on one's ability to function) [30, 39, 41, 43, 54], COMDQ-26 (chronic oral mucosal diseases questionnaire) items [23], ABSIS (autoimmune bullous skin disorder intensity score) score [39], modified oral mucositis index [13, 16], and the Hospital Anxiety-Depression Scale [54].

Discussion

Factors like extra-oral lesions, medical history, co-morbidities, and oral cavity idiosyncrasy influence OLP treatment duration. The treatment strategy focuses on pain control, lesions healing, and plaque reduction to reduce malignancy risk, based on clinical form criteria and prior experiences.

Glucocorticoids are commonly prescribed for OLP treatment, with effects varying among individuals and no evidence of superiority in effectiveness. There are a variety of corticosteroids that can be employed to treat OLP, but the most commonly prescribed are triamcinolone acetonide 0.1% [10-12, 16-18], clobetasol propionate 0.05% [20-22], betamethasone 0.05% [26, 41], and dexamethasone 0.05% [35, 37]. For both triamcinolone and clobetasol, the most commonly utilized forms were oral paste and gel, while dexamethasone was prescribed as an oral solution for mouthwash in the majority of these trials. The medication should always be applied after brushing and flossing, and the patient should not eat, drink, or smoke for half an hour after application [12, 20, 28]. Distinct trials have proposed different treatment procedures in terms of intervention duration (Table 1). In summary, most of the papers studied suggested a 4-week treatment period with 2-4 applications each day. Triamcinolone acetonide is an intermediate-acting glucocorticoid with a dosing regimen of 2–4 times per day and duration of 2 weeks to 6 months**.**

Calcineurin inhibitors are immunosuppressant drugs that block calcineurin. It is a calcium-dependent protein that inhibits the early activity of T cells and is involved in the immunological response [58]. Tacrolimus, pimecrolimus, and cyclosporine are among the medications in this class. In seven trials, tacrolimus was used [20, 25, 27, 31–34]. Pimecrolimus, on the other hand, was used in

four trials [27–30]. Tacrolimus and pimecrolimus, notably pimecrolimus, are well-tolerated medications in the treatment of OLP [28]. Burning mouth and altered taste sensation were the most common adverse effects observed with tacrolimus and pimecrolimus medication [27, 34]. The efficacy of a topical calcineurin inhibitor (tacrolimus or pimecrolimus) versus a topical steroid (clobetasol or triamcinolone) was studied in six RCTs: clobetasol and tacrolimus [20, 33], triamcinolone and tacrolimus [20, 31], and triamcinolone and pimecrolimus [28–30]. One study compared the efficacy of tacrolimus and pimecrolimus [27].

Sivaraman*et al.* [20] reported that steroids are notably more efficient than tacrolimus, while another study [31] showed no statistically considerable differences. Hettiarachchi *et al.* [33] concluded that tacrolimus was more effective than clobetasol. Both tacrolimus and pimecrolimus had been found to be effective in alleviating symptoms and lowering the clinical presentation of lesions; however, there were no statistically meaningful differences in effectiveness between the two medications [**27**]. Mahdi *et al.* [32] showed that tacrolimus is more efficient than topical isotretinoin in alleviating pain and swelling. Pakfetrat*et al.* [29] found no statistical significance between pimecrolimus cream and triamcinolone. Arunkumar*et al.* [28] showed that pimecrolimus cream exhibited statistically meaningful improvement in clinical score reduction when compared to triamcinolone. Riaz *et al.* [30] reported that pimecrolimus cream was found to be more effective than triamcinolone paste. Singh *et al.* [25] found that patients treated with dapsone, tacrolimus, or retinoid showed significant statistical clinical remission and concluded that these treatments were effective as steroidal therapy.

Photodynamic therapy (PDT) has recently been proposed as a new, side-effect-free treatment choice for erosive-atrophic OLP. Jajram*et al.* [35] assess the effects of local corticosteroids and toluidine blue-mediated photodynamic therapy (TB-PDT) for treating erosive-atrophic OLP. The study revealed that TB-PDT with laser was successful in treating OLP. According to Mirza *et al.* [37], PDT and LLLT are successful in treating adult patients with erosive-atrophic types of OLP. Mostafa *et al.* [36] used methylene blue-mediated diode laser therapy (MB-PDT) to treat erosive OLP, and they came to the conclusion that this method was superior to topical steroid therapy since it was considerably more effective at reducing pain and regressing lesions. Saleh *et al.* [38] also reported that MB-PDT performed better than topical corticosteroids in treating erosive OLP. PDT seems to be a fairly effective course of treatment for OLP. More RCTs should be performed to confirm the effectiveness of PDT in treating OLP.

The Zingiberaceae family plant, Curcuma longa, contains compounds called curcuminoids. Due to its anti-oxidant, anti-inflammatory, anti-carcinogenic, anti-microbial, anti-proliferative, and wound-healing qualities, it is a well-liked beneficial treatment choice [59]. When 0.1% triamcinolone acetonide is used in conjunction with 1% nanocurcumin, the extent of healing of the lesions can be increased in comparison to when triamcinolone acetonide is used independently. [51] Because of its advantageous anti-inflammatory benefits and negligible adverse effects, Kia *et al.* [52] reported using curcumin for the treatment of OLP. Curcumin, according to Amirchaghmaghi*et al.* [49], had no discernible impact on the therapy of OLP. Although curcumin oral gel can enhance clinical outcomes for OLP patients, it should not be the primary treatment. Rather, it can be administered as a maintenance medication following the patient's primary treatment with corticosteroids [50].

Conclusion

The reviewed trials demonstrate that topical corticosteroid therapy, which is still the standard of care for this kind of lesion, is the most efficient and effective medication for individuals with symptomatic OLP. While systemic corticosteroids should only be used for individuals whose condition is not responding to topical application first- and second-line treatments or who have a significant presence in the oral mucosa, the use of intralesional steroids, although relatively not common, may represent a valid alternate for cases that only partly respond to topical steroid therapy.

The review of RCTs suggests that second-line therapy for relapsed or refractory OLP involves calcineurin inhibitors, curcumin and retinoids topical preparations, photodynamic therapy, and excisional surgery for circumscribed lesions.Nutraceutical treatments should be investigated further with randomized trials, and used in conjunction with common first-line therapies. Topical steroids are superior for managing OLP, so use should be reserved for extensive lesions.

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