Received: 5 May 2021 | Revised: 25 June 2021 | Accepted: 14 July 2021

DOI: 10.1111/odi.13966

ORAL DISEASES Leading in Oral, Maxillofacial, Head & Neck Medicine WILEY

REVIEW ARTICLE

The effectiveness of topical forms of dexamethasone in the treatment of oral lichen planus— A systematic review

Magdalena Łukaszewska-Kuska | Zuzanna Ślebioda | Barbara Dorocka-Bobkowska

Department of Gerodontology and Oral Pathology, Poznan University of Medical Sciences, Poznan, Poland

Correspondence
Zuzanna Ślebioda, Department of Gerodontology and Oral Pathology, Poznan University of Medical Sciences, ul. Bukowska 70, 60-812 Poznań, Poland.
Emails: zslebioda@ump.edu.pl; zuzia_slebioda@o2.pl

Abstract

The goal of this systematic review was to assess the efficacy of dexamethasone compared to other treatments in oral lichen planus (OLP). The literature search used the following inclusion criteria: randomized controlled trials (RCT) comparing dexamethasone and other treatment strategies in patients with OLP. The outcome measures included relief of symptoms, decrement of erosive area size, and changes in quality of life. A computer and manual search was performed in Pubmed, Web of Science, and Cochrane Library up to January 31, 2021. The risk of bias was measured with the Revised Cochrane risk-of-bias tool for randomized trials. Eight trials with 131 study participants and 132 controls were identified. The following interventions were compared dexamethasone mouthwash, and 5% methylene blue-mediated photodynamic therapy, low-level laser therapy, amlexanox, clobetasol mouthwash, ketoconazole with amitriptyline, and thalidomide 1% paste. The therapeutic outcomes were more advantageous for dexamethasone in comparison with photodynamic therapy (PDT) (2 RCT) and low-level laser therapy (LLLT). Comparable effects were observed for dexamethasone, amlexanox, thalidomide, and PDT (1 RCT). Clobetasol showed more effective action than dexamethasone. Given the small sample sizes, heterogeneity and the few studies included, there is limited evidence to support the selection of treatment for OLP.

KEYWORDS
dexamethasone, oral lichen planus, oral pathology, treatment

1 | INTRODUCTION

Lichen planus (LP) is a common mucocutaneous disease of an uncertain etiology, affecting up to 2% of the population with a higher prevalence in middle-aged and elderly women (Gupta and Jawanda, 2015; Lavanya et al., 2011). To date, the background of the condition remains unclear, but most likely it involves both antigen-specific and non-specific mechanisms, leading to the damage of the basal cell layer in the epithelium (Lavanya et al., 2011; Thornhill, 2001; Sugerman et al., 2002). It is characterized by periods of remissions and exacerbations, where environmental factors like stress, anxiety, depression, and elevated salivary cortisol play an essential role in the aggravation of the disease (Akay et al., 2002; Shah et al., 2009).

Most common forms of LP include oral, cutaneous, and genital, with possible concurrent expression in different locations in one person (Cheng et al., 2016). Intraoral lesions present as white, non-removable striae on an inflammatory background, occasionally accompanied by erosive or bullous eruptions (Yang et al., 2016; Gorouhi et al., 2014). Oral lichen planus (OLP) may develop in over 70% of people with skin lesions. It seems to occur more often than the cutaneous form and tends to be more therapy-resistant

Magdalena Łukaszewska-Kuska, Zuzanna Ślebioda equal contribution.

(Mostafa and Tarakji, 2015). OLP was identified as a potentially malignant disorder by the World Health Organization working group, with a risk of malignant transformation ranging from 0.4% to 3.3% over a period 0.5 to>20 years, and with higher rates occurring in patients with atrophic-erosive lesions (Cheng et al., 2016; Epstein et al., 2003). However, the results of several studies on carcinogenesis in LP have been inconclusive and inconsistent; therefore, this issue remains controversial and requires further examination (Cheng et al., 2016).

The treatment of OLP is mainly symptomatic, and no effective causative therapeutic option is currently available (Yang et al., 2016; Carrozzo and Thorpe, 2009; Scully et al., 2000; Canjuga et al., 2010). The standard treatment regime includes local application of steroids or non-steroidal anti-inflammatory agents, substances to enhance the epithelial regeneration, and the elimination of predisposing factors. Herbal rinses, coating salve, retinoids, and laser therapy have been also utilized (Lavanya et al., 2011; Yang et al., 2016). Topical corticosteroids remain the mainstay of the therapy; however, their long-term use may cause adverse effects. Local complications include *Candida* overgrowth, thinning of the oral mucosa, and discomfort on application of the medication, while the systemic side effects include adrenal suppression, gastrointestinal upset, hypertension, and hyperglycemia (Scully et al., 2000; Gebremedhin et al., 2014; Gorsky et al., 1996). In addition, some patients may not respond effectively to only topical steroid application or may develop resistance to this form of therapy (Bakhtiari et al., 2017).

The aim of the present systematic review was to evaluate the efficacy of dexamethasone in the treatment of oral lichen planus.

2 | MATERIALS AND METHODS

In this report, PRISMA guidelines for systematic reviews were implemented. The study followed a pre-designed protocol registered in PROSPERO (International Prospective Register of Systematic Reviews).

2.1 | Search strategy

The PubMed/MEDLINE, Cochrane Library, and Web of Science databases were searched up to January 31, 2021. The PubMed/MEDLINE database was searched using the following terms: ("lichen planus"[MeSH Terms] OR ("lichen"[All Fields] AND "planus"[All Fields]) OR "lichen planus"[All Fields]) AND ("dexamethason"[All Fields] OR "dexamethasone"[MeSH Terms] OR "dexamethasone"[All Fields] OR "dexamethasone s"[All Fields] OR "dexamethasones"[All Fields]) with filters: Clinical Trial, Randomized Controlled Trial. The Cochrane Library database was searched using the terms: "oral" AND "lichen" AND "planus" AND "dexamethasone." The Web of Science (WoS) was searched on topic "oral" AND "lichen" AND "planus" AND "dexamethasone."

A language restriction was implemented by the researchers when assessing the records and only the full-text articles in English were finally qualified for the further evaluation. Additionally, a manual search of the bibliographies and the publications identified from a database search in Pubmed, Web of Sciences, and Cochrane Library for potentially eligible references was performed. In order to identify missing information or data, we attempted to contact the authors of the relevant studies. The gray literature was not searched for the purpose of this review.

Initially, the records were assessed by two independent authors according to the relevance of title and/or abstract. In doubtful cases, at this stage, the full reports were assessed independently by the same reviewers. Studies considered potentially eligible by at least one of the reviewers in the initial search were then verified in their entirety by the same two authors. Further analysis included full texts describing the studies which met the following inclusion criteria: randomized controlled trials (RCTs) performed on patients with OLP, comparison of dexamethasone with one or more other treatment strategies. The reviewers were not blinded to the authorship of the analyzed studies.

The data from each study entered in this analysis were extracted independently by the two reviewers and included year of publication, country of origin, details of the participants including demographic characteristics, type of intervention and comparisons, study design, and outcomes.

The outcome measures included relief of symptoms, decrement of the size of erosive area, and changes in quality of life. The primary outcome was the assessment of pain, while the resolution of the clinical symptoms and changes in quality of life were the secondary outcomes. Any disagreements between researchers were resolved after consultation with the senior author.

2.2 | Assessment of study quality

The bias assessment was performed by two independent authors in accordance with the recommendations of the Revised Cochrane risk-of-bias tool for randomized trials (RoB 2). In this evaluation five bias domains, including bias arising from the randomization process, deviations from the intended intervention, missing outcome data, measurement of the outcome, and selection of the reported results, were assessed (Sterne et al., 2019). Each domain was mandatory. The risk of bias in each category was assigned as high, low, or as raising some concerns. The overall risk of bias for each study corresponded to the worst risk of bias in any of the domains, although a study judged to have "some concerns" about risk of bias for multiple domains, could also be judged as at high risk of bias overall. In case of disagreement, the senior author performed the final evaluation.

3 | RESULTS

3.1 | Characteristics of the studies included

A total of 8 studies were selected from 73 potentially eligible publications identified in the initial database searches. Figure 1 shows a flow diagram of the study selection.

A detailed description of the included studies is shown in Table 1.

The primary outcomes related to pain relief were measured using Visual Analogue Scale (VAS), Chronic Oral Mucosal Diseases Questionnaire (COMDQ), evaluation of the pain improvement, self-assessment of symptom relief, and subjective assessment of oral symptoms. Post-treatment changes in the clinical appearance of lesions were evaluated with Thongprasom sign scoring, Reticulation/erythema/ulcer score (REU), Clinical severity index (SI), Efficacy index (EI), Piboonniyom clinical data scale, comparisons of clinical photographs, measurement of erosive area size, and reduction in severity of the lesion. Additional methods were used to assess other effects of the therapy. They included Treatment Satisfaction Questionnaire for Medication-9 (TSQM-9), 3-month recurrence rates, and adverse effects at 1 year.

The evaluated studies compared the effects of several topical forms of dexamethasone to a wide spectrum of other therapeutic strategies in the treatment of OLP. The following forms of dexamethasone were used: 0.5 mg tablet dissolved in 5 ml aqueous mouthwash, 0.5 mg tablet crushed, and mixed with up to 20 ml water, 0.5 mg tablet dissolved in 5 ml of water in combination with nystatin (100,000 units) and diphenhydramine elixir, 0.043% drug powder dissolved in pure glycerol, compounded 0.5 mg/2ml drug mouth rinse, compounded 0.1 mg/ml drug solution in Mucolox, and pure 0.1 mg/ml drug solution. Other treatment modalities analyzed in the reviewed studies included 5% methylene blue-mediated photodynamic therapy (PDT), toluidine blue-mediated photodynamic therapy (PDT), low-level laser therapy (LLLT), amlexanox paste, mouthwash containing clobetasol, ketoconazole and amitriptyline, and thalidomide 1% paste.

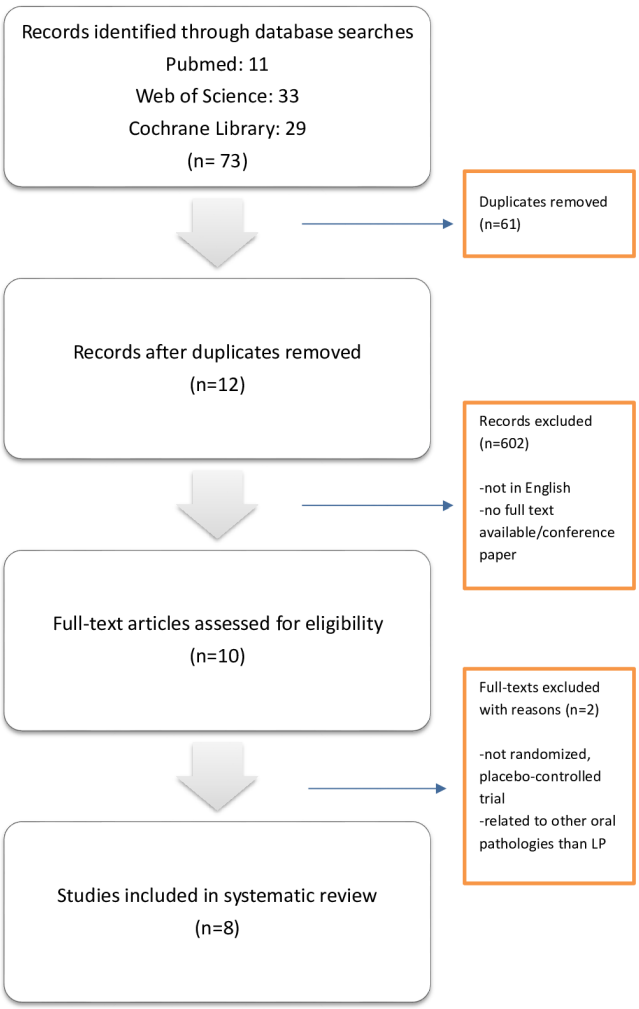

FIGURE 1 Flowchart of the study selection

Photodynamic therapy was tested in 3 studies, in 2 of which a 5% methylene blue was utilized as a mediator (Bakhtiari et al., 2017; Mirza et al., 2018), while the remaining study used toluidine blue (Jajarm et al., 2015). In all studies, the efficacy of treatment was compared to dexamethasone mouth rinse (0.5 mg/5 ml). In Mirza's study, these treatment strategies were additionally compared to low-level laser therapy (LLLT) (Mirza et al., 2018). In the Bakhtiari study, no significant differences regarding VAS, Thongprasom sign score, and efficacy and clinical severity indices were revealed between the compared groups (Bakhtiari et al., 2017). Contrary to those results, Jajarm demonstrated a significantly greater pain improvement and a higher efficacy index in the dexamethasone group in comparison with the PDT (Jajarm et al., 2015). Also in the Mirza et al., 2018. study, the corticosteroid application resulted in a significantly greater pain reduction compared to both LLLT and PDT groups (Mirza et al., 2018). There was also a significantly lower risk of relapse for corticosteroid group in comparison with PDT. The efficacy index improved most significantly in the PDT group.

Low-level laser therapy (LLLT) was evaluated in one study only (Mirza et al., 2018). Diode laser irradiation with an exposure time 2.5 min, fluence of 1.5 J/cm^2 per session, and irradiance 10 mW/cm^2 was repeated every third day for a maximum of 10 sessions. As mentioned above, in the Mirza study, the mean pain improvement in patients treated with this option was comparable to PDT but it was less significant than in subjects treated with corticosteroids (Mirza et al., 2018).

Amlexanox paste (2-amino-7-isopropyl-5-oxo-5H-chromeno[2,3-b]pyridine-3-carboxylic acid), which was tested in a study by Fu et al., appeared to be as effective as 0.043% dexamethasone paste (Fu et al., 2012). The authors did not reveal any significant differences between the tested groups in the reduction of erosive areas and VAS scores after the treatment.

Mouthwash containing clobetasol, ketoconazole, and amitriptyline, which was compared to dexamethasone mouth rinse (0.5 mg/5 ml) administered in combination with nystatin (100000 units) and diphenhydramine elixir in the Javadzaneh study (Javadzadeh et al., 2008), showed several advantageous effects of the first treatment approach compared to the other. There was a significantly greater improvement of the lesions in the clobetasol/ketoconazole/amitriptyline group compared to the dexamethasone group. The mean time of drug use for complete resolution of lesions was significantly shorter for the clobetasol/ketoconazole/amitriptyline group. The patient satisfaction was also higher for this treatment option, while the probability of the persisting disease was lower when compared to the dexamethasone group.

TABLE 1 Summary of the studies reviewed and sorted by the author

Authors (Years)	Intervention	Study population (country)	Study group (*n*)	Control group (*n*)	Outcome assessment	Results
Bakhtiari et al. (2017)	• 5% methylene blue-mediated PDT (630 nm) • Dexamethasone 0.5 mg/5 ml + Nystatin 100.000 IU	Iran	15	15	• VAS • Thongprasom sign scoring • SI • EI	• No significant differences between the groups in VAS, sign score, efficacy index, and clinical severity
Fu et al. (2012)	• Amlexanox paste (250 mg: 5 g per tube) • Dexamethasone powder 0.043% dissolved in pure glycerol	China	18	20	• VAS • Erosive area (mm^2)	• No significant differences between the groups in the reduction of erosive areas and VAS
Hambly et al. (2017)	• Self-formulated Dexamethasone rinse (0.5 mg Dexamethasone/20 ml) • Dexamethasone (0.5 mg/2 ml)	Australia	9	9	• VAS • TSQM-9 • Comparisons of clinical photographs • Self-assessment of symptom relief, compliance, and QoL	• Compounded formulation superior to self-formulated rinse in terms of convenience of use, positive compliance, patient-perceived faster onset of action, and symptom relief (the difference not confirmed statistically due to the small sample size)
Jajarm et al. (2015)	• Toluidine blue-mediated PDT (630 nm) • Dexamethasone 0.5 mg/5 ml + Nystatin 100.000 IU	Iran	14	11	• VAS • Thongprasom sign scoring • EI	• No significant differences between the two groups before and after treatment in sign score • Mean amount of reduction of pain significantly greater in the Dexamethasone group in comparison with the PDT group • EI of the Dexamethasone group improved significantly more compared to the PDT group
Javadzadeh et al. (2008)	• Clobetasol + Ketoconazole + Amitriptyline (5 ml) • Dexamethasone 0.5 mg/5 ml + Nystatin 100.000 IU + Diphenhydramine	Iran	16	17	• Piboonniyom clinical data scale • Reduction in severity of the lesion • VAS • Reduction of pain	• Significantly greater improvement of pain and lesions in Clobetasol/Ketoconazole/Amitriptyline group • Significantly shorter mean time of drug use for complete resolution of lesions in Clobetasol/Ketoconazole/Amitriptyline group • Significantly higher patient satisfaction in the Clobetasol/Ketoconazole/Amitriptyline group • Significantly lower probability of the disease persisting for the Clobetasol/Ketoconazole/Amitriptyline group

TABLE 1 (Continued)

Authors (Years)	Intervention	Study population (country)	Study group (*n*)	Control group (*n*)	Outcome assessment	Results
Mirza et al. (2018)	• Methylene blue-mediated PDT (630 nm) • LLLT (630 nm) • Dexamethasone 0.5 mg/5 ml + Nystatin 100.000 IU	Saudi Arabia	15	15	• Thongprasom sign scoring • EI • VAS	• Mean improvement in pain significantly greater in the Dexamethasone group in comparison with the PDT and LLLT groups. • The pain outcome was comparable in PDT and LLLT groups • The EI of the PDT group significantly better than in the LLLT and corticosteroid groups • Statistically significant lower relapse risk for corticosteroids group in comparison with PDT
Villa et al. (2020)	• Dexamethasone 0.1 mg/ml solution in Mucolox+ Fluconazole 200 mg or Nystatin suspension • Dexamethasone 0.1 mg/ml + Fluconazole 200 mg or Nystatin suspension	USA	12	8	• REU score • Subjective assessment of oral symptoms • COMDQ	• Significantly better REU scores and higher improvement in the total COMDQ score in Dexamethasone + Mucolox group • No significant differences between the groups in the overall self-reported responses
Wu et al. (2010)	• Thalidomide 1% paste • Dexamethasone 0.043% paste	China	32	37	• Size of erosive area • VAS • 3-month recurrence rates • Adverse effects at 1 year	• No significant differences in the diminution of erosive areas, VAS scores, recurrence rates, and the adverse effects between the groups

Abbreviations: COMDQ, chronic oral mucosal diseases questionnaire; EI, efficacy index; REU, reticulation/erythema/ulcer score; SI, clinical severity index; TSQM-9, treatment satisfaction questionnaire for medication-9; VAS, visual analogue scale.

Thalidomide 1% paste was also evaluated in 1 study only (Wu et al., 2010), where it was compared to 0.043% dexamethasone paste. The authors did not reveal any significant differences between these two treatment strategies regarding VAS, reduction of erosive area size, recurrence rate at 1- and 3-month follow-up, and the occurrence of the adverse effects during the therapy.

Self-formulated and *compounded dexamethasone mouth rinses* were compared in two studies. In the Villa et al. study (Villa et al., 2020), dexamethasone 0.1 mg/ml solution in Mucolox (mucoadhesive polymer) was compared to dexamethasone 0.1 mg/ml solution alone, while in the Hambly et al. study (Hambly et al., 2017) a self-formulated mouth rinse composed of 0.5 mg dexamethasone tablet crushed and mixed with up to 20 ml water was compared to a compounded mouth rinse of dexamethasone (0.5 mg/2 ml). Although there were no statistically significant differences between the 2 groups in the overall self-reported responses in the first study, and the treatments for both groups were effective at lowering the REU scores, the group on Mucolox solution had statistically better outcomes. There was also a significantly higher improvement in the total COMDQ score in Mucolox group compared to dexamethasone group alone. In the second study, a statistical analysis was not feasible due to the small sample size. However, a compounded formulation was found to be superior to existing therapy due to its convenience, positive contribution to compliance, patient-perceived faster onset of action, and improved symptom relief.

3.2 | Quality of the studies included

The evaluation of the study quality is presented in Figure 2.

The risk of bias related to the randomization process was estimated as low in 4 studies and as raising some concerns in remaining 4 studies. The random numbering tables, coin tossing, and computer-generated random lists were applied in each of the 2 studies. Unbiased randomizer software was used in one study, while in remaining study the method of randomization was not clearly defined by the authors. Bias due to deviations from intended interventions was estimated as raising some concerns in all of the studies. Most of the authors (75%) did not specify clearly whether the participants were aware of their assigned intervention during the study. Only two studies clearly indicated that the patients were blinded to the type of intervention until the end of the treatment (Javadzadeh et al., 2008; Wu et al., 2010). In some studies, people delivering the intervention were not blinded to the participants' assignment or their awareness was not clearly stated in the text. Because of the failure to blind the nature of some kind of interventions (comparisons of the drug therapy and photodynamic treatment) some studies were evaluated as "raising concerns" in this section. Again only in Wu et al. and Javadzadeh et al. studies (Javadzadeh et al., 2008; Wu et al., 2010), it was clearly shown that the medical staff was also blinded to the type of intervention while evaluating the patients' condition. None of the authors described whether an analysis of the estimated effect of the assignment was performed. Bias due to missing outcome data

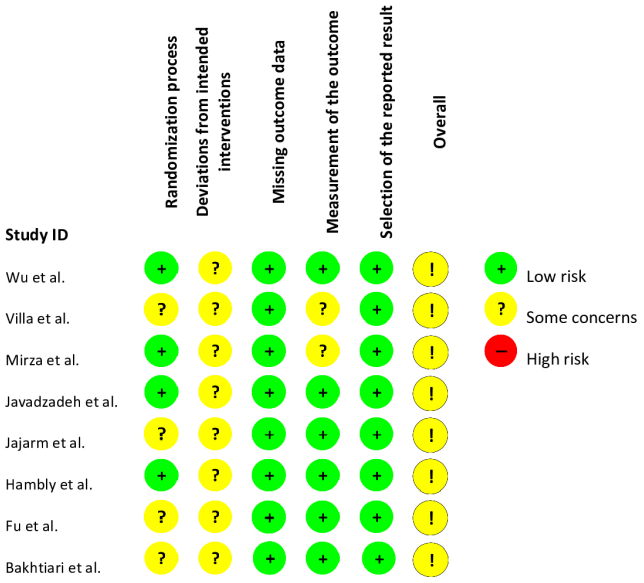

FIGURE 2 Evaluation of the risk of bias in the studies reviewed

was evaluated as low for all the studies. Bias in measurement of the outcome was assessed as raising some concerns for 2 studies (Mirza et al., 2018; Villa et al., 2020), and as low for the remaining six studies (Bakhtiari et al., 2017; Fu et al., 2012; Hambly et al., 2017; Jajarm et al., 2015; Javadzadeh et al., 2008; Wu et al., 2010). Bias related to the selection of the reported results were estimated as low for all the studies reviewed. Although for most of the domains the reviewed studies were evaluated as having a low risk of bias, according to the current recommendations on using RoB 2, the overall risk of bias for a specific result reflects the worst risk of bias in any of the domains. Therefore, if a study is judged to raise some concerns in at least one of the evaluated domains, the overall risk is defined as "at some concerns." In the case of this review, all the studies were evaluated as raising some concerns. It should be emphasized that none of the studies indicated a high risk of bias in any of the domains, and for three studies, all the domains except one were estimated as at low risk of bias (Hambly et al., 2017; Javadzadeh et al., 2008; Wu et al., 2010).

4 | DISCUSSION

For several years, oral lichen planus has generated heated discussions and has been probably associated with more controversy than any other disease in oral pathology and medicine (Cheng et al., 2016). The etiology of OLP is still unclear. Various potential triggers and contributing factors to OLP have been proposed, including local and systemic inducers of cell-mediated hypersensitivity, stress, autoimmune response to epithelial antigens, and microorganisms. As the background of the condition has not been fully explained, the current therapeutic approaches are mainly symptomatic and are concerned with the alleviation of symptoms (Gupta and Jawanda, 2015), but a permanent cure is not yet possible. Variations in the disease

activity within an individual patient and also between patients make the management with a single and definitive therapeutic strategy very challenging (Gupta and Jawanda, 2015).

Several therapies have been described for OLP including pharmacotherapy with topical, locally injected, and systemic corticosteroids, doxycycline, topical retinoids, topical calcineurin inhibitors, hydroxychloroquine, azathioprine, mycophenolate, mofetil, methotrexate, dapsone, and thalidomide, biological agents (e.g., efalizumab, etanercept, alefacept, and rituximab), surgery, psoralen with ultraviolet light A (PUVA), phototherapy, topical aloe vera, oral curcuminoids, and laser (Gupta and Jawanda, 2015; Ślebioda and Dorocka-Bobkowska, 2020). Novel, currently developed treatment options are focused on blocking activity of interleukins, interferon, tumor necrosis factor, and matrix metalloproteinases (Gupta and Jawanda, 2015).

Topical corticosteroids are widely accepted as the primary treatment of choice in OLP. They present potent anti-inflammatory actions, mainly by decreasing the production of cytokines and by reducing the number of several immune cells at the site of inflammation (Thongprasom and Dhanuthai, 2008). Patients unresponsive to topical therapy require systemic application of steroids, which are generally reserved for acute exacerbations of OLP. Multiple or widespread lesions, where the application of a topical drug is difficult and may affect the patient compliance, are also an indication for a systemic approach. Complications due to corticosteroid treatment in the oral cavity include developing secondary *candidiasis*, relapse of treatment, and refractory cases (Gorsky et al., 1996). Prolonged use of corticosteroids may induce tachyphylaxis, a decrease in the biological effectiveness of the drug (Bakhtiari et al., 2017). Several steroids have been widely used in topical treatment of OLP, including clobetasol, clobetasol propionate (0.025%–0.05%), fluocinonide (0.025%–0.05%), triamcinolone acetonide (0.05%–0.5%), fluticasone propionate, betamethasone sodium phosphate, and dexamethasone. The purpose of this systematic review was to investigate the efficacy of topical dexamethasone therapy in comparison with different treatment approaches of OLP. The compared therapeutic strategies included PDT, LLLT, amlexanox, mouthwash containing clobetasol, ketoconazole and amitriptyline, and thalidomide. Dexamethasone appeared to be more effective than PDT in pain reduction and reducing the risk of relapse of OLP in two studies, while in one study the effects of action of these approaches were comparable. Dexamethasone was also more effective than LLLT, but comparable to amlexanox and thalidomide in terms of the diminution of erosive areas, VAS scores after the treatment, the recurrence rate at follow-ups, and the occurrence of adverse reactions (Fu et al., 2012; Mirza et al., 2018; Wu et al., 2010). Amlexanox, which is an inhibitor of phosphodiesterase and inflammatory mediators, had been originally developed for the treatment of recurrent aphthous stomatitis. Considering the comparable effectiveness of this drug in comparison with topical steroid in the study by Fu et al., it could be used as an alternative, especially in patients refractive to steroids or with contraindications for steroidal treatment (Fu et al., 2012). No serious, long-term side effects of amlexanox used topically on oral mucosa have been described so far, which makes it a promising treatment alternative to dexamethasone. Thalidomide shows anti-inflammatory properties due to its ability to decrease the production of TNF-α and to suppress T-cell function. As the systemic administration of this drug may lead to serious adverse effects such as teratogenicity, neuropathy, somnolence, and rash, topical application has been also recently considered in several oral ulcerative conditions, for example, in HIV induced recurrent aphthous stomatitis. In the Wu et al. study (Wu et al., 2010), the effectiveness of thalidomide was comparable to dexamethasone, and no adverse effects were observed in the thalidomide group; nevertheless, it should be restricted to selected patients with precautionary measures.

Meanwhile, the mouth rinse composed of clobetasol, ketoconazole, and amitriptyline showed a higher efficacy than dexamethasone, which was evaluated based on treatment duration, patient's satisfaction, and the risk of relapse (Javadzadeh et al., 2008). Clobetasol has been recommended by many authors as a first-line topical steroid in the treatment of OLP. It is classified as US Class I (Europe: class IV) corticosteroid, making it one of the strongest available (Ference and Last, 2009).

Self-formulated dexamethasone mouth rinses appeared to be less acceptable to patients when compared to compound solution and mouth rinse of dexamethasone mixed with Mucolox, for which a patient-perceived faster onset of action was reported (Hambly et al., 2017; Villa et al., 2020).

A comparison of the effects of the interventions tested was severely restricted by the paucity of relevant placebo-controlled studies; therefore, the evidence for the effectiveness of any specific palliative treatment for symptomatic OLP is not sufficiently robust. Variability of the metrics used in the evaluation of the results and heterogeneous study design, short follow-up periods, relatively low numbers of participants, and lack of a placebo group were the main limitations of the reviewed studies. A sample size was justified in one study only (Jajarm et al., 2015). In most of the studies, the efficacy of treatment was measured by the reduction of pain, evaluated with various scales, mostly with VAS. As pain is a subjective impression, not measurable with standard tools that may interfere with the objective evaluation of the results reported. An objective comparison of topical treatment approaches is also partially impeded by the diversity of drug delivery routes, described in the cited studies. Several approaches were considered in this review, including water and glycerol mouth rinses, pastes, mucoadhesive polymers, LLLT, and PDT. Transdermal and transmucosal delivery is well recognized, as it allows a controlled transfer of a drug with minimal side effects, good efficiency, and maintenance of a therapeutic dose throughout topical administration. Percutaneous absorption of drug molecules is pivotal as the drug must be absorbed to an optimum concentration in the restricted area of the organ (Sharadha et al., 2020). OLP affects the basal cells and the adjacent connective tissue. To reach this goal, a drug needs to cross the permeability barrier and penetrate deeply into the epithelium. A perfect agent for oral topical application should provide a targeted penetration, good retention, and easy uptake by cells. Unfortunately, there are

very few topical formulations that have been designed specifically for oral pathologies, and dermatological drugs commonly used as replacements have not been designed for the aqueous oral environment (Sharadha et al., 2020). Having regard to the diversity of preparations analyzed in this review, the results need to be treated with caution.

Nevertheless, based on our analysis, the most promising therapeutic effects in the treatment of OLP were observed for a mixed mouth rinse containing clobetasol. Dexamethasone also appeared to be more effective than most of the compared treatment approaches; therefore, it can be recommended as an effective therapeutic strategy in OLP treatment. Although dexamethasone is an effective therapeutic strategy for OLP, it is not better than clobetasol combined with ketoconazole/amitriptyline. It should be emphasized, however, that there is limited evidence to support the treatment selection for OLP considering the small number of studies with relatively low sample sizes which have qualified for this review.

ACKNOWLEDGEMENTS

There are no sources of funding for this report. The authors contributed to the design of the study, data acquisition, and interpretation. They drafted and critically revised the manuscript.

CONFLICT OF INTERESTS

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Magdalena Lukaszewska-Kuska: Conceptualization; Investigation; Methodology; Resources; Validation; Writing-original draft; Writing-review & editing. **Zuzanna Slebioda:** Conceptualization; Investigation; Methodology; Resources; Visualization; Writing-original draft; Writing-review & editing. **Barbara Dorocka-Bobkowska:** Formal analysis; Funding acquisition; Supervision; Writing-review & editing.

PEER REVIEW

The peer review history for this article is available at https://publons.com/publon/10.1111/odi.13966.

ORCID

Magdalena Łukaszewska-Kuska https://orcid.org/0000-0002-4163-0995
Zuzanna Ślebioda https://orcid.org/0000-0002-5482-3964
Barbara Dorocka-Bobkowska https://orcid.org/0000-0003-3659-7761

REFERENCES

Akay, A., Pekcanlar, A., Bozdag, K. E., Altintas, L., & Karaman, A. (2002). Assessment of depression in subjects with psoriasis vulgaris and lichen planus. *Journal of the European Academy of Dermatology and Venereology*, *16*(4), 347–352.

Bakhtiari, S., Azari-Marhabi, S., Mojahedi, S. M., Namdari, M., Rankohi, Z. E., & Jafari, S. (2017). Comparing clinical effects of photodynamic therapy as a novel method with topical corticosteroid for treatment of Oral Lichen Planus. *Photodiagnosis and Photodynamic Therapy*, *20*, 159–164.

Canjuga, I., Mravak-Stipetic, M., Loncar, B., & Kern, J. (2010). The prevalence of systemic diseases and medications in patients with oral lichen planus. *Acta Stomatologica Croatica*, *44*, 96–100.

Carrozzo, M., & Thorpe, R. (2009). Oral lichen planus: A review. *Minerva Stomatologica*, *58*(10), 519–537.

Cheng, Y. S., Gould, A., Kurago, Z., Fantasia, J., & Muller, S. (2016). Diagnosis of oral lichen planus: a position paper of the American academy of oral and maxillofacial pathology. *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology*, *122*(3), 332–354.

Epstein, J. B., Wan, L. S., Gorsky, M., & Zhang, L. (2003). Oral lichen planus: Progress in understanding its malignant potential and the implications for clinical management. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology*, *96*(1), 32–37. https://doi.org/10.1016/S1079-2104(03)00161-6

Ference, J. D., & Last, A. R. (2009). Choosing topical corticosteroids. *American family physician*, *79*(2), 135–140.

Fu, J., Zhu, X., Dan, H., Zhou, Y., Liu, C., Wang, F., Li, Y., Liu, N., Chen, Q., Xu, Y., Zeng, X., & Jiang, L. (2012). Amlexanox is as effective as dexamethasone in topical treatment of erosive oral lichen planus: A short-term pilot study. *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology*, *113*(5), 638–643. https://doi.org/10.1016/j.oooo.2011.10.013

Gebremedhin, S., Dorocka-Bobkowska, B., Pryliński, M., Konopka, K., & Duzgunes, N. (2014). Miconazole activity against Candida biofilms developed on acrylic discs. *Journal of Physiology and Pharmacology: An Official Journal of the Polish Physiological Society*, *65*(4), 593–600.

Gorouhi, F., Davari, F., & Fazel, N. (2014). Cutaneous and mucosal lichen planus: A comprehensive review of clinical subtypes, risk factors, diagnosis, and prognosis. *The Scientific World Journal*, *10*, 742826. https://doi.org/10.1155/2014/742826

Gorsky, M., Raviv, M., Moskona, D., Laufer, M., & Bodner, L. (1996). Clinical characteristics and treatment of patients with oral lichen planus in Israel. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology*, *82*, 644–649.

Gupta, S., & Jawanda, M. K. (2015). Oral lichen planus: An update on etiology, pathogenesis, clinical presentation, diagnosis and management. *Indian Journal of Dermatology*, *60*(3), 222–229.

Hambly, J. L., Haywood, A., Hattingh, L., & Nair, R. G. (2017). Comparison between self-formulation and compounded-formulation dexamethasone mouth rinse for oral lichen planus: A pilot, randomized, cross-over trial. *Journal of Investigative and Clinical Dentistry*, *8*(3), e12225.

Jajarm, H. H., Falaki, F., Sanatkhani, M., Ahmadzadeh, M., Ahrari, F., & Shafaee, H. (2015). A comparative study of toluidine blue-mediated photodynamic therapy versus topical corticosteroids in the treatment of erosive-atrophic oral lichen planus: A randomized clinical controlled trial. *Lasers in Medical Science*, *30*(5), 1475–1480. https://doi.org/10.1007/s10103-014-1694-1

Javadzadeh, A., Vatanpour, H., Delavarian, Z., Momajed, A., Esmaeily, H., Vatanpour, M., & Shirazian, S. (2008). Efficacy of clobetasol, ketoconazole and amitryptiline mouthwash on oral lichen planus. *Iranian Journal of Pharmaceutical Research*, *7*(3), 171–178.

Lavanya, N., Rao, U. K, Jayanthi, P., & Ranganathan, K. (2011). Oral lichen planus: An update on pathogenesis and treatment. *Journal of Oral and Maxillofacial Pathology*, *15*(2), 127–132.

Mirza, S., Rehman, N., Alrahlah, A., Alamri, W. R., & Vohra, F. (2018). Efficacy of photodynamic therapy or low level laser therapy against steroid therapy in the treatment of erosive-atrophic oral lichen planus. *Photodiagnosis and Photodynamic Therapy*, *21*, 404–408.

Mostafa, D., & Tarakji, B. (2015). Photodynamic therapy in treatment of oral lichen planus. *Journal of Clinical Medicine Research*, *7*(6), 393–399.

Scully, C., Eisen, D., & Carrozzo, M. (2000). Management of oral lichen planus. *American Journal of Clinical Dermatology*, *1*(5), 287–306.

Shah, B., Ashok, L., & Sujatha, G. P. (2009). Evaluation of salivary cortisol and psychological factors in patients with oral lichen planus. *Indian Journal of Dental Research*, *20*(3), 288–292.

Sharadha, M., Gowda, D. V., Vishal Gupta, N., & Akhila, A. R. (2020). An overview on topical drug delivery system – Updated review. *International Journal of Research in Pharmaceutical Sciences*, *11*(1), 368–385. https://doi.org/10.26452/ijrps.v11i1.1831

Sterne, J. A. C., Savović, J., Page, M. J., Elbers, R. G., Blencowe, N. S., Boutron, I., Cates, C. J., Cheng, H. Y., Corbett, M. S., Eldridge, S. M., Emberson, J. R., Hernán, M. A., Hopewell, S., Hróbjartsson, A., Junqueira, D. R., Jüni, P., Kirkham, J. J., Lasserson, T., Li, T., McAleenan, A., Reeves, B. C., Shepperd, S., Shrier, I., Stewart, L. A., Tilling, K., White, I. R., Whiting, P. F., & Higgins, J. P. T. (2019). RoB 2: A revised tool for assessing risk of bias in randomised trials. *BMJ*, *366*, l4898.

Ślebioda, Z., & Dorocka-Bobkowska, B. (2020). Low-level laser therapy in the treatment of recurrent aphthous stomatitis and oral lichen planus: A literature review. *Postępy Dermatologii I Alergologii*, *37*(4), 475–481.

Sugerman, P. B., Savage, N. W., Walsh, L. J., Zhao, Z. Z., Zhou, X. J., Khan, A., Seymour, G. J., et al. (2002). The pathogenesis of oral lichen planus. *Critical Reviews in Oral Biology and Medicine : An Official Publication of the American Association of Oral Biologists*, *13*(4), 350365.

Thongprasom, K., & Dhanuthai, K. (2008). Steriods in the treatment of lichen planus: A review. *Journal of Oral Science*, *50*(4), 377–385.

Thornhill, M. H. (2001). Immune mechanisms in oral lichen planus. *Acta Odontologica Scandinavica*, *59*(3), 174–177.

Villa, A., Sankar, V., Bassani, G., Johnson, L. B., & Sroussi, H. (2020). Dexamethasone solution and dexamethasone in Mucolox for the treatment of oral lichen planus: A preliminary study. *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology*, *129*(6), 585–590.

Wu, Y., Zhou, G., Zeng, H., Xiong, C. R., Lin, M., & Zhou, H. M. (2010). A randomized double-blind, positive-control trial of topical thalidomide in erosive oral lichen planus. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology*, *110*(2), 188–195. https://doi.org/10.1016/j.tripleo.2010.03.034

Yang, H., Wu, Y., Ma, H., Jiang, L., Zeng, X., Dan, H., Zhou, Y., & Chen, Q. (2016). Possible alternative therapies for oral lichen planus cases refractory to steroid therapies. *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology*, *121*, 496–509.

How to cite this article: Łukaszewska-Kuska, M., Ślebioda, Z., & Dorocka-Bobkowska, B. (2022). The effectiveness of topical forms of dexamethasone in the treatment of oral lichen planus— A systematic review. *Oral Diseases*, 28, 2063–2071. https://doi.org/10.1111/odi.13966