

Efficacy of Herbal Interventions in Oral Lichen Planus: A Systematic Review

Abstract

Introduction: Oral lichen planus (OLP) is a chronic autoimmune condition requiring prompt treatment to alleviate the signs and symptoms. There is weak evidence emphasizing the efficacy of any one therapy. Steroids, of all the therapies, have proved to be effective and hence considered as the standard care for OLP. However, the complications associated with it further worsen the patient's condition. Alternative safe approaches such as herbal interventions (HIs) have been tried in OLP. Their efficacies could only be evaluated from properly designed research protocols such as randomized controlled trials (RCTs). The present systematic review aims to assess the efficacy of HIs compared to steroids in RCTs involving OLP. **Materials and Methods:** An extensive search for HIs in OLP was conducted in PubMed, MEDLINE, Cochrane Central Register of Controlled Trials, Scopus, and gray literature. Eight studies fulfilled the eligibility criteria. **Results:** In all the studies, clinical severity was significantly reduced in within-group comparisons, whereas between-group comparisons showed nonsignificant results, except for total glucosides of paeony capsules. **Conclusion:** Efficacy of herbal therapy in OLP should be weighed against the high bias in the studies.

Keywords: Herbal, intervention, oral lichen planus, randomized controlled trial, steroid.

Introduction

Oral lichen planus (OLP) is a chronic, T cell-mediated autoimmune disease characterized by periods of exacerbations and remissions.^[1-5] A female predominated condition, OLP could also be associated with systemic conditions such as diabetes mellitus and hypertension.^[5-7] It manifests in various forms such as plaque, reticular, papular, atrophic, erosive, and bullous.^[8] Periods of exacerbations are usually associated with atrophic or erosive forms which lead to severe pain or burning sensation. Various treatment strategies have been tried, with variable results.^[9,10] Corticosteroids have been the main drug of choice in these patients.^[11] However, considering the chronic nature of the condition, associated systemic diseases, and frequent use of steroids, the number of patients affected by the complications is uncountable. In addition to the systemic complications, long-term topical corticosteroids can lead to secondary candidiasis, taste alterations, mucosal atrophy, and burning sensation, further worsening the condition.^[12-14] Therefore, an alternative and safe therapy

which could be equally effective or superior to steroids should be explored.

One such therapy is the herbal medicines which have been tried for many chronic conditions including OLP.^[15,16] Randomized controlled trials (RCTs) of herbal interventions (HIs) with steroids as standard control will give an unbiased insight to the current scenario of range of herbal therapies which could be alternatively given in OLP patients. Thus, the present systematic review was planned with the basic research question: "How efficacious are the herbal medicines as compared to corticosteroids in RCTs on symptomatic OLP patients?"

Materials and Methods

Eligibility criteria

1. Types of studies: The studies included were RCTs comparing herbal medicine with corticosteroid, with or without blinding of the participants and the outcome assessors. Quasi randomized trials, nonrandomized trials, crossover studies, case reports, and split-mouth studies were excluded
2. Intervention types: Studies with herbal and corticosteroid interventions in any

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Submitted : 22-Apr-2020

Revised : 24-Aug-2020

Accepted : 23-Sep-2020

Published : 20-Dec-2020

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Access this article online

Website:
www.contempclindent.org

DOI: 10.4103/ccd.ccd_320_20

Quick Response Code:



How to cite this article: Kalaskar AR, Bhowate RR, Kalaskar RR, Walde SR, Ramteke RD, Banode PP. Efficacy of herbal interventions in oral lichen planus: A systematic review. Contemp Clin Dent 2020;11:311-9.

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form, either topical or systemic or intralesional and in varying doses, were included. In addition, studies comparing different HI or trials with placebo as one of the groups along with steroid intervention were also included. Studies not involving corticosteroids were excluded

3. Participants: Studies involving histopathologically confirmed and symptomatic cases of OLP of any age, gender, or race were included. Whereas, participants with idiopathic, plaque type, nonsymptomatic OLP, or individuals with lichenoid drug reaction or showing evidence of dysplasia and those who have missed the follow-up or recall visits were also excluded
4. Primary outcome: Studies assessing relief in symptoms such as pain, burning, or discomfort as stated by the participants measured by visual analog scale (VAS) or numeric rating scale (NRS) or any other related scale were included.
5. Secondary outcome: Studies involving following secondary outcome measuring parameters were included:
 - a. Reduction in clinical signs that is the size and severity of the lesions measured by appropriate clinical scoring system
 - b. Improvement in clinical response or restoration of normal function judged by the improvement index
 - c. Reduction in the interference with daily activities or improvement in quality of life judged by quality of life index/questionnaire
 - d. Reduction in the severity and flare
 - e. Relapse after discontinuation of medicine
 - f. Adverse effects if any reported.

The outcomes should have been assessed periodically either in days, weeks, or months.

The protocol of the study was registered in PROSPERO with the registration no: CRD42018114116.

Searching sources and strategy

The sources for search of relevant RCTs were from electronic databases of PubMed, MEDLINE, Cochrane Central Register of Controlled Trials, and Scopus from January 2000 to October 2018 with no restrictions for any language. In addition, National Institute of Health Trials, knowledge Hub e-library, Clinical Trials Registry of India, Google Scholar, and EBSCOhost along with manual searching from citations, bibliographies, review articles, and major journals related to the topics were also searched. The search strategy is shown in Table 1. The keywords were validated by the MeSH (Medical Subject Headings) dictionary, and the Boolean operator AND was used to relate them.

Screening and selection

The studies in the form of titles and/or abstracts obtained after using search strategy (including all sources) were

screened independently by two review authors (A and C). The duplicate studies were removed, and the full texts of those studies which fulfilled the eligibility criteria mentioned above were retrieved and independently assessed for eligibility. Any disagreements between the reviewers were resolved by discussion with the third reviewer (B) [Table 1].

Data extraction and quality assessment

The data were extracted from the selected articles independently by two reviewers (D and E) in a standardized pre-piloted form [Table 2], and discrepancy if identified was resolved by discussion with the third reviewer (B). Contacts were established with the authors of articles having missing data and were requested to provide the same. Quality assessments of RCTs were done by Cochrane risk-of-bias tool for RCTs.^[17]

Results

Search and selection results

After an extensive search of database and other sources as mentioned previously, the data were gathered. Details of data collection, screening, and selection procedure are summarized in flowchart shown in Figure 1. After removal of the duplicate articles and retrieval of full-text articles (14) for screening for the eligibility criteria, six articles were excluded and finally the remaining eight articles were considered for systematic review.

Table 1: Search strategy keywords

Concepts	Search strategy
Lichen planus	Oral lichen planus OR lichen planus, oral
Herbal therapy	Herbal therapy OR herb therapy OR phytotherapy OR plant extracts OR plants, medicinal OR herbalism OR curcumin OR aloe vera OR anthocyanins OR quercetin OR lycopene OR propolis OR honey OR Chinese herbs
Steroids	Steroids OR Corticosteroids OR triamcenolone acetonide OR clobetasole propionate OR dexamethasone OR prednisolone OR betamethazone

Table 2: Points included in data extraction form

Study setting
Study population
Participant demographics and baseline characteristics
Details of herbal intervention and steroid intervention
Study methodology
Recruitments and study completion rates
Scales used to measure the outcomes
Outcomes and times of measurement
Indicators of acceptability by user and adverse effects
Risk of bias assessment

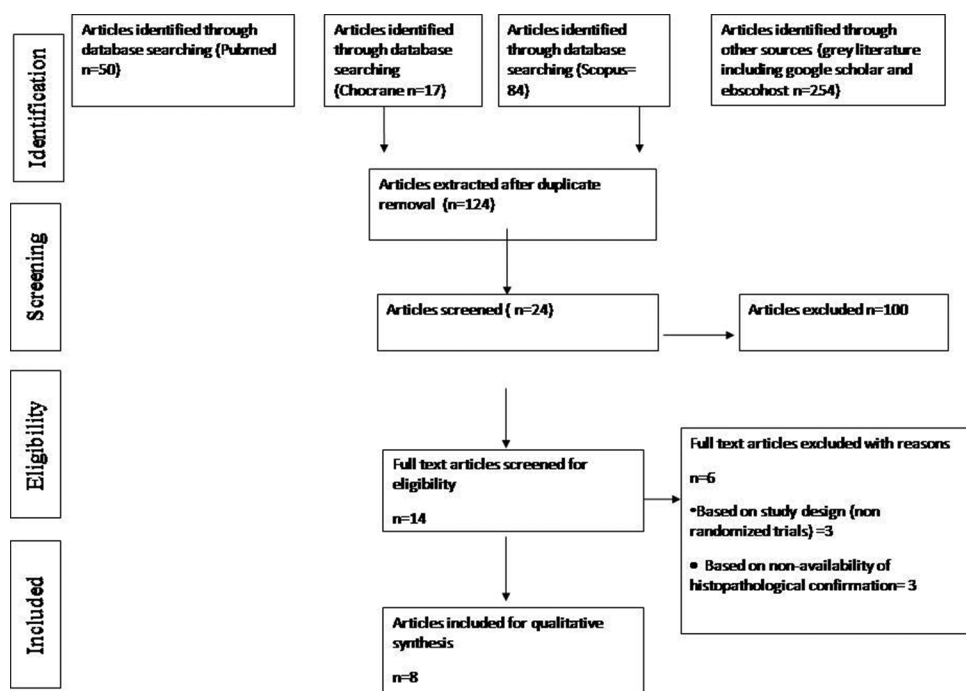


Figure 1: Flowchart summarizing article selection process

Characteristics of eight studies included for the systematic review [Table 3]

All the included studies were prospective RCTs carried out in secondary care centers. Studies included clinically and histopathologically were proven cases of OLP. A total of 354 (males = 117 and females = 237) symptomatic OLP participants participated in the trials with a mean of 44 per study, female predominance, and an age range of 18–75 years. The commonly involved oral mucosal areas were buccal mucosa followed by tongue and gingiva. Types of lesions commonly observed in the participants were mixed, erosive, atrophic, and reticular types in descending order. The trials included steroids in topical form in all studies except one.^[18-25] In this last study, two types of steroids, dexamethazone (0.1% gel) and prednisolone (capsule 15mg), were given topically and orally, respectively, in two different arms.^[25] The topical steroids included triamcinolone acetate 0.01% in gel and paste forms and dexamethazone acetate 0.1% in gel and mouthwash (0.5mg) forms.^[18-25] Two studies had an additional placebo group.^[20,23] HIs included curcuminoids in three studies and aloe vera, cedar honey, quercetin, glucosides of paeony, and lycopene in the remaining five studies each.^[18-25] The modes of administration of HI were as follows: curcuminoids were administered systemically in the form of tablets^[23] and topically in the form of paste and gel, and total glucosides of paeony and lycopene were administered systemically in the form of capsules and pills, respectively, and aloe vera mouthwash in the form of topical therapy had to be expectorated whereas cedar honey liquid had to be swished and swallowed.^[18,19,21-25] One study included the same intervention in different

arms with different dosing patterns (curcuma longa extract 10 mg in gel form thrice for 3 months in one arm and six times for 3 months in another arm).^[24] Antimycotic drugs, fluconazole capsules 100 mg and nystatin suspension 10,000 U, were administered in two studies, whereas 1% sodium bicarbonate rinse was administered in another study.^[19,20,22,23]

Outcomes

Assessment criteria for outcome were found to vary across the studies. For the evaluation of burning sensation and pain, out of the eight included studies, four studies used only VAS, two studies used NRS, and two studies used VAS and pain index.^[18-25]

Clinical response of decrease in size and severity of lesion was measured in all trials but by different grading methods. Thongprasom clinical grading criteria were used by five studies and modified oral mucositis index (MOMI) in one study.^[18,21-25] Two studies evaluated clinical response by severity index and severity improvement.^[19,20] Size measurements were done with sterile caulis, periodontal probe, and grids, whereas few studies did not specify their methods of measurements of lesion size.^[18-25]

Times of follow-up measurement

Six studies had a total follow-up time of 4 weeks, one had a follow-up time of 3 months, whereas another study had 6 months of follow-up time.^[18-25]

Effects of herbal intervention versus steroids

Statistically nonsignificant difference was noted between the HIs and the steroid interventions in terms of relief

Table 3: Details of randomized controlled trials of herbal interventions with steroids with their relevant results

Studies	Number of participants in each and type of intervention received	Herbal intervention type with dose and duration	Steroid intervention type with dose and duration	Adverse effects	Outcome evaluations		
					Relief in burning sensation and pain	Decrease in the size and severity of lesion	Other
Mansourian <i>et al.</i> , 2011 ^[18]	G1=23 Intervention: Herbal G2=23 Intervention: Steroid	Aloe Vera mouthwash 2 tablespoons for 2 min, QID for 1 month	Triamcinolone acetate 0.1%, thin layer application, QID for 1 month	-	Evaluated by VAS: Statistically nonsignificant difference between the two groups	Evaluated by Thongprasom criteria: Statistically nonsignificant difference between the two groups	-
Sanatkhami <i>et al.</i> , 2014 ^[19]	G1=15 Intervention: herbal + steroid G2=15 Intervention: steroid	Cedar honey, 20 ml TDS via the swish and swallow technique for 4 weeks	Dexamethasone mouthwash, 0.5 mg QID and fluconazole capsule 100 mg OD for 4 weeks	Mild burning sensation in G 1 cases	Evaluated by VAS and pain index: Statistically nonsignificant difference between the two groups	Evaluated by severity index and severity improvement index : Statistically nonsignificant difference between the two groups	Improvement of severity index and Improvement of pain index: Statistically nonsignificant difference
Amirchaghmaghi <i>et al.</i> , 2015 ^[20]	G1=15 Intervention: herbal + steroid G2=15 Intervention: steroid + Placebo capsules	Quercetin hydrate Capsule 250mg, two capsules BD for 4/8 weeks	Dexamethasone mouthwash 0.5 mg, QID along with nystatin suspension 10,0000 U	Well tolerated	Evaluated by VAS and pain index: Statistically nonsignificant difference between the two groups	Evaluated by severity index: Statistically nonsignificant difference between the two groups	Improvement of severity index and Improvement of pain index: Details not provided.
Kia <i>et al.</i> , 2015 ^[21]	G1=25 Intervention: herbal G2=25 Intervention: steroid	Curcuminoid 5% paste, TDS for 4 weeks	Triamcinolone acetate 0.1% paste TDS for 4 weeks	G 1=Burning sensation, itching, mild swelling, xerostomia and yellowish discoloration of gingiva G 2=Burning sensation, mucosal desquamation	Evaluated by VAS : Statistically nonsignificant difference between the two groups	Evaluated by Thongprasom criteria: Statistically nonsignificant difference between the two groups	Improvement index=Statistically nonsignificant difference

Contd...

Table 3: Contd...

Studies	Number of groups (G) with number of participants in each and type of intervention received	Herbal intervention type with dose and duration	Steroid intervention type with dose and duration	Adverse effects	Relief in burning sensation and pain	Outcome evaluations Decrease in the size and severity of lesion	Other
Zhou <i>et al.</i> , 2016 ^[22]	G1 ROLP [¶] A: n=17 Intervention: topicalsteroid B: n=22 Intervention: herbal + topical steroid G2 EOLP C: n=17 Intervention: systemic steroid D: n=17 Intervention: herbal + systemic steroid	Total glucosides of paeony capsule 200 mg capsules, 400 mg TDS, once a month for 6 months	Topical: Dexamethasone acetate 0.1%, BD until symptom resolution 1% sodium bicarbonate rinses Systemic: prednisolone 15mg daily for 1 month until symptom resolution followed by tapering	Diarrhea	Evaluated by VAS: Statistically significant difference between ROLP A and ROLP B ($P<0.05$) and EOLP C and EOLP D ($P<0.01$), at 4 th and 6 th months	Evaluated by Thongprasom criteria: Statistically significant difference between ROLP A and B ($P<0.05$) and EOLP C and EOLP D ($P<0.01$), at 4 th and 6 th months	Effective rates: significantly higher in ROLP B and EOLP D as compared to ROLP A and EOLP C respectively.
Amirchaghma-ghi <i>et al.</i> , 2016 ^[23]	G1=12 Intervention: herbal + steroid G2=8 Intervention: steroid + Placebo capsules	Curcuminoid tablets 500 mg, four tablets BD for 4 weeks	Dexamethasone mouthwash 0.5 mg, QID alongwith nystatin suspension 10,0000 U	Well tolerated	Evaluated by VAS: Statistically nonsignificant difference between the two groups	Evaluated by Thongprasom criteria: Statistically nonsignificant difference between the two groups	-
Thomas <i>et al.</i> , 2017 ^[24]	G1=25 Intervention: steroid G2=25 Intervention: herbal (a) G3=25 Intervention: herbal (b)	Curcuma longa extracts 10 mg gel thrice for 3 months Curcuma longa extracts 10mg gel six times for 3 months	Triamcinolone acetonide 0.1% oral paste thrice with tapering	Well tolerated	Evaluated by numeric rating scale: Statistically nonsignificant difference between the three groups	Evaluated by MOMI: Statistically nonsignificant difference between the two groups	-
Arbabi-Kalati and Farahmand 2017 ^[25]	G1=15 Intervention: herbal + steroid G2=15 Intervention: herbal	Lycopene pill of 15 mg OD for 1 month	Triamcinolone acetonide 0.1% oral paste QID for a month	-	Evaluated by numeric rating scale: Statistically nonsignificant difference between the two groups	Evaluated by Thongprasom criteria: Statistically nonsignificant difference between the two groups	-

QID: Four times daily, VAS: Visual analog scale; TDS=Thrice daily, OD: Once daily, BD: Twice daily, ROLP: Reticular oral lichen planus, EOLP: Erosive oral lichen planus, MOMI: Modified oral mucositis index

in burning sensation and decrease in size and severity of lesions in all the RCTs, except one in which statistically significant difference was noted.^[18-22,23-25] In this last study, the HI groups received total glucosides of paeony capsules (TGPC) along with topical dexamethasone 0.1% in one group and TGPC along with prednisolone 15 mg in another group, which were compared with only steroid intervention groups receiving dexamethasone 0.1% and prednisolone 15 mg, respectively.^[22] The effect measures at different follow-up periods also showed higher improvement rates in HI groups along with steroid groups as compared to steroid intervention group alone. Improvement index done by three studies showed statistically nonsignificant difference.^[19-21]

Adverse effects [Table 3]

Quercetin capsules and curcuminoids in gel and tablet forms were well tolerated, but participants receiving curcuminoids in paste form reported of burning, itching, desquamation, and discoloration of gingiva and xerostomia.^[20,21,23,24] Mild burning and diarrhea have been reported by cedar honey and TGPC.^[19,22] Adverse effects related to the use of aloe vera and lycopene were not reported. Adverse effects to steroids were reported as burning sensation and mucosal desquamation.^[18,21,25]

Only two studies followed up the participants after discontinuation of the intervention for 1 month and no recurrences were reported by any of the studies.^[18,20]

Risk of bias assessment [Table 4]

The included RCTs (n = 8) were assessed for risk of bias by the Cochrane risk-of-bias tool for RCTs [Appendix D].^[17] The studies were individually assessed under the following five domains: selection, performance, attrition, reporting, and other bias. The judgment of risk of bias was given as low, unclear, or high for each of the five domains and accordingly the quality was graded as having low risk, moderate risk, or high risk of bias. Table 2 summarizes the risk of bias assessment of the eight studies included in the present review.

Selection bias

Random allocation of the participants to the study arms ensures minimization of selection bias. Out of the 8 shortlisted studies, few used an electronic random number generator to create a list of random number, whereas others used random numbering table and simple randomization method.^[18-20,22,25] Block randomization was used by two studies with block size of six in one study and quota sampling method in another.^[21,24]

Allocation concealment

Pharmacy controlled randomization was advocated in four studies, whereas others did not specify their method of allocation concealment.^[18-25]

Selective reporting

All the studies reported their prespecified outcomes, except one. This study did not specify the outcomes during the follow-up visits.^[25]

Other bias

All the eight studies appeared free of other sources of bias.

Blinding

In four studies, both participants and outcome assessors were blinded.^[18,20,21,23] In two studies, only outcome assessors were blinded, whereas in two studies, nothing has been addressed about blinding.^[19,22,24,25]

Incomplete outcome data

Primary and secondary outcomes were adequately reported by all the studies. Four studies reported the number of attrition or exclusions along with the reasons, whereas two studies did not address anything on this matter as all the enrolled participants completed the study.^[18,19,21-25] Less than 10% dropout rate was observed in three studies, whereas dropout rate between 10% and 20% was observed in one study.^[19,21,22,24]

Meta-analysis of the pooled data could not be performed due to marked heterogeneity among the included studies. The main reasons were as follows: variations in the HIs and the steroid interventions along with variations in the modes of drug delivery and dosing patterns, variations in the assessment criteria of outcome variables, and variations also in their reporting.

Discussion

Efficacy of a new therapy could be judged only when it is compared with the standard or active intervention under standard conditions. Corticosteroids for OLP could be considered as standard intervention as its efficacy has already been proven earlier, but its use could be limited due to the complications associated with it.^[26,27] Currently, natural therapies have gained lots of momentum. Being natural, they are abundant, safe, and cost-effective which could have let to their trials in various health-related problems. OLP is one such condition, in which herbal therapies have also been tried. Being a chronic autoimmune condition, OLP is associated with interference in daily life activities which could adversely affect the psychological well-being of the patient. Till date, complete cure of OLP has not been evidenced. Most of the patients experience recurrence of lesions with symptoms and this could lead to a poor quality of life. Evidence from the clinical trials could help researchers and clinicians to provide a safe and effective therapy for long term. Furthermore, the various constituents in a single herb accommodate a host of responses which could be beneficial from complete health point of view. Considering this perspective, a systematic

Table 4: Risk of bias assessment of the eight included randomized control trials

Studies	Random sequence generation	Allocation concealment	Selective reporting	Other bias	Blinding of participants	Blinding of outcome assessment	Incomplete outcome data	Quality assessment
Mansourian <i>et al.</i> , 2011 ^[18]	Low (random number generated through software)	Low (identical sealed packet of medication to be picked up from the pharmacist)	Low (all outcomes reported)	Low (no other bias detected)	Low (subjects were blinded)	Low (outcome assessors blinded)	Low (outcome data was complete)	Low risk of bias
Sanatkhani <i>et al.</i> , 2014 ^[19]	Low (electronic random number generator was used)	Unclear (not described in sufficient detail)	Low (all outcomes reported)	Low (no other bias detected)	High (subjects not blinded)	Low (outcome assessors blinded)	Low (outcome data was complete)	High risk of bias
Amirchaghmaghi <i>et al.</i> , 2015 ^[20]	Low (Random number generated through software)	Low (identical capsules of interventions provided by the pharmacist)	Low (all outcomes reported)	Low (no other bias detected)	Low (subjects were blinded)	Low (outcome assessors blinded)	Low (outcome data was complete)	Low risk of bias
Kia <i>et al.</i> , 2015 ^[21]	Low (Blocked randomization was done)	Low (similar oral pastes provided)	Low (all outcomes reported)	Low (no other bias detected)	Low (subjects were blinded)	Low (outcome assessors blinded)	Low (outcome data was complete)	Low risk of bias
Zhou <i>et al.</i> , 2016 ^[22]	Low (Random numbering table was used)	Unclear (not described in sufficient detail)	Low (all outcomes reported)	Low (no other bias detected)	High (subjects not blinded)	Low (outcome assessors blinded)	Low (outcome data was complete)	High risk of bias
Amirchaghmaghi <i>et al.</i> , 2016 ^[23]	Low (Computer-generated random number table was used)	Low (identical tablets in identical containers were provided)	Low (all outcomes reported)	Low (no other bias detected)	Low (subjects were blinded)	Low (outcome assessors blinded)	Low (outcome data was complete)	Low risk of bias
Thomas <i>et al.</i> , 2017 ^[24]	Low (simple randomization was done)	Unclear (not described in sufficient detail)	Low (all outcomes reported)	Low (no other bias detected)	Unclear (not described in sufficient detail)	Unclear (not described in sufficient detail)	Low (outcome data was complete)	High risk of bias
Arbabi-Kalati and Farahmand 2017 ^[25]	Low (blocked randomization was done)	Unclear (not described in sufficient detail)	Unclear (insufficient information regarding outcomes during the follow-up visits)	Low (no other bias detected)	Unclear (not described in sufficient detail)	Unclear (not described in sufficient detail)	Low (outcome data was complete)	High risk of bias

review to evaluate the efficacy of HI as compared to standard intervention by corticosteroids was planned.

Adjuvant therapy is given with the motive of providing synergistic action and enhancing faster relief. In the present review, seven RCTs showed nonsignificant differences between the HI and SI.^[18-21,23-25] Out of these, in four RCTs, the participants received HI as an adjuvant to corticosteroids.^[19,20,23,25] In these studies, it is difficult to comment on the role of herbal medicines, as in all these four studies, the result is statistically nonsignificant. If the results would have been statistically significant, it would have been easy to comment on the synergistic action of HI with that of steroid in enhancing faster relief. On the contrary to this, in one study, TGPC was given as an adjuvant to steroid and had shown significant result, but the study was at a very high risk of bias.^[22] In the remaining three RCTs, the participants received only HI compared to only steroid intervention. The results were nonsignificant, indicating that HI was equally effective to that of SI in resolving the signs and symptoms of OLP.^[18,21,24] The HI included in these studies were aloe vera mouthwash, curcuminoid paste, and curcuma longa extract gel.^[18,21,24] Thus, aloe vera mouthwash and curcuminoid paste could be considered equally effective to that of steroid as the risk of bias in these studies was also low.^[18,21] Alternatively, aloe vera mouthwash and curcuminoid paste could be considered as a substitute therapy in place of steroids in OLP patients. However, it would be difficult to comment on the efficacy of curcuma longa extract gel, as the study has a higher risk of bias.^[24]

Curcumin has shown to exhibit antioxidant, anti-inflammatory, antimicrobial, and anticarcinogenic activities.^[28] It is safe even at high doses, albeit with occasional side effects such as diarrhea.^[23,29] Aloe vera also exhibits anti-inflammatory action by virtue of its cyclooxygenase inhibition action and decrease in the leukocyte adhesion molecules and tumor necrosis factor alpha levels.^[30] In addition, it also has antioxidant properties.^[31]

Herbal therapy has the advantage of providing multiple pharmacological effects mainly due to the combination of various phytoconstituents available in a single herb. This could be the reason for its utilization in various health-related problems. The herbal medicines tried in OLP mainly curcumin, aloe vera, honey, propolis, quercetin, lycopene, and glucosides of paeony, all have proved to have anti-inflammatory, antioxidant, and immunomodulatory properties. However, their mostly nonsignificant results in the trials could be due to the insufficient doses or the forms, in which they might have been tried. Thus, more stringent protocols of RCTs with varying doses and forms of intervention should be carried out to provide evidence for the efficacy of herbal therapies in OLP.

Previous systematic reviews on interventions in treating OLP included RCTs involving all types of

interventions (including herbal) compared with placebo or other active treatment. They stated insufficient evidence to comment on the effectiveness or superiority of any specific intervention in reducing signs and symptoms of OLP.^[32,33] In the present systematic review, only those RCTs on OLP patients were included which had HIs compared to standard treatment (corticosteroids). Apart from the two RCTs involving curcumin and aloe vera, in the present review also, the remaining RCTs provided questionable evidence to support herbal therapy effectiveness.

Limitations and recommendations

The relatively less number of RCTs with different HIs, in different forms and doses, varying study designs, different scoring patterns for outcome evaluations, and different follow-up intervals warrant more research in this area, but with uniformity in the abovementioned aspects. Efforts should also be taken to reduce the amount of bias in the RCTs.

This would enable one to draw a meta-analysis to further confirm the efficacy of individual herbal medications over steroids in a larger sample. Furthermore, the RCTs should encourage herbal medications either alone or as an adjuvant therapy to steroids to confirm their respective efficacies. To ensure long-term benefits of medications, longer follow-up periods should also be planned along with assessment of quality of life.

Conclusion

Although two RCTs involving curcumin (Mansourian *et al.* 2011) and aloe vera (Kia *et al.* 2015) as the herbal therapy have shown promising results in resolving the signs and symptoms of OLP, the present systematic review suggests insufficient evidence to support most of the other herbal therapies.^[18,21] To confirm their efficacy, more research in standard conditions (RCTs with low risk of bias) is required.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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