



Effectiveness of Clobetasol Propionate in the Treatment of Oral Lichen Planus - A Systematic Review

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Abstract

Background: Lichen planus is an inflammatory disease affecting skin and oral mucosa with a typical Wickham's white striae and keratotic cap. Clobetasol propionate is a corticosteroid used for minimizing pain and discomfort associated with the disease.

Aim: To pool the data on the effectiveness of topical application of Clobetasol propionate in oral lichen planus patients.

Methodology: Search strategy was framed and relevant articles were identified through titles, abstract and full text read in PubMed and Google scholar published between 1st January 2000 and 31st October 2019. Other language articles were translated as required. Only randomized controlled trial, clinical studies using Clobetasol propionate in any form and dosage and assessing its effectiveness in oral lichen planus were included. Case reports and series, reviews, editorials, conference proceeding were excluded.

Results: A total of nine studies were included in the final synthesis of this review from the initial count of 88. The reasons for exclusion were duplicate articles, irrelevant titles, study design and no required data provided. All the studies favoured the use of topical clobetasol propionate in various concentrations with presence of few side effects.

Conclusion: Topical application of Clobetasol propionate is a promising drug to be used in oral lichen planus to reduce the signs and symptoms of lesion size, pain and burning sensation. The widely used concentration was 0.05% followed by 0.25%. Future studies with malignant transformation with longer follow-ups are recommended.

Keywords: Oral Lichen Planus; Corticosteroids; Clobetasol Propionate; Pain; Burning Sensation; Lesion Size

Introduction

Lichen planus is an inflammatory disease of skin. The counterpart of this disease in the one affecting oral mucosa and is known as oral lichen planus. Oral lichen planus usually affect the individuals in the 4th decade of their life. The predilection for women is more over men with a ratio of 14:1. The overall burden shared by this disease accounts to 1.27% [1]. Clinically oral lichen planus appears either as atrophic type consisting erythematous lesions that are surrounded by reticular components, asymptomatic reticular type identified clinically, plaque type, erosive type, papular type or bullous type [2]. The most widely recognized type of Oral lichen

planus is the reticular type, which shows up as a network of overlapping white striae, followed by ulcerative (erosive), atrophic and plaque types [3]. The lesion shows a peculiar period of remissions wherein symptoms appear and regress at particular intervals [4]. Oral lichen planus often appears reciprocally on the buccal mucosa, and as often as possible appears on the tongue, gingiva, mucobuccal fold or numerous other oral sites. Anxiety and stress are reported to be the main etiological factors of oral lichen planus [5].

Literature reports various treatment modalities in an attempt to reduce the pain and burning sensation. Corticosteroids, retinoids,

ultraviolet radiation of the lesion and use of lasers like CO₂ are used for providing palliative care to the patients [6]. Corticosteroids are the most widely accepted therapeutic options available for oral lichen planus. Though various other options are available along with steroids but none have provided a definitive cure. All the measures are focused on reducing the pain and discomfort [7]. Amongst the steroids the topical corticosteroids (TCSs), including betamethasone, clobetasol, topical calcineurin inhibitors, dexamethasone and triamcinolone [6]. Topical steroids are always preferred as the first-line treatment for various muco-cutaneous conditions. They help in limiting the irritation caused over dermis and upper dermis [8].

Clobetasol is a highly potent steroid among all the topical steroids that helps to reduce inflammation in the body. It has immunosuppressive and antimetabolic effect thus has a great influence of the differentiation and inhibition of cells [9]. Clobetasol topical is used to treat inflammation and itching caused by plaque psoriasis or skin conditions that respond to steroid medication. It has proved its effectiveness in the treatment of atopic dermatitis and vulvar lichen sclerosus [9]. Its use is contraindicated in infants, toddlers, and children under 12 years of age [7]. Since it is a high potency drug, it surely has positive effects over the lichen planus lesion. But since there is no literature found on the pooled effectiveness of Clobetasol propionate on oral lichen planus this systematic review was initiated with a focused question of “What is the effectiveness of clobetasol propionate in the treatment of oral lichen planus?”.

Methodology

Literature search

A systematic search was carried out in database of PubMed and Google scholar. Search terms relevant to the topics were selected with the help of MeSH library related to Clobetasol propionate, oral lichen planus and effectiveness. Free text terms were also used and a search strategy was framed to obtain relevant articles through PubMed (Table 1). Filters were set for article type at clinical trial, clinical study, comparative study, randomized controlled trials and human species with best match option. Apart from search strategy the articles were also selected by chasing cross references of the selected studies, speciality journals and grey literature.

Eligibility criteria

All *in-vivo* studies with study designs of randomized controlled trials and clinical studies containing clobetasol propionate as a medicament in treating oral lichen planus regardless of dose, fre-

quency, duration the dosage; all forms of clobetasol propionate used like ointments, gels and creams used as an intervention were eligible for the review. The articles published between 1st January 2000 and 31st October 2019 available in English language or were possible of getting translated into English language were included. While studies wherein other high potency steroid was used apart from clobetasol propionate; were non-clinical studies and studies reporting data through letter to editors, patents, short communications, review articles and conference proceedings were excluded from the review.

Sr. No.	Search strategy	Articles in hit	Articles selected
1	Oral lichen planus[ti] and clobetasol[ti]	12	10
2	Oral lichen planus[ti] and clobetasol propionate	32	10
3	Lichen planus oral and clobetasol gel	7	4
4	Lichen planus oral and clobetasol gel and recurrence	2	1
5	Lichen planus oral and clobex and healing	3	0
6	Lichen planus oral and cormax and recurrence	9	3
7	Oral lichen planus and clobetasol mouthrinse	0	0
8	Oral lichen planus[ti] and temovate and malignant transformation	4	0
9	Oral lichen planus and (temovate or clobetasol or dermovate) and malignant transformation	4	0
10	Oral lichen planus and (temovate or clobetasol or dermovate) and (malignant transformation OR recurrence)	13	3
11	Others (Google scholar)	2	2
	Total	88	33

Table 1: Search strategy used in PubMed database.

Study selection

The screening process was conducted by one author independently. At stage 1, the titles of all the studies were screened. The articles that were not eligible through the titles were excluded and at stage 2 the abstracts of the remaining articles were read. This

was followed by further exclusion to read the full text. After obtaining the full texts of the articles they were screened by reading the whole article and then decided if they met the inclusion criteria. Uncertainties encountered were resolved by the help of second author.

Data extraction

A standardized data extraction form was prepared in Microsoft Excel with the help of an expert. The sheet included information on author’s name and publication year, the place of the study, study design, age of the patients included in the respective studies, details about the intervention used, duration of the drug and outcomes in the form of clinical improvement, pain improvement and compliance to the drug along with the side effects observed. Finally a brief inference of the study was provided along with the remarks if any.

Results

The articles included at each step of this review are presented in the form of PRISMA flow chart (Figure 1). A total of 88 articles were found through PubMed and three through Google scholar. The initial screening of titles yielded 33 studies which were subjected

for duplicate removal. Around 19 articles were duplicates. The abstracts of the remaining fourteen articles were read and four were excluded. After reading full texts of remaining ten articles, one was excluded as it was a review. All the studies included in the final synthesis compared Clobetasol with some other drug or treatment modality. The data characteristics of the included studies are provided in table 2.

Campisi G., *et al.* [10] reported that Clobetasol with 0.025% concentration was effective as a new drug in the treatment of lichen planus. Conrotto D., *et al.* [11] through their trial inferred that Clobetasol though effective in inducing clinical improvement, but possess side effects. Moreover, the effectiveness diminished post treatment duration. The patients in Rafdar L., *et al.* [12] study were provided with 0.05% Clobetasol ointment for 6 weeks and showed reduction in size and pain measures. Corrocher G., *et al.* [13] too assessed the same concentration as found it to be an effective measure in reducing symptoms scores in lichen planus patients. Symptoms improvement after 2 month follow-up was reported by the use of 0.05 and 0.025% clobetasol [14].

Study Id	Authors	Year of publication	Country	Study design	Sample size	Age	Intervention	Duration of the drug	Outcome			Side effects	Inference	Remark
									Clinical improvement	Pain score improvement	Compliance to the drug			
1	Campisi G et al	2004	Italy	Randomized controlled trial	18	61.1 years	Clobetasol propionate	2 months	82.35%	48.9	29.4% good compliance	Acute oral candidias	Clobetasol is appropriate treatment for OLP lesions	
2	Conrotto D et al	2006	Italy	Randomized controlled trial	19	66 years	Clobetasol propionate	2 months	95.00%	57.89%	Less compliance	Dyspepsia, skin rashes and parotid swelling	Clobetasol propionate gel is effective in treating oral lichen planus	Less expensive
3	Rafdar L et al	2008	USA	Randomized controlled trial	14	58.2 years	Topical clobetasol 0.05%	6 weeks	92.85%	62%	Not reported	None	Clobetasol showed a significant role in treating oral lichen planus	Short duration study
4	Corrocher G et al	2008	Italy	Randomized controlled trial	16	43.6 years	0.05% clobetasol ointment	4 weeks	Not reported	50%	100%	None	Clobetasol propionate ointment is effective in treating oral lichen planus	Short week study
5	Carbone M et al	2009	Italy	Randomized controlled trial	15	57.7 years	0.05% clobetasol propionate gel	2 months	93.30%	60%	100%	None	Clobetasol propionate gel is effective in treating oral lichen planus	
6	Sonthalia S and Singal A	2012	India	Randomized controlled trial	20	34.7 years	0.05% clobetasol ointment	8 weeks	40%	90%	Not reported	None	Clobetasol propionate ointment can be considered as a choice of drug in treating oral lichen planus	Small sample size, short observation period
7	Dillenburg CS et al	2014	Brazil	Randomized controlled trial	21	>21 years	0.05% clobetasol gel	8 weeks	>56%	mean 4.29 score	Not reported	Transien local burning sensation, gastrointestinal distress	Clobetasol is appropriate treatment for OLP lesions but sideeffects should be considered	27.3% patients showed recurrence
8	Hettiarachchi PVKS	2017	Sri Lanka	Randomized controlled trial	34	46.7 years	0.05% clobetasol propionate cream	5 weeks	Significant improvement seen	mean 1.59 score	Not reported	Development of candidiasis	Clobetasol is appropriate treatment for OLP lesions	Small sample size, short observation period
9	Arduino PG et al	2018	Italy	Randomized controlled trial	16	66.28 years	0.05% clobetasol propionate cream	8 weeks	87.50%	87.50%	100%	Abdominal pain, mild hyperglycemia	Clobetasol is useful in treating oral lichen planus	Long lasting use is poor

Table 2: Data extraction sheet of the included studies (Attached as a supplement file).

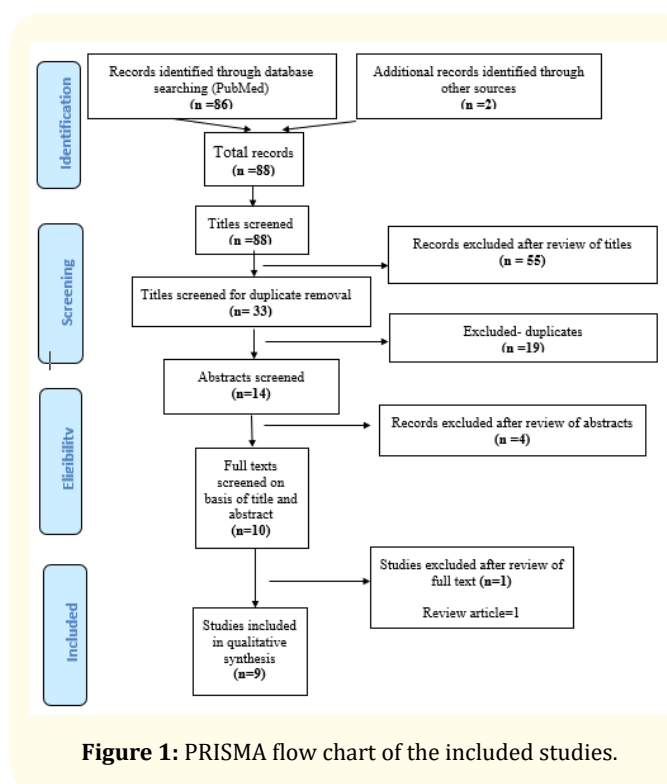


Figure 1: PRISMA flow chart of the included studies.

Similar was reported by Sonthalia S and Singal A [15] favouring clobetasol propionate 0.05%. On the contrary, Dillenburg CS., *et al.* [16] reported that though clobetasol is effective in treating oral lichen planus but in few it might show worsening of condition. Clobetasol propionate 0.05% cream was found to be an effective alternative to topical steroid in treating oral lichen planus [17]. Clobetasol use in symptomatic patients of atrophic-erosive oral lesions proved to be effective in reducing clinical signs in almost 87.5% patients [18].

Discussion

Clobetasol propionate has been used in the clinical setting to provide relief to the patients from the pain and burning sensation. Though it is not the cure but it does help in overcoming the agony of the patients by diminishing the clinical signs. In this systematic review only nine articles could fit into the eligibility criteria. Clobetasol is a high potency drug and is in use since a very long time in the treatment regimen of skin oral mucosal related diseases. The search for this review was kept for a period of last 19 years. Most of the studies reported were conducted among Indian patients.

The sample size ranged from 14 patients with oral lichen planus in Rafdar L., *et al.* [12] study to a maximum of 34 reported in Het-

tiarachchi PVKS., *et al.* [17] study. Most of the studies have a sample ranging between 10-15 patients. Overall the sample size in all the studies was very small. When it came to age, almost all the studies except one had patients between their 5th to 6th decade of life. All the patients were quite old. Study reported by Dilleburg CS., *et al.* [16] did not represent a clear age of their sample but even in their study all the patients were above 21 years of age. Clobetasol propionate was topically applied in all the studies in the form of either gel, ointment or a cream.

All the studies introduced clobetasol in the concentration of 0.05% except few studies like Campisi G., *et al.* [10] and Corotto D., *et al.* [11] did not report about the form of medicament used. The drug was asked to apply topically for a maximum of 2 months in Campisi G., *et al.* [10] and Conrotto D., *et al.* [11] study and was applied least in Corrocher G., *et al.* [13] study. Overall the duration of dose differed a lot between the included studies. When outcome was assessed in the included studies of this systematic review the interest was to know about the overall clinical improvement, pain reduction as an improvement and compliance of the drug by the patients. Overall all the studies showed remarkable percentages of improvement in their clinical parameters. The maximum improvement of 95% was observed in Corotto D., *et al.* [11] study while the lowest percentage of clinical improvement was reported by Sonthalia S and Singal A [15] study. Dillenburg CS., *et al.* [16] did not give a clear percentage but reported that the overall improvement was greater than 56%. A significant improvement was observed in study conducted by Hettiarachchi PVKS., *et al.* (2017).

Pain improvement in most of the included studies stood at average. A range of 48% to 62% was found in majority of the studies. Dillenburg CS., *et al.* [16] and Hettiarachchi PVKS., *et al.* [17] did not provide any percentage improvement in pain sensation but gave a mean improvement value while studies by Arduino PG., *et al.* [18] and Sonthalia S and Singal A [15] has a good pain score improvement in the oral lichen planus patients.

According to the reports of WHO non-compliance of any medication is accounted to the five elements namely; socioeconomic stats governed by education, income and employment; health care framework which includes poor medicine circulation, deficient or non-existent repayment or an absence of criticism on execution; treatment related elements; severity of the medications and patient's awareness including convictions, inspirations [19].

With the same concern as raised by WHO, the non-compliance towards the medication in one of the study included in this review was a result of complications suffered by patients due to clobetasol propionate. Dyspepsia, skin rashes and parotid swelling were the complications observed and thus patients avoided the daily dosages. While in other studies a high compliance was observed for the drug. Few studies like Sonthalia S and Singal A [15], Dillenburg CS., *et al.* [16], Hettiarachchi PVKS [17] and Rafdar L., *et al.* [12] did not report anything about the compliance towards the drug. In most of the studies the compliance was evaluated by the number of drugs remaining beyond the required numbers. Overall the included studies reported a clobetasol propionate a good choice of steroids for treating oral lichen planus. Though the cure does not yet exist but the drug surely helps to provide palliative care and reduce signs and symptoms of the patients. The review has limitation with respect to data searching with only two databases searched; there is a chance of missing out data from other databases.

Conclusion

Compiled data on clobetasol propionate proves to the drug to be effective in treating oral lichen planus. Drug, whether present in the form of cream, ointment or gel does not make any difference in its effectiveness. 0.05% is the widely used concentration. Compliance towards the drug plays major role in enhancing the clinical improvements with respect to lesion size, pain and burning sensation which comes in hand with the side effects like development of candidiasis making it essential to streamline the drug appropriately. To obtain further details, studies should report on the recurrence rate, malignant transformation through long follow-ups with larger sample size.

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