

# Topical Clotrimazole/Betamethasone use in Oral Erosive Lichen Planus

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## Abstract

Oral Lichen Planus (OLP) is a mucosal subtype of lichen planus, a chronic inflammatory disorder that affects the skin and mucous membranes. The manifestations of oral lichen planus vary from reticular, white papules and plaques to erythematous, atrophic, and erosive, with frank ulcers. Reticular OLP is often asymptomatic, but atrophic and erosive form can cause symptoms from burning to severe pain. The buccal mucosa and gingiva are commonly involved. The specific pathology is not understood, however a common theory is that an immune reaction against an exogenous antigen triggers the onset of an aberrant immune response, resulting in the onset of the disease. Oral lichen planus is considered to be a T-cell mediated chronic inflammatory tissue reaction against epithelial basal cells. The pain and discomfort of this condition can significantly impair the quality of life of patients is often the reason most seek treatment<sup>[1]</sup>.

Oral lichen planus is not a curable condition, and as such, treatment is mostly palliative and focused on alleviating symptoms and minimizing scarring. This includes both non-pharmacologic and pharmacologic therapy. Non-pharmacologic measures may help to reduce exacerbations of oral lichen planus, and include the following: good oral hygiene, elimination of mechanical irritation from dental equipment, avoidance of chewing on lips or mucosa, smoking cessation, and minimization of consumption of acidic, salty, spicy, hot, or sharp foods<sup>[1]</sup>.

Topical corticosteroids including triamcinolone acetonide, fluocinonide acetonide, betamethasone, clobetasol, and dexamethasone are commonly used first-line due to their ability to modulate inflammation and immune response. Local treatment with steroids is preferred over systemic treatment to reduce risk of serious adverse events. However, the biggest disadvantage in using topical steroids is their lack of adherence to the mucosa for a sufficient period of time. Systemic treatment is typically reserved for those who fail to respond to sufficient local therapy or for patients with both oral and extra oral mucosal involvement. Topical corticosteroids when applied for a short duration have been shown to be safe, but prolonged use can produce side effects such as the development of secondary candidiasis<sup>[2]</sup>, which necessitates antifungal treatment, atrophy of the oral mucosa<sup>[3]</sup>, and the risk of adrenal suppression is not insignificant<sup>[4]</sup>.

**Received date:** April 14, 2016

**Accepted date:** August 19, 2017

**Published date:** August 30, 2017

**Citation:** Courtney Schultz. Topical Clotrimazole/Betamethasone use in Oral Erosive Lichen Planus. (2017) J Pharm Pharmaceutics 4(2): 142- 144.

**DOI:** 10.15436/2377-1313.17.019

**Keywords:** Oral lichen planus (OLP); Betamethasone; Cochrane; Clotrimazole; Candidiasis.



## Introduction

### Evidence Using Betamethasone in Oral Lichen Planus

As patients with oral lichen planus are managed with medications that were neither developed nor intended for oral diseases, adequate efficacy studies are lacking. Thus, such factors as optimal dose, duration of treatment, safety and true efficacy remain to be elucidated.



The Cochrane collaborations, a non-profit organization that systematically reviews primary literature, published a systematic review Interventions for erosive lichen planus affecting mucosal sites. The review included 28 trials with a total of 1204 patients that evaluated all forms of treatment for symptomatic oral lichen planus. Local steroids were the active intervention in 14 studies. Six trials compared two different steroids in the treatment arms; two trials compared the same steroid with or without an anti-mycotic drug. Clobetasol was used in six trials, triamcinolone in seven trials, betamethasone in two trials, fluocinolone, fluticasone and dexamethasone all in one trial. One study by Hegarty et al., compared betamethasone sodium phosphate mouth rinse with fluticasone propionate spray and found that both interventions were effective in symptomatic management of oral lichen planus by reducing the surface area of the lesion and improving pain scores. There was no significant difference between the two interventions. The second study compared betamethasone oral mini-pulse therapy with topical triamcinolone acetonide oral paste. Systemic treatment with oral betamethasone 5 mg 2 days a week for 3 months was shown to significantly improve pain scores. The authors concluded that from this review that although topical steroids are considered first line treatment for oral lichen planus, there are currently no randomized controlled trials that compared steroids with placebo and there was no evidence to suggest that one steroid is any more effective than another<sup>[3]</sup>.

A study excluded by the Cochrane review showed that treatment with betamethasone valerate aerosol resulted in remarkable clinical improvement compared with placebo. Another study showed that treatment with betamethasone valerate pellets was significantly superior to hydrocortisone pellets<sup>[4,5]</sup>. The efficacy of betamethasone cream, ointment, lotion and gel in oral lichen planus has not been established. The package inserts for betamethasone ointment, lotion, cream, and gel recommend against its use orally with concern for increased absorption and systemic side effects<sup>[6-8]</sup>.

However, a number of studies have demonstrated the safety of topical steroids when applied to mucous membranes for short intervals and even up to 6 weeks. A small study by Lehner et al., reported that administration of betamethasone valerate did not affect plasma cortisol levels or suppress adrenal function in patients when administered anywhere from two days up to 8 months<sup>[9-12]</sup>.

Another study found that betamethasone dipropionate gel (augmented) was shown to cause inhibition of the HPA axis following application for one, two, or three weeks to diseased skin in some patients with psoriasis or atopic dermatitis. Patients should not be treated with betamethasone dipropionate gel (augmented) for more than 2 weeks at a time<sup>[16]</sup>.

### Evidence Using Clotrimazole in Oral Lichen Planus

Several studies have shown clotrimazole troches to be effective in curing and preventing oral candidiasis<sup>[17-19]</sup>. These findings are consistent with the clinical practice guidelines for the management of candidiasis by the Infectious Diseases Society of America. However there is no current evidence to support the use of clotrimazole cream or ointment for oral use.

### Conclusion

Topical betamethasone is a valid treatment option for patients with oral lichen planus, but there are currently no randomized, controlled trials comparing the efficacy of topical betamethasone to placebo for efficacy in oral lichen planus. However, the safety of using topical betamethasone valerate has been demonstrated in a small study and serious adverse events secondary to systemic absorption are reportedly rare. Risk versus benefit should be discussed with patients, when making a decision to trial betamethasone for use in oral lichen planus.

Careful consideration should also be given to the vehicle of the medication because clinical trials that have compared the strength of corticosteroids in various bases in the oral cavity are generally lacking. With higher potency steroids the potential for adrenal suppression with prolonged use, especially for a disease that is chronic like oral lichen planus, necessitates careful and frequent follow up.

If the decision is made to use a topical corticosteroid for oral lichen planus, patients should be instructed to apply the agent several times daily, maintain prolonged contact of the medication with the mucosa, and refrain from eating and drinking for 1 h afterwards. It is advisable to lower the strength of the preparation as soon as erosions heal and become asymptomatic. Once the disease becomes inactive and there is either an absence of lesions or the presence of only white reticular lesions, therapy may be temporarily discontinued.

It has been well established that the use of clotrimazole troches is effective in the prevention and treatment of oral candidiasis. However the efficacy and safety of clotrimazole cream and ointment have not been established for use in oral candidiasis. Further studies using this dosage form would need to occur before recommending their use in this indication.

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