Original Article

Comparison of Two Corticosteroids Mouthwashes in Treatment of Symptomatic Oral Lichen Planus

Ahadian H.[a], Akhavan Karbassi MH.[a], Vahidi AR.[b], Owlia F.[a]

[a] Dept. of Oral Medicine and Diagnosis, School of Dentistry, Yazd Shahid Sadoughi University of Medical Sciences, Yazd, IRAN
[b] Dept. of Toxicology and Pharmacology, School of Pharmacy, Yazd Shahid Sadoughi University of Medical Sciences, Yazd, IRAN

KEY WORDS
Oral Lichen Planus, Dexamethasone, Triamcinolone Acetonide, Corticosteroid mouthwashes

Received Nov. 2011;
Received in revised form April 2012;
Accepted: May 2012

ABSTRACT

Statement of Problem: Oral Lichen Planus (OLP) is a common chronic inflammatory mucocutaneous disease and has different types. If they are symptomatic, they must be treated. Corticosteroid, especially in topical form, is commonly used.

Purpose: The purpose of this study was to compare the therapeutic effects of two corticosteroid mouthwashes on treatment of symptomatic OLP.

Materials and Method: The participants of this single-blind study were 44 symptomatic OLP patients. They included 27 females and 17 males. They were randomly divided into two groups and were given drug A (Dexamethasone 0.1%) or B (Triamcinolone acetonide 0.2%) for four weeks. Extension of lesions (mm^2) and severity of symptoms (based on Visual Analogue Scale) were recorded before and after treatment (weeks 1, 2, 4). Finally, SPSS 12 was used and Man-Whitney test was run to analyze the data.

Results: In both groups extension of lesions and burning sensation decreased significantly during the four weeks of treatment. There was no statistically significant difference between the two groups. However, Dexamethasone 0.1% was more efficacious, in the fourth week, in reducing the size of lesions than Triamcinolone acetonide 0.2% ($p = 0.02$).

Conclusion: Both mouth washes were useful in diminishing pain and decreasing the size of lesions. However, Dexamethasone 0.1% was recommended for treatment of OLP because it was more efficacious than Triamcinolone acetonide 0.2%.

*** Corresponding author.** Owlia F. Dept. of Oral Medicine and Diagnosis, School of Dentistry, Yazd Shahid Sadoughi University of Medical Sciences, Yazd, IRAN
Tel: 0098-0351-6233933 Fax: 0098-0351-6250344 Email: dr.olia@ssu.ac.ir

Introduction

Oral Lichen Planus (OLP) is a relatively common chronic inflammatory muco-cutaneous disease with an incidence rate of 0.6-2% .It is manifested as reticular, papular, plaque-like, bullous and ulcerative lesions. In case of erosions or ulcers, since the patients may experience pain or discomfort, it is mandatory to take therapeutic measures to treat the disease [1-3].

The patients are recommended to be under regular follow-up examinations due to the premalignant nature of OLP [4].

Unlike the skin lesions, oral lesions of OLP are rarely resolved completely. One of the main goals of taking therapeutic measures in treating OLP is to relieve patients' pain and discomfort. Patients' problems vary from burning sensation or pain to difficulty in speech and swallowing [2-3].

If the lesions do not respond to treatment, there will be a probability of dysplasia and toluidine blue application should be considered for suspected cases.

So far different topical and systemic agents have been prescribed for treatment of OLP. Topical corticosteroids are the first treatment of choice [1]. Not only do they repair mucosal damages, but also they control the disease by having varied effects on lymphocytes [5-7].

Steroids, even in topical forms, can significantly reduce the number of HLA DR/T6 in langerhans cell per mm^2 desquamated epidermal cells. Mucosal and skin cells have the same properties in this regard. Another efficacy of corticosteroids is reducing T lymphocytes activity, which is dependent on langerhans cells [5-7]. Because of different side effects associated with systemic prescription of corticosteroids [1, 8], it seems that topical forms are better choices [8].

Some forms like pastes, ointments and lotions have been applied in different studies [9-12]. Topical agents had some success in controlling the disease [9-10]. Due to a better access to posterior areas of mouth and extensile surfaces, mouthwashes are more useful than other topical forms [3, 6, 12-13].

Clinicians frequently prescribe 0.2% Triamcinolone acetonide [6] and 0.1% Dexamethasone [13] mouthwashes for treatment of OLP. Therapeutic efficacy of these two agents in one trial has not been compared yet. Consequently, this study was an attempt to compare the therapeutic effects of two mouthwashes on treatment of symptomatic OLP.

Materials and Method

The participants of this single-blind randomized clinical trial were 44 patients with symptomatic OLP who referred to Yazd Medical University, Faculty of Dentistry, Department of Oral Medicine from October 2010 to May 2011.

As a rule, treatment must only be prescribed for symptomatic OLP [1]. Treatment manners were not influenced by the type of lesions. It is possible that a patient with erosive OLP shows no symptoms and be considered as a false negative case because of his high pain threshold. Papular, plaque-like lesions and reticular forms are never symptomatic. They are false positive. All forms of symptomatic OLP belong to one of these forms (erosive, atrophic or bullous). In this study all of them were treated similarly.

Diagnosis of OLP was made through approved histological and clinical criteria (Wickham's striae) [12]. Then patients, with the informed consent, were registered for the study. The participants were enrolled in two groups; A and B. The sample comprised of 44 people; 22 in each group. Randomization was done through simple random sampling and random number table was used to select the participants. The participants were then allocated to either of the two groups through using the sealed envelope method.

For the participants to take part in this study, they had to have symptomatic OLP and those having any systemic disease, pregnancy, allergy to these two drugs, dysplastic features in histological view and lichenoid lesions were set aside [17-20]. Furthermore, in following the arranged protocol among the patients, in case of any disorder, the relevant participant was excluded from the study. Patients were also withdrawn in case of the occurrence of any adverse effects which warranted the withdrawn of the drug.

At first, a complete description of situation was provided and lesions were assessed by a transparent grid calibrated to $1mm^2$ [12] Pain was evaluated by 0-10 scored VAS. Each patient was reassessed for all these aspects in the first, second and fourth weeks.

In group A, the 22 patients were treated with 0.1% Dexamethasone and in group B with 0.2% Triamcinolone acetonide mouthwashes. The drugs were prepared by the druggist and they were in similar

Table 1 Comparison of P-value and median of VAS before and after treatment

Mann-Whitney P-value	Triamcinolone acetonide median	Dexamethasone median	Group / VAS
0.31	6.5	6	VAS_0
0.59	3	3	VAS_1
0.55	0	0	VAS_2
0.75	0	0	VAS_4

Before treatment:VAS_0 VAS_1 first week:
VAS_2 second week: VAS_4 fourth week:

Table 2 Comparison of P-value and average of size of lesion before and after treatment

Mann-Whitney P-value	Triamcinolone acetonide median	Dexamethasone median	Group / Size of lesion mm2
0.3	930	725	S_0
0.15	541.5	455	S_1
0.1	370	268	S_2
0.02	209.5	100.5	S_4

S_0 Before treatment S_1 First week:
S_2 Second week: S_4 Fourth week

bottles. Bottle A consisted of 5cc of Dexamethasone ampoule 8mg/2ml (manufactured by Iran Hormone) in combination with 15cc normal saline [13]. Bottle B consisted of 1cc of Triamcinolone acetonide ampoule 40mg/ml (manufactured by Iran Hormone) and combined with 19cc normal saline [6]. The patients were instructed to rinse their mouths with mouthwashes 4 times daily for 4 weeks; after meals and before sleep at night. Each time they were treated with 5cc of prepared drug for 5 minutes. They had been informed not to drink or eat for 30 minutes after rinsing [6].

The results of patients' assessment were compared with their primary measures. Mann-Whitney and Wilcoxon tests were used to analyze the data, using SPSS 12.

Results

The participants of this study were 44 patients with symptomatic OLP (27 females and 17 males).The age range in group A, consisting of 8 males and 14 females, was 19-65 years. The age range in group B was 22-65 years and there were 9 males and 13 females in this group. The mean, standard deviation and median values of VAS among group A were 5.86, 2.03, and 6. They were also 6.4, 2.28, and 6.5 for group B, respectively.

The mean and standard deviation for extension of lesion in mm^2 for group A were 863.04 and 529.05 and for group B 1076.95 and 650.66 with the median of 725 and 930 for them respectively.

The use of drugs in both groups led to a dramatic decrease in pain and burning sensation among OLP patients and the change was statistically significant (p =0.0001). The difference between the two groups, as Mann-Whitney test revealed, was not statistically significant (p >0.05). Also this value was significant in long term usage of two groups with superiority of Dexamethasone (p =0.02).

Discussion

Topical forms of corticosteroids are preferred to systemic ones, because they are less harmful. On the other hand, corticosteroids are the first treatment of choice for autoimmune diseases like OLP [1]. Some side effects of corticosteroids in systemic use are an increase in serum glucose, cholesterol, blood pressure and peptic ulcer [1].

Mouthwash was selected as the treatment of choice for this study because it, compared to Orabase which was the form available in Iran, was much easier to be applied for all parts of mouth. Of course the patient was free of nausea after Orabase application [12].

The design of this study and frequent patient assessment made it impossible to have more than 44 participants. In this study, the number of participants was more than some of trials [2, 6, 13-18] and less than some others [19-21].

Furthermore, there was no need to match both groups for gender and age, because the participants in each group had self-examination before and after treatment.

In this study, 0.1% Dexamethasone and 0.2% Triamcinolone acetonide mouthwashes were compared with regard to their treatment efficacy. The results of this study were not parallel to those of other studies.

In Javadzade's study, 0.1% Dexamethasone mouthwash was used for treatment of OLP and pemphigus. He stated that symptoms of OLP patients weren't decreased significantly [13]. They tested that drug for the two diseases without any comparison. Another form which was mentioned in Bakhtiari's review article was 0.5 mg/5ml Dexamethasone elixir. It must be used four times daily, each time 1 teaspoon and for 2 minutes. However, it was recommended for moderate disease [3] and her article was just a review and recommended some therapeutic measures [3].

Although Triamcinolone acetonide is less potent than some corticosteroids, based on literature on this disease, it has therapeutic effects on OLP lesions [2, 14, 20].

Thongprasom and Laeijendecker compared 0.1% Triamcinolone acetonide in form of orabase to cyclosporine and tacrolimus [2, 17]. The results of their study revealed that the last two mentioned agents were not better than 0.1% Triamcinolone acetonide. P-value wasn't statically significant. Also burning sensation at the site of application was the frequent side effect of cyclosporine [1]. Due to the probability of dysplasia development in the long term use of tacrolimus,

application of this medicine must be limited to resistant cases [1].

They further stated that Triamcinolone was preferred to cyclosporine because the latter had some side effects, such as burning and itching sensation, swelling of lips and petechia-like bleeding. However, the results of their study weren't statistically significant [2], perhaps due to the low percent of Triamcinolone.

Motta compared 0.05% clobetasol propionate to placebo in a double-blind, crossover trial that was consisted of 22 cases of desquamative gingivitis [22].

With regard to the evaluation of the efficacy of 0.1% Dexamethasone mouthwash and 0.05% clobetasol propionate ointment for treatment of OLP, the findings of the present study were in contrast to those of the previous studies, in which the patients did not have a meaningful response to treatment [13, 22]. However, they were consistent with the findings of the previous studies on the evaluation of the efficacy of topical corticosteroids for treatment of OLP [2, 6, 10, 12].

Dalirsani divided their patients into two groups. The groups were treated with 0.2% Triamcinolone acetonide mouthwash with or without vitamin A. The results revealed that both agents were effective in reducing the size of lesion, pain and irritation. However, the patients who were treated with vitamin A had a relatively more desired improvement [14].

In this study, the amount of time which was needed to rinse with mouthwashes, four times daily, was 5 minutes. If orabase or ointment is used in the trials, the amount of time for rinsing cannot be specified because it is related to oral factors and can vary from patient to patient.

One pitfall in most of the previous studies is that they have not made any mention of the amount of time necessary for rinsing with mouth washes. Some researchers, such as Bakhtiari and Azizi considered one to two minutes as the appropriate amount of time to rinse the mouth and to increase the efficacy of agents on lesions [3, 12].

Four weeks were enough to improve the lesions and the participants were assessed prior to treatment and also in the first, second, and fourth weeks. Most of lesions were completely repaired in this short time. Through using the agents, VAS was reduced to zero in the second week and treatment was discontinued after four weeks. Fortunately, in this study, all of the patients responded well to treatment. Any kind of poor response is attributed to drug resistance. If any case was existed, it is rational to prescribe systemic approach of corticosteroids (40 mg/kg/day) for several days and taper gradually [1].

Considering the limited time, patients did not follow by clinician to evaluate the recurrence of the disease.

Conclusion

Based on the results of this study, there were no significant differences in reducing VAS and the extension of lesions between the two groups. Again, it is noteworthy that Dexamethasone can be used as the preferred treatment of choice because it is cost-effective and within reach. There was a statistically significant difference between the two groups in the fourth week in that 0.1% Dexamethasone was preferred to 0.2% Triamcinolone acetonide mouthwashes.

Acknowledgement

This study was done under the support of the members in Research Council of Yazd Shahid Sadoughi University of Medical Sciences and as a thesis. The authors would like to thank the council for their helps in carrying out this study. This study was a single-blind randomized clinical trial registered by code IRCT201011275256n1.

References

[1] Greenberg M, Glick M.Ship j. Burkets oral medicine diagnosis & treatment. 11th ed., Hamilton: BC Decker inc; 2008; p.85-95.

[2] Thongprasom K, Chaimusig M, Korkij W, Sererat T, Luangjarmekorn L, Rojwattanasirivej S. A randomized-controlled trial to compare topical cyclosporin with triamcinolone acetonide for the treatment of oral lichen planus. J Oral Pathol Med 2007; 36: 142-146.

[3] Bakhtiari S, Azimi Hosseini S, Ghaem Maghami A. Review of routine therapeutic management of common oral lesions. J Dent Sch, Shahid Beheshti Univ Med Scien 2008; 25: 348-356.

[4] Rad M, Hashemipoor MA, Mojtahedi A, Zarei MR,

Chamani G, Kakoei S, Izadi N. Correlation between clinical and histopathologic diagnoses of oral lichen planus based on modified WHO diagnostic criteria. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2009; 107: 796-800.

[5] Sharma S, Saimbi CS, Koirala B. Erosive oral lichen planus and its management: a case series. JNMA J Nepal Med Assoc 2008; 47: 86-90.

[6] Mansourian A, Momen-Heravi F, Saheb-Jamee M, Esfehani M, Khalilzadeh O, Momen-Beitollahi J. Comparison of aloe vera mouthwash with triamcinolone acetonide 0.1% on oral lichen planus: a randomized double-blinded clinical trial. Am J Med Sci 2011; 342: 447-451.

[7] Saxon A, Stevens RH, Ramer SJ, Clements PJ, Yu DT. Glucocorticoids administered in vivo inhibit human suppressor T lymphocyte function and diminish B lymphocyte responsiveness in vitro immunoglobulin synthesis. J Clin Invest 1978; 61: 922-930.

[8] Ashworth J, Booker J, Breathnach SM. Effects of topical corticosteroid therapy on Langerhans cell antigen presenting function in human skin. Br J Dermatol 1988; 118: 457-469.

[9] Buajeeb W, Pobrurksa C, Kraivaphan P. Efficacy of fluocinolone acetonide gel in the treatment of oral lichen planus. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2000; 89: 42-45.

[10] Rabiee M, Sahebjamee M. Effect of aqueous Triamcinolone Acetonide %0.2 suspension in treatment of oral Lichen Planus. J Guilan Univ Med Scien 2003; 12: 1-5.

[11] Carbone M, Arduino PG, Carrozzo M, Caiazzo G, Broccoletti R, Conrotto D, et al. Topical clobetasol in the treatment of atrophic-erosive oral lichen planus: a randomized controlled trial to compare two preparations with different concentrations. J Oral Pathol Med 2009; 38: 227-233.

[12] Azizi A, Lawaf Sh, Amani B. Comparsion treatment efficacy of adcortyl ointment (Triamcinolon in orabase) & triamcinolon mouthwashes in oral lichen planus. Shiraz Univ Dent J 2009; 10:25-30.

[13] Javadzade A, Javidi Z, Pakfetrat A. Evaluation of treatment effect of Dexamethazone 0.1% on oral lesions of pemphigus & erosive lichen planus patients. Mashhad Univ Dent J 2003; 27: 116-121.

[14] Dalirsani Z, Mehdipour M, Taghavi Zenooz A, Alavi F, Javadzadeh Y. The comparison of combination of triamcinolone acetonide and vitamin A mouthwash with triamcinolone mouthwash alone on oral lichen planus. J Dent Res Dent Clinic Dent Prospect 2010; 4: 21-24.

[15] Youngnak-Piboonratanakit P, Dhanuthai K, Thongprasom K, Luckprom P, Sarideechaigul W, Luangjarmekorn L, Azuma M. Expression of IFN-gamma before and after treatment of oral lichen planus with 0.1% fluocinolone acetonide in orabase. J Oral Pathol Med 2009; 38: 689-694.

[16] Kaliakatsou F, Hodgson TA, Lewsey JD, Hegarty AM, Murphy AG, Porter SR. Management of recalcitrant ulcerative oral lichen planus with topical tacrolimus. J Am Acad Dermatol 2002; 46: 35-41.

[17] Laeijendecker R, Tank B, Dekker SK, Neumann HA. A comparison of treatment of oral lichen planus with topical tacrolimus and triamcinolone acetonide ointment. Acta Derm Venereol 2006; 86: 227-229.

[18] Kapoor S. Management of oral lichen planus: treatment of steroid refractory lesions. Maturitas 2008 20; 59: 413-414.

[19] Lo Muzio L, Mignogna MD, Favia G, Procaccini M, Testa NF, Bucci E. The possible association between oral lichen planus and oral squamous cell carcinoma: a clinical evaluation on 14 cases and a review of the literature. Oral Oncol 1998; 34: 239-246.

[20] Malhotra AK, Khaitan BK, Sethuraman G, Sharma VK. Betamethasone oral mini-pulse therapy compared with topical triamcinolone acetonide (0.1%) paste in oral lichen planus: A randomized comparative study. J Am Acad Dermatol 2008; 58: 596-602.

[21] Eisen D. Hydroxychloroquine sulfate (Plaquenil) improves oral lichen planus: An open trial. J Am Acad Dermatol 1993; 28: 609-612.

[22] Motta AC, Domaneschi C, Komesu MC, Souza Cda S, Aoki V, Migliari DA. Double-blind, crossover, placebo-controlled clinical trial with clobetasol propionate in desquamative gingivitis. Braz Dent J 2009; 20: 231-236.