Original Article

Zahedan Journal of Research in Medical Sciences

Journal homepage: www.zjrms.ir

Comparison of Effectiveness of the Bioadhesive Pastes Containing Licorice 5% and Topical Corticosteroid for the Treatment of Oral Lichen Planus: A Pilot Study

Fateme Arbabi-Kalati,[1] Tahereh Nosratzehi,*[2] Hamed Hamishehkar,[3] Abbas Delazar[3]

1. Department of Oral Medicine, Genetics of Non-Communicable Disease Research Center, Zahedan University of Medical Sciences, Zahedan, Iran
2. Department of Oral Medicine, Dental Research Center, Zahedan University Of Medical Science, Faculty of Dentistry, Zahedan, Iran
3. Drug Applied Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

Article information

Article history:
Received: 2 Feb 2013
Accepted: 27 Feb 2013
Available online: 28 Apr 2013
ZJRMS 2014 July; 16(7): 7-9

Keywords:
Oral Lichen Planus
Licorice
Corticosteroid

*Corresponding author at:
Department of Oral Medicine, Zahedan University of Medical Sciences, Zahedan, Iran.
E-mail:
nosratzehi@yahoo.com

Abstract

***Background*:** Lichen planus is a chronic inflammatory mucocutaneous disease with immune system's origin. There is no definite cure for that and present treatment methods are symptomatic. According the effects of topical medications and anti-inflammatory properties of licorice, this study is designed for comparison the effectiveness of the adhesives containing licorice with topical steroid on treatment of oral lichen planus.

***Materials and Methods*:** In this double-blind clinical trial, 40 patients randomly divided into two groups: licorice and topical corticosteroid therapy and were followed up for 12 weeks, we asked patients used the drugs four times in a day and after applying drugs avoid of eating, drinking and smoking for an hour. Data were analyzed by SPSS-19, using the independent samples *t*-test and Mann-Whitney *U* tests.

***Results*:** In this study the use of topical licorice as topical corticosteroids were effective in reducing pain, but the improvement of clinical signs was not effective as corticosteroids. The severities of lesion according Thongprasom classification were 1.2±1.03 in corticosteroid group and 2.6±0.9 in licorice group. There was a statistical significant difference between groups (p=0.006).

***Conclusion*:** Based on the findings of this study topical licorice 5% is not a good alternative for topical corticosteroids in the treatment of lichen planus.

Introduction

Lichen planus is an inflammatory disease that involves skin and mucosa. Oral mucosa is involved in 50%. Oral Lichen Planus (OLP) is mainly seen in women and characteristically the lesions are symmetrical, involving the buccal mucosa, tongue, gingival, floor of the mouth, lips, and palate. Two basic types of lesion occur: totally white (keratotic) and white (keratotic) with red (atrophic, erosive and bullous) [1, 2].

Till now high-potency topical corticosteroids in an adhesive medium is the best method for management of OLP, it seems has many side effects including fungal infection, mucosal atrophy and systemic absorption [3].

Licorice is one of the most herbal drugs in Iran. Glyceric acid in licorice can inhibit an enzymatic way of cyclooxygenase and lipoxygenase. In the other hand, it can prevent the production of oxygen free radical also prevents of cell immigration, the recent event results in inhibit of arachidonic acid metabolism. All of them reduce inflammatory reaction [4]. Licorice has been used in the treatment of various rang from tuberculosis to peptic ulcer [5], but there is a few study about licorice effect on oral lesions, some studies showed the licorice extract improved the healing time and reduced pain in patients with aphthous ulcer, on the other hand one study showed bioadhesive patch containing licorice extract was not effective more than bioadhesive patch without licorice extract [6-9], but there is no study about effect of licorice on OLP, so we design this study to evaluate the effect of bioadhesive paste containing 5% licorice extract in management of OLP.

Materials and Methods

This randomized controlled double blind study has been carried out 40 patients with OLP. They were recently referred to the clinic of oral medicine at the school of dentistry in Zahedan University of Medical Sciences. This study was approved by Ethical committee of Zahedan University of medical sciences before the patient's enrolled. All patients filled and signed consent forms.

Patients with clinical and histopathological diagnosis of OLP were enrolled in this study. The exclusion criteria were systemic disease, pregnancy, smoking, systemic drug therapy for OLP during 3 past months, topical drug therapy, which had lesion/lesions with dysplasia, lesions adjacent to amalgam filling site.

Before procedure all patients under went careful examination by an oral medicine specialist. Patients were divided in 2 groups by block randomization method. Patients in group a received bioadhesive paste containing 5% of licorice extract, 4 times in a day; three times after meal and one time before sleeping for 15 days. We advised patients to keep away of eating, drinking and smoking for an hour after applying drug. Patients in group

B were treated by bioadhesive paste with triamcinolone 0.1% which was similar in shape, taste and color to licorice tape. Patients, applied drug in same way as patients in group B. Patients were evaluated by an oral medicine specialist for demographics, medical history, symptoms, duration of disease, type, site, size of the lesions (cm^2), and history of cutaneous lesion and these data were recorded. Reduction in sign scores were assessed by Thongprasom sign score.

For evaluating the efficacy of treatment, sign and symptoms were recorded by the blind examiner on follow up sessions. Visual analogues scale (VAS) was used for symptom (pain) evaluation the patients were requested to record the level of pain of lesion in follow up period. Reductions in size of lesions were measured with periodontal prob. The grounds roots of licorice were defatted using n-hexane and then obtained powder were dried using rotary evaporator. Extraction was done by 50% methanol solution using maceration technique. Obtained extraction was filtrated and then dried in rotary evaporator (Heidolph, Laborota 4002). Deglycyrrhin ization was done in acidic medium. For this mean, powders were purred in distillated water and pH adjusted with 20% sulfuric acid solution. Finally precipitated glycyrrhizine was separated from the medium. For neutralization of the medium, calcium hydroxide was also added. Obtained extraction was dried in rotary evaporator and used for preparations of bioadhesive formulate [10].

Licorice extract powder, gelatin, pectin and sodium carboxy methyl cellulose were milled in a plenary ball mill (PM100, Retsch, Germany) and sieved in an automatic sieve shaker (AS200, Retsch, Germany). The size fractions under 45 µm were separated and dried an overnight in a 60ºC oven (Behdad, Iran) for complete dehydration. The same proportion of mucoadhesive excipients (gelatin, pectin and NaCMC) were mixed together completely after addition of licorice extract (5% w/w of total formulation weight). Powders were mixed with Plastibase (5% poly ethylene in liquid paraffin) in the ratio of 40/60 at 2000 rpm (IKA, Germany) until a substantially homogeneous ointment was obtained. A placebo formulation was prepared in the same method without licorice extract. Both formulations were filled into the identical tubes and coded randomly to be used in the double blind manner. Data were analyzed by SPSS-19, statistical significancy was tested by in dependent *t*-test for pain levels and Mann-Whitney *U* tests for evaluated of change in signs, the level of statistical significance was set at a tow-tailed value of 0.05.

Results

Forty patients enrolled in this study were divided in two groups. Distribution of age, sign and symptoms of lesions before treatment were the same in groups (Table 2).

Improvements in sign and symptom scores after 12 weeks are represented in table 3, there is a statistical significance between reduction in size of lesions (p=0.006). Group B has Clinical improvement more than group A, but there is no statistical significance between mean of pain.

Number of lesions in any score before and after treatment is shown in table 4, in both groups score 3 and score 4 were the most frequent ones. After treatment there was complete remission in 12 lesions of group A, but in group B there was no complete improvement.

Table 1. Thongprasom sign score for OLP

Sign	Definition
Score 5	White striae with erosive area>1 cm^2
Score 4	White striae with erosive area<1 cm^2
Score 3	White striae with atrophic area >1 cm^2
Score 2	White striae with atrophic area <1 cm^2
Score 1	Mild white striae only
Score 0	No lesions, normal mucosa

Table 2. Demographic data and sign and symptom scores in two groups before treatment

Group	Age (year)	Mean of pain	Sign according Thongprasom scoring	Disease
Licorice	49.5±2.3	4.6±1.1	3.1±7.3	2.8±0.42
Topical corticosteroid	45.6±3	4.5±1.0	3.2±0.78	2.3±0.8
p-Value	0.6	0.8	0.7	0.1

Table 3. Sign and pain score after treatment in two groups

Group	Mean score of pain	Sign according Thongprasom scoring
Licorice	1.9±0.9	2.6±0.9
Topical corticosteroid	1.2±1.6	1.2±1.03
p-Value	0.2	0.006

Table 4. Sign scores before and after treatment in each group

Thongprasom scoring	Topical corticosteroid		Licorice	
	Before treatment	After treatment	Before treatment	After treatment
Score 5	0	0	0	0
Score 4	12 (30%)	0	16 (40%)	8 (20%)
Score 3	20 (50%)	4 (10%)	16 (40%)	12 (30%)
Score 2	8 (20%)	12 (30%)	8 (20%)	16 (40%)
Score 1		12 (30%)	0	4 (10%)
Score 0	0	12 (30%)	0	0

Discussion

Oral lichen planus is a chronic disease that currently management the signs and symptoms are not satisfactory. Among available treatments topical high potency corticosteroids are more effective. Although topical cyclosporine and tacrolimus, topical and systemic retinoids are used for resistant lesions however, outcomes are often disappointing. Our results showed topical licorice is significantly reduced pain and so can lead to smaller lesions although in comparison with topical corticosteroids, the shrinkage was not noticeable. Licorice is a plant with very anti-inflammatory effects and was used for treatment of many diseases. Different mechanisms were explained for its anti-inflammatory effect including inhibition of glucostroid metabolism and complement. We could not find any study about effect of licorice on oral lichen planus but this drug has been used in treatment of aphthous ulcers. Moghaddamnia et al.

used bioadhesine pachte containing %1 licorice extract for treatment of RAS. They showed this therapy reduced pain and size of lesion, but compared with the bioadhesine patch without drug this reduction was not significant [6]. They concluded patch therapy was effective on pain control and licorice was not useful. Burges et al. showed dissolving oral patch can have the same effect as amelexanox. Martin et al. investigated the efficacy of intraoral adhesive patch with licorice and placebo patch on healing of aphthous ulcer, he reported in comparison with placebo group ulcer size and pain were improved in case group [9]. Das et al. showed that the use of mouthwash containing licorice extract could relief the pain and improved the healing time in patients with aphtous ulcer [11]. Despite the anti-inflammatory mechanisms of licorice, the drug had little effect on the control of oral lichen planus; it can be explained by the fact that the concentrations used in this study (5%) are not sufficient to exert anti-inflammatory effects.

Due to the lack of side effects among users of the drug and the relative effectiveness of licorice on lichen planus lesions, maybe the high dose composition of this drug can be effective as topical corticosteroid (without complications). It is suggested that future studies with larger sample size and drug doses should be made.

Acknowledgements

This study is extracted from research project with the code 90-2247 and supported by Shahid Beheshti University. This study is registered on Iranian Registry of clinical trial and its code is IRCT IRCT201110123133N4, it is available on www.irct.it and www.who.int /trialsearch.

Authors' Contributions

All authors had equal role in design, work, statistical analysis and manuscript writing.

Conflict of Interest

The authors declare no conflict of interest.

Funding/Support

Zahedan University of Medical Sciences, Zahedan.

References

1. Aghahosseini F, Arbabi-Kalati F, Fashtami LA, et al. Treatment of oral lichen planus with photodynamic therapy mediated methylene blue: A case report. Med Oral Patol Oral Cir Bucal 2006; 11(2): E126-9.
2. Aghahosseini F, Arbabi-Kalati F, Fashtami LA, et al. Methylene blue-mediated photodynamic therapy: A possible alternative treatment for oral lichen planus. Lasers Surg Med 2006; 38(1): 33-8.
3. Seherfiled JF, Black MM, Challacombe SJ. The management of oral lichen planus. Clin Exp Dermatol 2000; 25(3): 176-82.
4. Inoue H, Mori T, Shibata S and Koshihara Y. Modulation by glycyrrhetinic acid derivatives of TPA-induced mouse ear edema. Br J Pharmacol 1989; 96(1): 204-10.
5. Saeedi M, Morteza-Semnani K, Ghoreishi MR. The treatment of atopic dermatitis with licorice gel. J Dermatolog Treat 2003; 14(3): 153-7.
6. Moghadamna AA, Motallebnejad M, Khanian M. The efficacy of the bioadhesive patchescontaining licorice extract in the managemen of recurrent aphthous stomatitis. Phytother Res 2009; 23(2): 246-50.
7. Messier C, Epifano F, Genovese S and Grenier D. Licorice and its potential beneficial effects in common oro-dental diseases. Oral Dis 2012; 18(1): 32-9
8. Burgess JA, van der Ven PF, Martin M, et al. Review of over-the-counter treatments for aphthous ulceration and results from use of a dissolving oral patch containing glycyrrhiza complex herbal extract. J Contemp Dent Pract 2008; 9(3): 88-98.
9. Martin MD, Sherman J, van der Ven P and Burgess J. A controlled trial of a dissolving oral patch concerning glycyrrhiza (licorice) herbal extract for the treatment of aphthous ulcers. Gen Dent 2008; 56(2): 206-10.
10. Miremadi H, Ezzatpanah K, Larijani R, et al. [Comparison of different methods of obtaining glycyrrhizic acid from licorice extract powder] Persian. Food Technol Nutr 2011; 8(1): 21-28.
11. Das SK, Das V, Gulati AK and Singh VP. Deglycyrrhizinated liquorice in aphthous ulcers. J Assoc Physicians India 1989; 37(10): 647.

Please cite this article as: Arbabi-Kalati F, Nosretzehi T, Hamishehkar H, Delazar A comparison of effectiveness of the bioadhesive pastes containing licorice 5% and topical corticosteroid for the treatment of oral lichen planus: A pilot study. Zahedan J Res Med Sci. 2014; 16(7): 7-9.