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Original Article

Green tea relieves erosive, atrophic, and ulcerative lesions in patients with oral lichen planus: a pilot clinical trial study

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Abstract

***Background & Aims*:** Oral lichen planus (OLP) is a chronic inflammatory and autoimmune disease of stratified squamous epithelium. Numerous treatment approaches have been introduced for the treatment of OLP, but there is no substantial evidence to support the effectiveness of these methods. Green tea is a popular drink widely used to relief and treat inflammatory and autoimmune diseases. The present pilot study aimed to investigate the effect of green tea tablets on OLP.

***Materials & Methods*:** In this pilot clinical trial study, we recruited 10 patients (48.1 ± 12.44 years old) with erosive and atrophic OLP from Western Azerbaijan, Urmia, in Iran. All patients received a green tea tablet (450 mg) daily for one month. The patients were monitored and followed up for pain severity scale with a visual analog scale (VAS), lesion size, and number of lesions. Finally, the collected data were examined using statistical software.

***Results*:** The mean of VAS score before intervention was 4.1 ± 2.02, whereas it was 2.2 ± 2.25 at the end of the intervention. Statistical analysis indicated the decreased VAS score after 30 days of tablet consumption ($p < 0.001$). Moreover, lesion number and size were markedly decreased in patients after 30 days of tablet consumption. However, no complete recovery was observed in patients after 30 days.

***Conclusion*:** Our study indicates that using green tea tablets could be an effective and complementary therapy for patients with erosive, inflammatory, and atrophic lesions. However, further studies are required to investigate green tea tablets efficiency in long-term usage.

***Keywords*:** Green tea, Herbal medicine, Oral lichen planus, Oral lesion

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Introduction

Oral lichen planus (OLP) is a frequent chronic mucocutaneous disorder whose pattern varies according to different lesion types, including reticular, popular, plaque-like, bullous, atrophic, and erosive (1, 2). Lesions involve buccal mucosa in 80-90 % of cases

(3). Erosive OLP is the most advanced type of OLP with atrophic and erythematous ulcers covered by pseudomembrane, mucosal erosion, and white lace-like patterns (4). About 0.4-3.7% of lesions develop malignancy, and atrophic and erosive types have more malignancy potential, resulting in a worse prognosis (5, 6). Although the etiology of OLP is still unknown, the dysregulation of the T-cell-mediated immune system is the most likely cause of this condition (7, 8). It has been demonstrated that the upregulation of cytokines, such as tumor necrosis factor-α, interferon-γ, and IL-1, is mostly responsible for the occurrence of OLP (9, 10).

Even though various therapeutic approaches have been provided to reduce pain and heal the lesions, corticosteroids have been the most common drug for OLP management (11). Other treatment modalities, e.g. calcitonin inhibitors, immunostimulators, retinoids, low-level laser therapy, and photodynamic therapy, have also been used to treat OLP (12). However, despite the common use of corticosteroids, various side effects may occur, including adrenal suppression, secondary candidiasis, and increased blood pressure (11). Following the side effects reported, many herbal drugs with anti-inflammatory and antioxidant effects have been suggested for the management of OLP (13).

Green tea is a popular drink known for its immunomodulation effects. It has also shown anti-inflammatory, anti-oxidative, anti-carcinogenic, antimicrobial, antihypertensive and antidiabetic properties. Green tea has been recognized to have minimum toxicity and side effects and is safe for a wide range of patients (14, 15). Its anti-inflammatory activity is performed through downregulating critical inflammatory mediators and increased production of anti-inflammatory cytokines (16, 17).

OLP is one of the common inflammatory diseases of oral mucosa and corticosteroids and has various side effects on reducing pain and clinical symptoms. However, no study has been found to use green tea to manage OLP. Accordingly, this study aimed to evaluate the efficiency of green tea tablets in the management of OLP.

Materials & Methods

Participants:

The present pilot clinical trial study included 10 patients (aged between 37-65 years), with at least one clinical and histopathological proven OLP lesion, who were referred to the Department of Oral Medicine, Urmia Dental School, Urmia, Iran. The exclusion criteria entailed the presence of any visible oral lesion other than OLP, pregnant or breast-feeding women, immunodeficiency diseases, current malignancy or malignancy in history, severe or recurrent infections, lichenoid reaction, patients with allergy to botanical products, topical treatment or systemic therapy of OLP for one month before starting the study, increased blood pressure, ulcerative colitis, and history of organ transplant. All the patients signed an informed consent before the initiation of the study. This study was approved by the Ethics Committee of Urmia University of Medical Sciences (ethical code: 2852-35.-01-1395).

Interventions:

All the patients were asked to use green tea tablets (450 mg) daily for 30 days. The severity of pain, lesion size, and lesion number were investigated 30 days after interventions. The severity of pain and burning sensation was assessed by visual analog scale (VAS) before and after interventions. In addition, lesion size was investigated according to the Thongprasom criteria.

Statistical analysis:

The obtained data were analyzed by statistical package for the social sciences (SPSS version 22) software and presented as percentages, frequencies, mean, and standard deviation (mean ± SD). The difference between baseline and after interventions was analyzed by Mann-Whitney and analysis of variance (ANOVA).

Results

Demographic and clinical characteristics:

The present study included 10 patients (6 females and 4 males) with OLP in the age range of 37-65 years

old (mean 48.1 ± 12.44 years old). The most common sites of OLP lesions were bilateral buccal mucosal (40%) and right retromolar (20%), followed by anterior maxillary gingival, maxillary and mandibular gums, bilateral buccal, right buccal mucosa, left retromolar, and bilateral buccal mucosal (10% for each). The efficacy of OLP treatment by green tea tablets was investigated according to the severity of pain and burning (VAS score) and type and severity of the lesion (Thongprasom score). The number of lesions among patients was 1-6 (mean 2.3 ± 1.41), and the total number of lesions among all patients was 23. Also, the frequencies of the atrophic, erosive and inflammatory lesions were 10, 8, and 5, respectively. Before the intervention, the mean pain score for lesions was 4.1 2.02 (VAS scale), with a minimum of 2 and a maximum of 7. The other demographics and clinical characteristics are presented in Table 1.

Table 1. Demographic characteristics of the studied patients

Characteristics	Patients
Age mean (year)	48.1 ± 12.44
Male (n)	4
Female (n)	6
History of previous treatment (%)	10
Skin involvement (%)	2
Pain severity mean (VAS)	4.1 ± 2.02
Thongprasom score mean	3.47
Lesions number mean	2.3 ± 1.41
Site of OLP lesions (%)	
bilateral buccal mucosal	40
right retromolar	20
anterior maxillary gingival	10
maxillary and mandibular gums and bilateral buccal	10
right buccal mucosa and left retromolar	10
bilateral buccal mucosal	10

Efficacy of treatment:

All the patients were advised to use green tea tablets (450 mg) daily for one month, and then the lesions were followed up. The obtained results indicated that at the end of interventions (including five atrophic and one erosive lesions), three patients had an appropriate response, and more than 50% of the symptoms and findings of the disease reduced. In addition, four patients (with five atrophic and two erosive lesions) had a partial response to treatment and reduced symptoms and injuries by less than 50%. Moreover, three patients (with five erosive and ulcerative lesions) showed no response to treatment, and no patient indicated a complete response to treatment at the end of interventions (Table 2). The mean pain score at the end of interventions was 2.2 ± 2.25, with the lowest pain of 0 and the highest pain of 5. The difference between pain at the baseline and end of the interventions was statistically significant (Figure 1).

Table 2. The clinical response of patients to green tea tablets

Clinical response	Lesions type	Patients' number (%)
Complete response	Erosive	0 (0)
	Atrophic	0 (0)
Appropriate response	Erosive	1 (1)
	Atrophic	5 (5)
Partial response	Erosive	2 (2)
	Atrophic	5 (5)
Without response	Erosive	5 (5)
	Ulcerative	5 (5)
Total of lesions		**23**

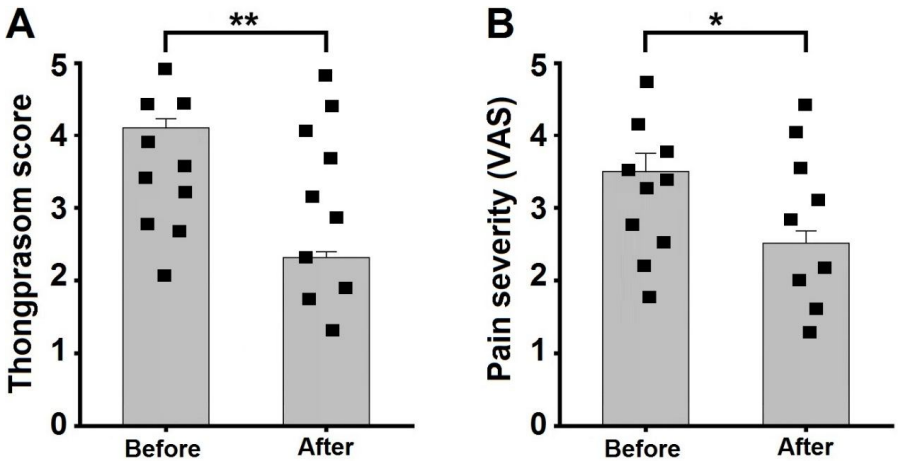

Fig. 1. Comparison of Thongprasom score (A) and VAS score (B) at the baseline and end of interventions (* $p<0.01$; ** $p<0.001$).

Discussion

OLP is a common T-cell-mediated inflammatory autoimmune disease with the features of disease chronicity, adult onset, female predilection, depressed immune suppressor activity, and autocytotoxic T-cell clones in lichen planus lesions (18). OLP is characterized by T-cell accumulation in the superficial lamina propria, basement membrane disruption, intraepithelial T-cell migration, and keratinocyte apoptosis, resulting from antigen-specific and non-specific mechanisms (19). Antigen-specific mechanisms in OLP comprise antigen presentation, lymphocyte activation, proliferation, and migration, as well as keratinocyte apoptosis mediated by $CD8^+$ cytotoxic T cells, whereas nonspecific mechanisms include mast cell degranulation and matrix metalloproteinase activation in OLP lesions (19). Moreover, deficient antigen-specific transforming growth factor-mediated immunosuppression may contribute to the pathogenesis of OLP (20, 21). Topical and/or systemic corticosteroids are the most common treatments for OLP. Despite the therapeutic effects of corticosteroids, their role in modulating inflammation and immune response are associated with adverse effects that reduce treatment efficacy (22).

Green tea is a rich source of the polyphenols known as catechins. It has recently been investigated because of its anti-inflammatory and immunomodulatory activities (23, 24). Findings have indicated that catechin supplementation might be beneficial to cases

with an abnormally excessive T-cell function, such as in autoimmune and inflammatory disorders (25). Evidence has also suggested that green tea could therapeutically be helpful for autoimmune diseases, particularly osteoarthritis, rheumatoid arthritis, autoimmune diabetes, Sjogren's syndrome, and lupus erythematosus (26, 27). However, research on the connection between green tea consumption and OLP is still inconclusive. In addition, current therapies for OLP are far from satisfactory because of various side effects (28). Thus, we speculate that green tea consumption may affect OLP at multiple levels through its anti-inflammatory and immunomodulatory activities. In this study, green tea tablets (450 mg/day) were administrated to 10 patients for 30 days. Based on our results, green tea tablets exhibited a more significant reduction in signs and symptoms, as well as decreased Thongprasom scale in erosive and atrophic lesions. These impacts could be explained by the anti-inflammatory and antioxidant properties of green tea. The phenols components of this herbal drug have been shown to play a role in immune-mediated pathways, therefore affecting inflammation or oxidation processes (16, 17).

Our study is the first report on the therapeutic effect of green tea on erosive, atrophic, and ulcerative lesions in patients with OLP. There are currently no studies on the role of green tea in treating OLP, and therefore, no comparison can be made. Despite this, green tea tablets have been used as a treatment for OLP disease and could be effective on a number of lesions, pain intensity, and recovery. Previous studies have suggested that green tea may have effects on the management of autoimmune diseases through immunomodulation (29, 30). Studies have also investigated the effects of green tea on the oral epithelium health through the modification of miRNA and microbiome of the oral epithelium (31, 32), showing that green tea has an effective the mechanism in the treatment of OLP.

In the present study, green tea was associated with some patient-reported adverse effects, including abdominal pain, in three patients. Side effects of green tea treatment have not been reported, and its short-term use has been associated with mild and reversible side effects, or it has been completely safe. The most frequent negative effects observed in our patients were gastrointestinal upsets. The strengths of the present research were optimal randomization and double-blindness of the study. Moreover, this study provided information that could contribute to the management of OLP, especially in cases where herbal drugs are preferred.

Conclusion

Our study demonstrates that the daily use of green tea tablets (450 mg) for one month could improve inflammatory and atrophic lesions and partially ameliorate erosive lesions in patients with OLP. However, further studies on different doses of green tea, larger sample size, long-term follow-up, and comparison with the control group that did not consume green tea are required to achieve more robust results.

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Conflict of interest

The authors have no conflict of interest in this study.

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Data availability

The raw data supporting the conclusions of this article are available from the authors upon reasonable request.

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