

# Comparison of the effect of Salvizan Gel with Teriident in patients with minor aphthous ulcers

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## Abstract

**Background and objective:** Recurrent Aphthous Stomatitis (RAS) is the most common inflammatory ulcer of the mouth that has involved humans throughout history. Relieving the pain and shrinking the ulcer size is of great importance for the patient. Finding an appropriate drug is of particular importance in relieving these sores.

**Materials and methods:** In this clinical trial study, the study population was 30 patients referred to the Department of Oral Disease of Faculty of Dentistry of Ahvaz Jundishapur University of Medical Sciences with the diagnosis of minor oral aphthous in the academic year 2015-2016. The participants were divided randomly into two groups of 15 persons. Each group was given one of the two drugs: salvizan gel or teriident ointment. The amount of pain was evaluated by VAS scale and ulcer size was measured in millimeters. The results were analyzed by using Mann-Whitney and Friedman tests. ( $P < 0/05$  was considered significant).

**Results:** No significant difference was seen between the two groups in the amount of pain and the ulcer size before use of drugs; however, there was a significant difference between the two groups in terms of the amount of pain and the ulcer size after use of drug on the second and sixth days ( $P \leq 0.05$ ); so, salvizan gel with a lower average rating has significantly better performance in reducing the ulcer size.

**Conclusion:** The results indicate the both medicines, have a significant effect on reducing the pain and the oral aphthous ulcer size; so, salvizan gel and teriident ointment are markedly effective respectively in the control of pain and in reducing the ulcer size.

**Key words:** Oral Aphthous; Pain, Salviza Gel; Teri-ident; Ulcer size

## Introduction

Recurrent Aphthous Stomatitis (RAS) is the most common inflammatory ulcers of the mouth (1) that has involved humans throughout human history (1). The Greek word "Aphtha" was used by Hippocrates for the first time for the definition of these oral ulcers (2).

RAS is a disease with unknown cause, but factors such as local trauma, systemic, genetic, immunological, and nutritional problems as well as allergy and microbial factors are suggested as its predisposing factors (3).

Sometimes the patient feels prodromal symptoms such as itching or burning feeling 2-48 hours before the advent of the ulcer in the place that turns gradually Erythematous and eventually turns into a small white papule that gets bigger during 48- 72 hours (3). The prevalence of RAS in a society is over 25% and its three-month recurrence reaches to 50% (4). The first occurrence of the disease is commonly in the second decade of life (3) but the faster incidence of the disease may be seen by slight trauma, menstruation, upper respiratory tract infection, or associated with certain foods (3). The percentage of incidence of RAS in children may be higher (approximately 39%) and influenced by the incidence of RAS in the parents (5). In this case in children with parents affected by the RAS, its incidence chance is 90% and in children whose parents have not been affected by RAS so far, this level is reduced to 20% (6).

The most important issue in the diagnosis and management of aphthous in dental science is that diagnosis of it is totally based on description and clinical symptoms and there is no laboratory test to prove any diagnosis (7).

The correct treatment of RAS depends on repeat (s), size, and the number of sores (8). The best treatment for aphthous, is a therapy where the wound is controlled over a long time and there are few risky side effects (9). In patients with a history of repeated courses of RAS the topical treatments reduce the risk of the disease (8). The use of topical antiseptics, topical antibiotics and topical corticosteroids are some therapies that are prescribed for patients with aphthous stomatitis (10).

Among the corticosteroids used for the aphthous patients in Iran is triamcinolone acetonide with a brand of teriident. Due to the loss of defensive mucous barrier of oral mucosa in aphthous disease, this drug is well absorbed and also due to the antiinflammatory features of the corticosteroids, it causes earlier regeneration of tissue (11). But since corticosteroids have systemic effects such as hypothalamic-pituitary-adrenal axis suppression, Cushing's syndrome, epithelial atrophy, hyperpigmentation, candidiasis, and acne, it is better that a drug with less complications is used (12, 13).

In the twenty-first century which is named as century of back to nature and the use of herbs in treatment, we see the increasing expansion of the research in the field of medicinal herbs and we see the supply of new

herbal medicines in the broader dimensions (14). One of the medicinal plants that is said to have many healing properties, is a plant known as *Salvia officinalis* (Common sage).

The leaves of the *Salvia officinalis* are very famous because of their antioxidant effect. This plant has a variety of properties such as antimicrobial, antifungal, antiviral, astringent effects and it reduces secretion of sweat and saliva and it is effective in the treatment of RAS (15). The extract of this plant HAS its antimicrobial effects more on gram negative bacteria and IT also HAS anti-fungal effects on *Candida albicans*. These effects are attributed to the active substance of  $\beta$ -thujone that the leaves of the *Salvia officinalis* contain. Active substances of  $\beta$ -thujone because of their antifungal and antimicrobial effects, remove the resulting inflammation of pathogens; on the other hand, ursolic acid contained in the herb has a powerful anti-inflammatory and antiphlogistic effect (16).

Salvizan gel in addition to  $\beta$ -thujone has tannins, phenolic acid, ursolic acid and so on, and reduce the inflammation through these substances and their effect on the lymph tissues (16). A pharmaceutical company called the Gol daru in Isfahan has prepared a therapeutic product from the herb *Salvia officinalis* for the treatment of aphthous, which is distributed under the commercial brand name of salvizan gel and is marketed as there is 28% of the hydro-alcoholic extract of *Salvia officinalis* per 15 g of gel (16) and according to the manufacturer's claims, it has been prepared and marketed in order to treat canker sores.

With regard to this point the policy of the Ministry of Health, Treatment, and Medical Education focuses on finding and using effective herbal drugs in the treatment of disease. (17), given the side effects of corticosteroids and to verify the claims of the manufacturer, this study was designed and conducted scientifically and practically to evaluate the hydro-alcoholic extract of a *Salvia officinalis* (Sage) compared with teriident ointment in the treatment of canker sores.

## Materials and Methods

In this clinical trial study, 30 patients, diagnosed as having minor oral aphthous, were referred to the department of oral diseases of Faculty of Dentistry of Ahvaz Jundishapur University of Medical Sciences, and were investigated in the academic year 2015-2016. This study was conducted in a pilot form, and a final sample size of 30 people was determined using random sampling and on the basis of the results of the initial pilot study.

In this study the inclusion criteria were: 1) patients referred to the Department of the oral diseases of the dental school; 2) patients who had a willingness to collaborate on this research; 3) People who were perfectly healthy and without systemic problems; 4) people with a maximum 24- hour history of minor RAS since the incidence of ulcers. Exclusion criteria were: 1) any sensitivity to NSAID drugs; 2) asthma patients; 3) a history of heart disease;

4) pregnant women; 5) people with gastrointestinal tract diseases such as peptic ulcers; 6) people with liver and kidney diseases; 7) patients with any periodontal surgery in the last six months; 8) the presence of systemic diseases such as diabetes. Participants were randomly divided into two groups of 15 people. Age, sex and features of minor RAS and ulcer size and amount of pain were recorded before treatment and matched at each group.

After a full explanation of the terms and methods, the basic situation of pain in patients was measured with the use of the scale VAS (Visual Analogue Scale). This scale is used to measure the amount of pain, and patients were asked to rate their pain to a number between zero to 10. The number zero represents the absence of pain and the number 10 represents the greatest amount of pain. Furthermore, the initial size of the ulcer was calculated and recorded using a disposable paper ruler by mm square ( $\text{mm}^2$ ) at baseline.

In the control group, 0.1% teriident ointment (Raha , Isfahan, Iran) was used and in the case group, salvizan gel (Goldaru, Isfahan, Iran) containing an amount of 28% of the hydroalcoholic extract of *Salvia officinalis* per 15 g of gel, was used. Before beginning the design, tubes of both drugs were covered completely by a third party, so that type of medication was not identified for the patient and the investigator. Then, the tubes were marked with "a" and "b" marks, and were randomly given to patients.

For every drug use in each group, people were trained to impregnate a small piece of health cotton of about 3 to 5 cm in size, in the drug and hold it in the sore's location for 30 seconds. People were asked to repeat this operation three times daily and refuse eating and drinking or washing the mouth at least 30 minutes after doing this for the better impact of the medication. Patients also were prohibited to use any oral anti-inflammation and pain medication during treatment. Patients were asked to refer in the second and sixth days after receiving the drug and to be examined again and the amount of pain was recorded based on VAS and ulcer size was measured with a disposable paper ruler. The collected data were given to a statistics expert to analyze statistics.

#### Statistical methods of analysis of the results

to compare the three groups, the Friedman- Whitney test was used. The results of this research were analyzed using SPSS version 22. A significance level of  $P \leq 0.05$  for was considered for all statistical tests.

## Results

After providing data to the statistical consultant, they were evaluated and the following results were achieved; the number of patients participating in the study was 30 people; of these 15 persons were men (50%) and 15 were females (50%). The overall average age of the patients participating in the study was  $30.62 \pm 0.515$  for men it was  $559.0 \pm 2.31$  and for women it was  $57.29 \pm 913.0$ . The average amount of pain in patients receiving teriident

ointment and salvizan gel along with details is shown in Table 1 and the average size of the ulcer in Table 2.

In this study, it was shown that there are significant differences between the amount of pain in the patients before using teriident ointment and salvizan gel with the amount of pain after use of medications ( $P \leq 0.05$ ). Also, no significant differences were seen between the amounts of pain before the use of drugs between the two groups however, there were significant differences between the amount of pain after use of drugs in the two groups on the second and the sixth days ( $P \leq 0.05$ ). As it was shown, salvizan gel with a lower rank average has significantly better performance in the control of pain.

In this study, it was shown that there were significant differences between the size of the ulcer in patients before using teriident ointment and salvizan gel with the size of the ulcer after the use of medications ( $P \leq 0.05$ ). Also, this study showed that there was not a significant difference between the size of the ulcer prior to the use of drugs in the two groups but there was no significant difference between the two groups in the size of the ulcer after the use of drugs on the second day and the sixth day .

As it was shown that teriident ointment with a lower rank average has significantly better performance in reducing the size of the ulcer.

## Discussion

RAS is a recurrent inflammatory disease of the oral mucosa that can be seen as single or multiple or painful sores in patients without systemic disease. These sores are one of the most common oral diseases that are seen in 20% of the world's population (18, 19).

Diagnosis of RAS disease is based on history and clinical profile and there is no specific test for RAS (63). Several factors are discussed in the etiology of RAS. Heredity, blood factors and immunity are the three main factors in the incidence of aphthous ulcers (64). In addition to these various factors, such as local trauma, cigarette smoking, viruses, stress, medication and allergy are very involved in the creation of the RAS (20-24).

This study showed that there is a significant difference between the amount of pain and the size of the ulcer in the patients before the use of teriident ointment and gel salvizan with the amount of pain after the use of the medications.

In this study, it was shown that there is no significant difference between the groups in the amount of pain and the size of the ulcer in the patients before the use of the medications ( $P \geq 0.05$ ); however, there is no significant difference between the two groups in the amount of pain and ulcer size after the use of medicines on the second day and the sixth day ( $P \leq 0.05$ ).

**Table 1: The amount of pain in patients with oral aphthous by day and the type of gel**

The amount of pain in the days off Gel type	At the visiting day	On the second day after treatment	On the sixth day after the treatment	Test results
Teriident ointment	5.73±0.358	4.20±0.416	1.80±0.327	0.0001
Salvizan Gel	6.40±0.335	2.13±0.215	0.27±0.118	0.0001
Test results	0.206	0.0001	0.0001	

**Table 2: The extent of oral aphthous by the following time and the gel type**

Amount of pain in the days off Gel type	At the visiting day	On the second day after treatment	On the sixth day after the treatment	Test results
Teriident ointment	4.4±0.349	2.33±0.287	0.933±0.118	0.0001
Salvizan Gel	3.933±0.462	1.150±0.123	0.2±0.106	0.0001
Test's result	0.478	0.001	0.0001	

It was shown that salvizan gel with a lower rank average has significantly better performance in reducing the size of the ulcer.

Farokh Rad et al. (25) have compared the medical effect of topical intraoral triamcinolone ointments and herbal solution of myrtus in the treatment of minor oral aphthous ulcers. Contrary to the results obtained in the present study, they found that there is no significant difference between topical intraoral triamcinolone ointment and herbal solution of myrtus in the response rate to treatment. However, in this study it became clear that there was a significant difference between the teriident ointment and salvizan gel in the response rate to treatment, as salvizan gel has significantly better performance in reducing the pain of RAS and teriident ointment has significantly better performance in reducing the size of the ulcer. Perhaps the differences in the results achieved are in the higher number of patients under investigation (100 patients) compared with the present study (30 patients).

MM Fani et al. (26) have compared the effect of phenytoin syrup and triamcinolone acetonide ointment on aphthous ulcers. They found that the rate of the effectiveness of triamcinolone acetonide ointment in the treatment of aphthous ulcers is more than phenytoin syrup. However, in this study it became clear that salvizan gel has significantly better performance in reducing pain induced by aphthous, and teriident ointment has significantly better performance in reducing the size of the ulcer. Perhaps the differences in the results achieved is in the higher number of patients under investigation (60 patient) compared with the present study (30 patients) as well as differences in the used drugs. They also investigated patients with Behcet's syndrome to evaluate the impact of drugs on aphthous ulcers, but in this study, the subjects were completely healthy and lack any systemic disease and syndrome.

Jahanshahi et al. (27) conducted an introductory study of the effectiveness of triamcinolone in treatment of the minor oral aphthous ulcer. Similar to the present study, they found that triamcinolone has significant effect in relieving pain and reducing the sizes of the ulcers and it can be used in accelerating the improvement of aphthous ulcers. A difference between their study compared to the present study is less people under investigation (23 patients) and the methods in their study so that they have compared the effect of triamcinolone with placebo. But in the present study, the therapeutic effect of teriident ointment was compared to the salvizan gel. So it can be said that the results obtained from this study was more comprehensive and more accurate than their study.

Abbasi et al. (28) compared the effect of triamcinolone acetonide 0.1% and diclofenac 1% in patients with minor oral aphthous. This study showed teriident ointment and salvizan gel significantly are effective in reducing pain and the size of the ulcers. They also found that the amount of pain and the size of the ulcers has a significant decrease in triamcinolone gel and diclofenac gel. Contrary to the results obtained in the present study that showed the salvizan gel with a lower rank average, had significantly better performance in controlling the pain and teriident ointment with a lower rank average, had significantly better performance in reducing the size of the ulcer. In their study, they did not find significant differences between the two groups in the reduction of pain and the size of the sore. Perhaps because of the differences in the results achieved is in the lower number of patients undergoing their study (25 patients) compared with the present study (30 patient) as well as differences in the used drugs.



## Conclusions

Both teriadent ointment and salvizan gel have a significant effect on reducing the amount of pain and the size of the oral aphthous, so salvizan gel has significantly better performance in the control of pain, and teriadent ointment has significantly better performance in reducing the size of the ulcer.

## Acknowledgement

This work was Financially Supported by Grand: ( U-36 263 ) from Vice-chancellor for Research Affairs of Ahvaz Jundishapur University of Medical Science. This Paper Is Issued From Thesis Of (Reza Mirzaei)

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