Curcumin Gel in the Treatment of Minor Aphthous Ulcer: a Randomized, Placebo- Controlled Trial

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Abstract

Background: It has been reported that curcumin has anti inflammatory, antibacterial, anti tumor and analgesic properties.

Objective: The purpose of this study was to investigate the efficacy of curcumin in the treatment of minor aphthous stomatitis.

Methods: The study was a two week, randomized, double blind, placebo controlled of patients with minor aphthous. Patients between 18 and 65 years old were included if they presented with 1–5 aphthous ulcers of less than 24 h duration. Twenty-eight patients were randomly allocated to curcumin gel containing (2% curcumin) and 29 patients were allocated to placebo gel for a two week, double-blind, placebo-controlled study. The patients used the medication using a swap twice per day. After enrolment, the size of ulcers were measured by the investigator, and pain was evaluated by the patients based on Perceived Pain Rating Scale before drug application (day 0) and at days 4, 7, and 14. Patients overall satisfaction were assessed at the end of treatment.

Results: Curcimin gel significantly reduced pain intensity and size of aphthous ulcer compare to placebo. Significant group differences appeared at the end of the trial regarding overall satisfaction of the patients.

Conclusion: The results of present study provide evidence that curcumin gel is a well tolerated effective treatment modality for minor aphthous stomatitis.

Keywords: Curcumin, Minor aphthous stomatitis, Pain

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Introduction

Aphthous ulcers or Recurrent Aphthous Stomatitis (RAS), commonly referred to as canker sores, are inflammatory lesions of the mucous lining of the mouth which may involve the cheeks, gums, tongue, lips, and roof or floor of the mouth. It is usually painful and associated with redness, swelling, and occasional bleeding from the affected area (s) [1, 2]. Manifestation of the disease can range from mild to severe and, in extreme cases, even hinder a person's ability to ingest foods, thereby making the person susceptible to malnutrition [3]. The cause of RAS is unknown, although several factors are suspected including genetics, stress, nutritional deficiencies, diet, hormonal changes, and immunological disorders [4]. Due to the indeterminate etiology of the disease, it is difficult to find a definitive cure and current treatments are aimed towards ameliorating the symptoms [1, 3]. The less severe form of the disease is often known as minor aphthous stomatitis while the less common but more severe type is major aphthous stomatitis [2, 4]. Minor aphthous stomatitis is a very common self-limiting, recurrent disease of unknown cause. One or several painful ulcers appear on the lining mucosa of the mouth [2]. The ulcers heal in 7-10 days with or without treatment. Major aphthous stomatitis are larger recurrent ulcers of unknown cause appearing as deep, painful areas in the mouth that leave scars on healing. They last longer than minor aphthae [1 - 4].

Minor aphthous is amongst the most common form of oral ulcerative diseases and affects an estimated 15-20% of the population worldwide. In some populations, the prevalence has been documented as being as high as 50-66%5 and it is especially common in North America [1 – 4]. These aphthae can also occur as widespread lesions in association with systemic diseases including Behcet's syndrome, and gastrointestinal mal absorption disorders like Crohn's and Celiac diseases [1, 2, 5]. It is unclear whether these presentations are manifestations of the underlying disease or represent a separate oral disorder. Treatment for RAS is symptomatic; the goals being to decrease pain, healing time, number and size of the ulcer, and to increase disease-free periods. Current treatment options include topical agents, systemic and topical steroids, corticosteroids, cauterization and antibiotics, mouth rinses containing active enzymes, laser treatments and combination therapy [4].

The lack of predictability of the efficacy of a particular treatment mirrors the mystery surrounding the etiology of the condition [4]. Over the last decade evidence based herbal medicine in the treatment of psychiatric disorders and dermatological disease, has been considered [6-15]. There are some natural remedies that are being explored for the treatment of aphthae [16, 17]. Herbal medicine will relieve pain, reduce inflammation and prevent infection in the treatment of aphthae [17]. It has been reported that curcumin has anti inflammatory, antibacterial, anti tumor and analgesic properties [18-21]. Therefore, the objective of this study was to investigate the efficacy of curcumin in the treatment of minor aphthous stomatitis.

Methods

The study was a randomized, double blind, placebo controlled of patients with minor aphthous ulcer referred to Oral Medicine Clinic of Imam Khomeni Hospital (Tehran University of Medical Sciences, Tehran, Iran)

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from October 2011 to December of 2011.

Patients between 18 and 65 years old were included if they presented with 1 – 5 aphthous ulcers of less than 24 h duration. The ulcers diameter was not greater than 6 mm and they did not suffer from acute or chronic diseases of the oral mucosa. Patients were excluded from the study if they had concurrent clinical conditions including serious liver, kidney, and heart dysfunctions or if they had ulcers as a manifestation of a systemic disease process such as ulcerative colitis, Crohn's disease, Behcet's syndrome, or serious anemia.

To minimize the effect of confounding variables in the psycho- physiological component of the study, the patients could not have a history of alcohol or drug abuse nor could they be taking any narcotic analgesics. Patients were excluded if they had a history of systemic immunosuppressive therapy.

Pregnant or lactating women and those of reproductive age without adequate contraception were also excluded. The trial was performed in accordance with the Declaration of Helsinki and subsequent revisions and approved by the ethics committee at Tehran University of Medical Sciences (Approval No: 13676). Written informed consents were obtained before entering into the study. This trial is registered with the Iranian Clinical Trials Registry (IRCT201107311556N28).

Twenty-eight patients were randomly allocated to curcumin gel containing 2% curcumin (Curcumin fluid Gel 2%®; Orphanidis Pharma Research GmbH and Orphan Teb Pars) and 29 patients were allocated to placebo gel for a two week, double-blind, placebo-controlled study. The patients used the medication using a swap twice per day and the surface of lesions were covered by a thin layer of medications. The patients were advised not to eat or drink for 1 hour after using the medications.

Measurements

After enrolment, the size of ulcers were measured by the investigator, and pain was evaluated by the subjects based on Perceived Pain Rating Scale before drug application (day 0) and at days 4, 7, and 14 as well as subject overall satisfaction score at the end of treatment on four-point description scale (poor=1, moderate=2, good=3 and excellent=4) [22). Ulcer size was measured using a sterile calibrated dental probe with millimeter marking and the longest diameter was used as measurement. In addition, all subjects were requested to immediately inform investigators at any time for any side effect.

Data were presented as mean ± standard deviation (SD) for quantitative variables with normal distribution. Background and demographic data were summarized with descriptive statistics. To evaluate the efficacy the Mann-Whitney *U* test was used.

Results

All patients completed the study protocol. No adverse drug reaction to a treatment was reported as a reason for leaving the study. No significant difference was identified between patients randomly assigned to the group 1 or 2 condition with regard to basic demographic data including age, gender, level of education and smoking (Table 1).

Efficacy based on Perceived Pain Rating Scale

At the study entry, the mean ulcer pain of the 2 groups matched well (ns), but it was later significantly relieved in the turmeric group at day 4 ($p<0.05$; Table 2).

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Table 1- Characteristics of the patients

	Curcumin (n=28)	Placebo (n=29)
Gender, female, n (%)	13(46%)	12(41%)
Age, years, mean±SD	36.1±9.6	33.3 ±9.5
Education, n (%)		
• Under diploma	6(21%)	8(27%)
• Diploma	5(18%)	6(21%)
• Higher education	17(61%)	15(52%)
History of smoking, n (%)	0	0
Previous treatments, n (%)	15(54%)	11(38%)
Size of ulcer, largest diameter, mm, mean±SD	4.7 ±0.8	5 ±0.75
Number of ulcers, median (range)	1(1-3)	1(1-5)

Table 2- Efficacy of curcumin gel vs placebo gel in the treatment of minor aphthous stomatitis

	Overall Satisfaction	P	Pain Score day 0	P	Pain Score day 4	P	Pain Score day 7	P	Diameter of Ulcer day 0 (mm)	P	Diameter of Ulcer day 4	P	Diameter of Ulcer day 7	P
Curcumin	2.99±0.85	0.01	2.96±0.18	0.58	1.17±0.47	0.03	0.21±0.41	0.06	4.71±0.81	0.17	2.64±0.86	0.02	0.75±0.58	0.04
Placebo	2.24±1.05		2.93±0.25		1.51±0.68		0.44±0.50		5.00±0.75		3.20±1.013		1.06±0.59	

Efficacy based on global satisfaction

Significant group differences appeared at the end of the trial regarding overall satisfaction of the patients ($p \leq 0.01$; Table 2)

Efficacy based on size of the ulcers

Although the ulcer size of the treatment group and the placebo group matched well at the study entry ($p > 0.05$), significant group differences appeared at the later visits (day 4 and 7; $p < 0.05$) (Table 2).

Discussion

In fact, there is no consensus on an effective treatment for RAS that can efficiently reduce the signs and symptoms of the disease at a low daily dose and with minimal effects [1 - 4]. Treatment for RAS is symptomatic; the goals being to decrease pain, healing time, number and size of the ulcer, and to increase disease-free periods. Current treatment options include topical agents, systemic and topical steroids, corticosteroids, cauterization, antibiotics, mouth rinses containing active enzymes, laser treatments and combination therapy [1 - 4].

Our findings suggest that curcimin gel can reduce pain intensity and size of aphthous ulcer. To our knowledge this is the first published study of curcumin gel in the treatment of aphthous ulcer. Clinical characteristics of the patients, such as sex, age and type of aphthouse, did not differ between groups and cannot explain differences in the

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therapeutic outcome. So far, several studies have shown positive effects of curcumin as anti inflammatory, anti tumor, antibacterial and analgesic agent. Therefore, the results of our study are in line with these studies [18-21].

In conclusion, the results of this study provide evidence that curcumin gel is a well tolerated and effective treatment modality for RAS. Additional studies with higher number of patients and in the prevention of ulcer development if treatment is commenced at the prodromal stage may be needed to examine the role of curcumin in the treatment of RAS.

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