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Comparative Evaluation of 2% Curcumin and 2% Aloe Vera Gel in the Management of Chronic Recurrent Oral Aphthous Ulcers: A Clinical Study

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Abstract

Chronic recurrent oral aphthous ulcers are the most common type of inflammatory efflorescence of the oral mucosa, with no known effective treatment. Turmeric, a rhizome of *Curcuma longa*, and *Aloe vera* (A.V.) are herbs with anti-inflammatory and immune stimulant effects, which could be of benefit. The aim of this study is to do comparative evaluation of curcumin and aloe vera gel in the management of chronic recurrent oral aphthous ulcers. A randomized double-blind case control study was conducted on 60 patients suffering with chronic recurrent oral aphthous ulcers after obtaining their informed consent. The patients were randomly allocated in 2% curcumin, 2% aloe vera gel group and group receiving placebo gel. Patients were asked to apply the gels three times a day for two weeks. The clinical assessment of the size, number of ulcer, time taken for ulcer healing ,patient's pain score and the diameter of surrounding inflammation after gel application were recorded after 1, 7 and 14 days. The statistical evaluation of the obtained data was done using SPSS software. The mean age group of patients was 20±4.68 years. The 2% aloe vera gel was found to be more effective in reducing the pain, inflammation and burning sensation. 2% Curcumin gel was found to be effective in decreasing the size and duration of healing of the ulcerative lesion.

Keywords: Aloe Vera, Anti-Inflammatory, Aphthous Stomatitis, Curcumin, Immunomodulation, Recurrent Oral Aphthous Ulcers

1. Introduction

Chronic recurrent oral aphthous ulcers are one of the most common oral cavity lesions, with a prevalence of 5 to 50%. It is typically presented as painful, sharply circumscribed fibrin-covered mucosal defects with a hyperemic border. Most common sites of occurrence are the lips, soft palate and throat in children and young adults. The males are more commonly affected than females. The pain and discomfort caused by the ulcers affect the quality of life by interfering with swallowing, drinking, eating and speech[1]. As the etiology and histopathology is unclear, most of the treatment modalities offer symptomatic management. A variety of chemical drugs such as chlorhexidine, cyclosporine, levamoisole, steroids, sucralfate, tetracycline, in topical form, have been used for its management[2,3].

Ayurveda is a traditional natural system of medicine that advocates use of medicinal plants for numerous human diseases since ages. Turmeric (*haldi*), a rhizome

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of *Curcuma longa*, is a flavourful yellow-orange spice. Curcumin (diferuloylmethane) is a polyphenol derived from *Curcuma longa* plant, commonly known as turmeric. The active constituents of turmeric are the flavonoid curcumin (diferuloylmethane) and various volatile oils including tumerone, atlantone, and zingiberone. Other constituents include sugars, proteins, and resins. The best-researched active constituent is curcumin, which comprises 0.3-5.4% of raw turmeric. Curcumin has been used extensively in ayurvedic medicine for centuries, as it is nontoxic and has a variety of therapeutic properties including antioxidant, analgesic, anti-inflammatory, antiseptic activity, and anticarcinogenic activity[4,5]. *Aloe vera* (*Aloe barbadensis miller*) belongs to the *Liliaceae* family. The leaves contain colorless mucilaginous gel (98–99% water and 1–2% active compounds). *Aloe Vera* has been used for the treatment of recurrent aphthous stomatitis, herpes simplex, and herpes zoster infection, Oral lichen planus, oral submucous fibrosis, radiation-induced mucositis, burning mouth syndrome, candida-associated denture stomatitis, xerostomia, periodontitis[6].

Aims and Objective

1) To do the comparative evaluation of the efficacy of 2% Curcumin and 2% aloe vera gel in patients with chronic recurrent apthous ulcers.
2) To assess the efficacy of the gels under study in reduction of inflammation associated with chronic recurrent apthous ulcers.
3) To assess the efficacy of the gels under study in reduction of duration of healing associated with chronic recurrent apthous ulcers.

Guidelines prescribed by CONSORT were followed in designing and implementation of this randomized controlled trial.

2. Materials and Method

This study was conducted in the Government Dental College and Hospital, Aurangabad. The approval for clinical trial was obtained from the Institutional Ethical Committee (Approval No. 001108/GDCHA/EAC-TRE/EC/2016). All study was in accordance with the ethical standards of the Institutional Ethical Committee and with the Helsinki Declaration of 1975, revised in 2000 and 2008[5]. Informed consent was obtained from the patients both verbally and in writing. No incentives were offered to the patients for this study. The study was conducted between January 2019 till March 2019.

2.1 Inclusion Criteria

1) Voluntary patient with age more than 18 years.
2) Patients with a positive history of developing apthous ulcers on the oral mucosa during a period of 2–3 months.
3) Patients presently suffering from minor recurrent aphthous singular lesions on their buccal mucosa and mucosal zone of the lips measuring ≤5 mm in size.
4) Patients without any other medical diseases and complications.

2.2 Exclusion Criteria

1) Patients with systemic diseases and complications
2) Patients with major aphthous lesions and multiple minor lesions in the oral cavity.
3) Pregnant mothers and smokers.
4) Involuntary patients.
5) Patients with history of hypersensitivity to Curcumin and aloe vera.

60 patients with chronic recurrent apthous ulcers visiting the institute for their dental problems meeting the inclusion and exclusion criteria were selected. The entire sample of was randomly divided into three groups, 20 each, using computerized lottery method. Group A received 2% aloe vera gel and Group B patients received 2% curcumin gel. Group C was used as a control. They were given gels without any medicaments. The flow chart showing the plan of study is shown in Figure 1.

2.3 Preparation of 2% Curcumin Gel by Simple Dispersion Method[7]

Carbopol-940 was soaked in purified water containing 0.2% w/v sodium benzoate overnight. Using tissue homogenizer hydroxypropyl methylcellulose (HPMC) solution was mixed in propylene glycol. 2 mg of curcumin (Rajesh Chemicals, Mumbai) was transferred into HPMC solution and homogenized. This drug solution was transferred to carbopol solution and homogenized. Triethanolamine was added quantity sufficient (q.s.) to neutralize the pH. Then, distilled water was added to make q.s. to 100 ml. Control gel was prepared in the same manner. The gel was stored at ambient temperature. The formulation of 2% curcumin gel was prepared by

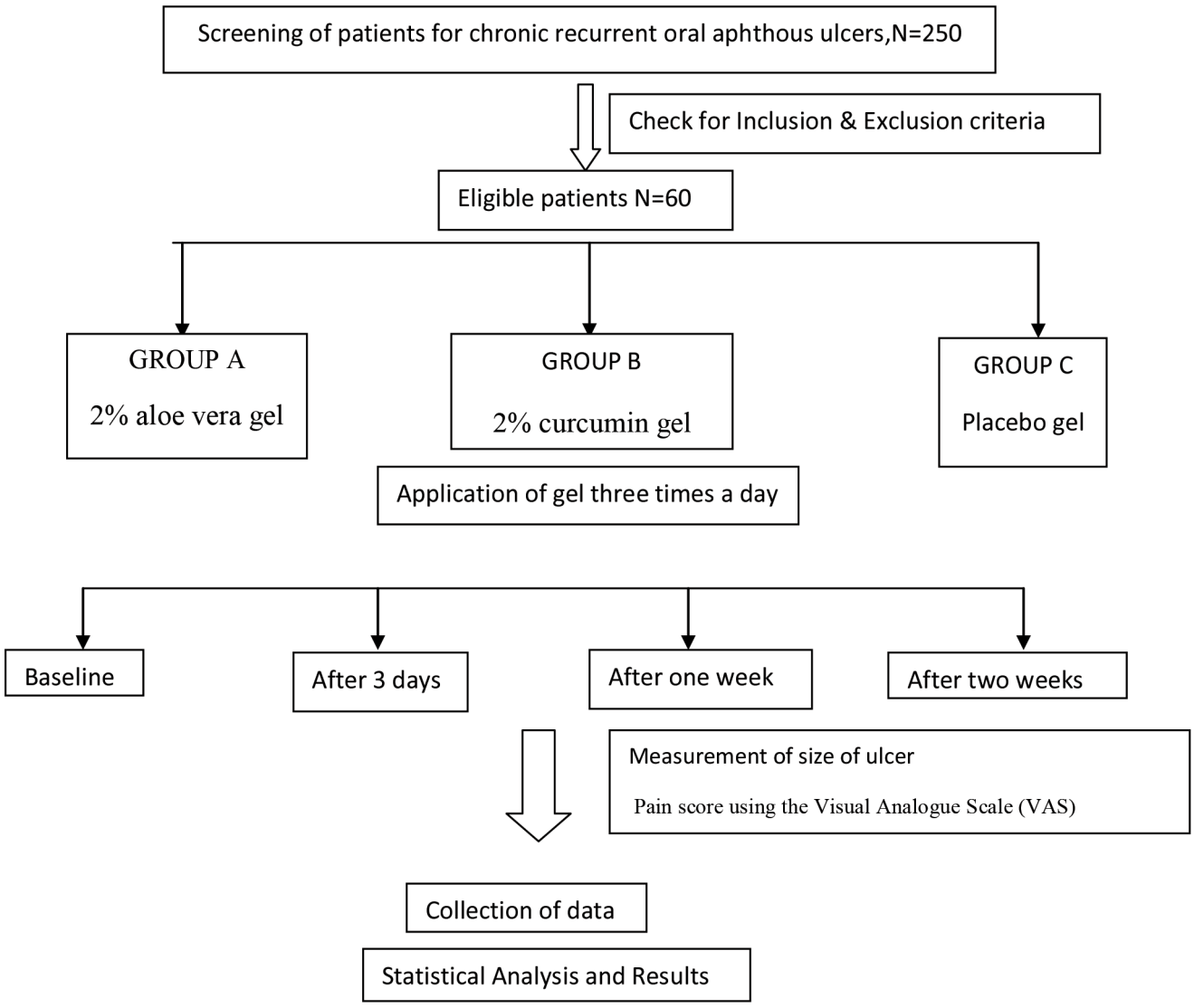


Figure 1. Study plan.

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2.4 Preparation of 2% Aloe Vera Gel[8]

Freshly purified leaf juice extract of A.V. gel (purchased from Kapoor Herbal Products, Nyay Nagar, Aurangabad) with 1.6% dry remnant and a density of 1.01 g/mL. Croscarmellose sodium (CCS), crospovidone (CLP) and sodium starch glycolate (SSG) (purchased from S.D. Fine Chem., Mumbai, India), microcrystalline cellulose - Avicel PH101 (procured from FMC Corporation, Philadelphia, USA.), Mannitol (purchased from Merck India Ltd, Mumbai, India). Anhydrous lactose, talc, magnesium stearate and hydrochloric acid were obtained from CDH Chemicals, Delhi, India. The inner mucilaginous parenchymatous tissues of leaves of Aloe vera plants were separated out with the help of a sterile knife and homogenized in a blender (National blender, Matushita Co. Japan) at 30 rpm.

2.5 Dispensing of gel

The prepared gels, 2% curcumin gel and 2% aloe vera gel, were dispensed aseptically in similar 50-mL pump–cap polystyrene-coded containers with appropriate nozzle.

2.6 Method of Application of Gel

The patients were asked to apply the gel on the ulcers three times a day after consumption of meals. They were instructed to avoid eating or drinking for atleast half an hour after gel application.

2.7 Clinical Observations and Scoring of Pain

The ulcers of the patients were clinically observed at days 0, 3, 7 and 14. On day 0, the number and size of ulcers and the pain score was noted. Ulcer size was measured along its longest diameter using a sterile vernier caliper. The pain score was noted from 0–14, using the Visual Analogue Scale (VAS). Patients with stimulated pain score of one and lesion diameters less than one mm were considered healed.

2.8 Statistical Analysis

At the end of 14 days the patients' median VAS scores, diameters, duration of healing of apthous ulcers were compared between the two groups using either Fisher exact or unpaired Student t-test. $P<0.05$ was considered statistically significant.

3. RESULTS

Thirty-three males and 27 females (Table 1) suffering from chronic apthous ulcers participated in this study.

Table 1. Demographic statistics of study samples

Gender	Number	Age(Mean± SD)
Male	33	20 .43±12.45
Female	27	21.10±11.45
Total	60	20±4.68

None of them suffered from any allergic reaction towards the curcumin and aloe vera gels. There was no significant difference between group A and B in terms of age, gender, size, duration and number of ulcers. There was statistically significant reduction in pain scores in both the groups in 14 days but there was no statistical significant difference between Group A and Group B when compared. Group A showed reduction in pain, inflammation and burning sensation (Table 2).

Table 2. Pain score in group A and group B along with *P* value

Day	Group A	Group B	*P* value
0	4.5±1.72	4.6±1.23	0.400
1	4.2±1.61	4.3±1.50	0.510
2	3.1±1.73	3.2±1.68	0.672
3	2.8±1.65	2.6±1.50	0.760
4	2.5±1.50	2.4±1.34	0.500
5	2.3±1.50	2.2±1.65	0.630
6	1.9±1.75	1.8±1.45	0.776
7	1.5±1.50	1.4±1.54	0.546
8	1.3±1.45	1.2±1.64	0.540
9	1.1±1.10	0.9±1.75	0.753
10	0.8±1.55	0.7±1.25	0.550
11	0.5±1.73	0.6±1.45	0.664
12	0.2±1.73	0.4±1.35	0.897
13	0	0.2±1.46	0.166
14	0	0	1

Group B was found to be effective in decreasing the size and duration of healing of the ulcerative lesion (Tables 3 and 4). Group C patients had ulcers without any reduction in pain, inflammation and burning sensation.

Table 3. Size of ulcer in group A and group B, with *P* value

Day	Group A	Group B	*P* value
0	2.8±1.21	2.7±1.33	0.640
7	0.06±0.26	0.01±0.42	0.421
14	0±0	0±0	1.000

Table 4. Duration of healing of ulcer in group A and group B, with *P* value

Group A	Group B	*P* value
4.9±1.52	4.1±1.08	0.516

4. Discussion

Chronic recurrent apthous ulcers are common ulcerative diseases of oral cavity with no definitive pathophysiology. The pain, inflammation, discomfort and inflammation associated with these ulcers affect the quality of life

of people suffering from it. Various pharmacological agents have been tested. Treatment for chronic recurrent apthous ulcers is mostly symptomatic with 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. However due to its unclear etiology, these medications are ineffective[9–11].

In this study the therapeutic effect of 2% curcumin and 2% aloe vera gel have been tested. A group of patient was used as control. To our knowledge this is the first published study of comparative evaluation of curcumin gel with aloe vera gel in the treatment of aphthous ulcer. Both herbs have shown promising results in reduction of pain, size and duration of healing of ulcers. Lower VAS scores in the patients observed in both the groups can be attributed to the anti-inflammatory properties of curcumin and aloe vera. The efficacy of aloe vera in reduction of inflammation has been shown in several previously conducted studies.[12-19] the duration of healing was also reduced in both the groups. The antioxidant properties of A.V. gel along with its inhibitory effects on prostaglandin E2 and interleukin-8 productions along with the presence of Acemannan, a mucopolysacharide, have a major contribution in A.V. wound healing effects[20].

Previous studies have shown that aloe vera has been effective in treatment of oral lichen planus, cancer, burn and skin infections. Results of our study are in accordance with previous randomized clinical trials where they have used 2% aloe vera gel along with a placebo.[8] Curcumin has been proved to be effective antioxidant, antiseptic, antibacterial, anti-inflammatory, immunomodulatory, and analgesic. A study conducted using 10% and 50% viscous curcumin solution on the healing of ulcer in patients with recurrent apthous ulcer showed a good percentage of complete healing of ulcers. Our results are in concurrence with previous randomized clinical trials done using 2% curcumin gel in treatment of minor recurrent apthous ulcer, which showed that it to be a well-tolerated effective antibacterial, anti-tumor agent with potent anti-inflammatory and analgesic properties[21].

5. Conclusion

2% Aloe vera gel and2% Curcumin gel had significant effect on the healing of recurrent apthous ulcers. Additional studies with more number of patients and additional parameters should be used to examine the role of curcumin and aloe vera in the treatment of recurrent apthous ulcer. It is recommended to use both the gels for treatment of oral ulcers to get benefits of both natural herbs.

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