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A systematic review on effectiveness of Aloe Vera in treating recurrent aphthous stomatitis

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Abstract

Background: Recurrent aphthous stomatitis is the most common ulcerative disease of oral mucosa affecting 5 to 25% of the population and cause severe irritation to the patients. Aloe Vera is a succulent plant with high level of water content and has anti-inflammatory and immunostimulant effects. Usage of aloe Vera could be therapeutically beneficial in treating recurrent aphthous stomatitis.

Aim: To assess the effectiveness of aloe Vera in treating recurrent aphthous stomatitis.

Study Design: A systematic review about clinical trials showing the effectiveness of aloe Vera in treating recurrent aphthous stomatitis. A total of 102 articles were retrieved. Among these 55 articles were screened. The intervention and outcomes were assessed in the study included for systematic review.

Results: A total of 4 studies were included which has clinical trials showing the effectiveness of aloe Vera done on patient with recurrent aphthous stomatitis. Studies performed in different countries were included. All the four clinical trials have shown supportive results towards the use of aloe Vera in treating RAS.

Conclusion: Since all the four clinical trials that have been done so far approved of using aloe Vera for treating RAS, hence aloe Vera can be used as an alternative for treatment of recurrent aphthous stomatitis.

Keywords: Aloe Vera, recurrent aphthous stomatitis, systematic review andtreatment

INTRODUCTION

Recurrent aphthous stomatitis is an ulcerative disease of oral mucosa. It is very common and affects 5 to 25% of the whole population[1].According to its size and number of ulcerations it can be classified into- i) Minor aphthous ulcer, ii) Major aphthous ulcer and iii) Herpetiform aphthous ulcer[2]. It presents as a painful round to oval shallow ulcerations of the oral epithelium with yellowish gray center circumscribed by marked erythematous margin. It is located mostly on the buccal and labial mucosa and tongue[3].

Minor aphthous ulcers usually affect the nonkeratinized oral mucosa and heal within a few days without scarring. Major aphthous ulcers are large, chronic, and usually solitary and heals with scarring. Herpetiform ulcers are multiple, shallow and pinpoint ulcers that may affect any part of the oral mucosa[4].

The etiological factors includes- genetic factors, virus and bacterial infections, deficiency of vitamins, systemic diseases such as lichen planus, pemphigus, ulcerative colitis, AIDS etc., stress and anxiety ,food allergies, hormonal defects and mechanical injuries[5].

The treatment for RAS aims at the reduction of pain as well as inflammation while promoting healing. There are various forms of RAS treatment which involves topical steroids and analgesics, anti-inflammatory, immunosuppressive agents, anti-microbial and laser therapy [6]. Herbal medicines such as Aloe Vera have been introduced as an alternate form of treatment to avoid the side effects cause by these drugs[7].

Aloe Vera is a succulent plant with high level of water content (99-99.5%) containing water and fat-soluble vitamins, minerals, enzymes, simple or complex polysaccharides, phenol compounds, and organic acids[8]. It stimulates the immune system and induces the growth of collagen as it has an anti-inflammatory affect[9].

The mucopolysaccharides present in aloe Vera is said to increase the proliferation of epithelial and fibroblast by activating the growth factors[10]. The acceleration of oral wound healing in animal experiments has also shown that aloe Vera is a good candidate for miRAS[6].

Aloe Vera gels are proven to be effective in topical management of minor RAS in decreasing ulcer size, erythema, and exudation[8]. Thus the aim of this study is to assess the effectiveness of aloe Vera in the treatment of recurrent aphthous stomatitis.

OBJECTIVES

To assess the effectiveness of aloe Vera in the treatment of recurrent aphthous stomatitis.

MATERIALS AND METHODS:

Study Design

A systematic review about clinical trials showing the effectiveness of aloe vera in treating recurrent aphthous stomatitis.

ELIGIBILITY CRITERIA

INCLUSION CRITERIA

1. Publications of studies in English with full text articles were included.
2. Compulsory inclusion of aloe Vera as one of the treatment modalities.
3. Publication from all years was included.
4. Clinical trial studies.

EXCLUSION CRITERIA

1. Articles published other than English were excluded.
2. Studies which do not use aloe Vera as one of the treatment modalities were excluded.

3. Conditions limiting abilities of patients to participate in the study.
4. Patients using oral topical anti-inflammatory agents during the course of study were excluded.

SEARCH STRATEGY

Published literature on assessing the effectiveness of aloe Vera in treating recurrent aphthous stomatitis which includes original articles and research papers in databases Pubmed Central, Cochrane Central Register of Controlled Trials, Wiley Online Library, Ovid Medline and Science Direct were taken to study review. A literature search to collect relevant data was performed using keywords Recurrent aphthous stomatitis AND aloe Vera. According to the Prisma guidelines the keywords were altered in each search engine went and the results were many or few.

SEARCH ENGINE

1. PUBMED
2. COCHRANE
3. MEDLINE
4. WILEY ONLINE LIBRARY
5. SCIENCE DIRECT
6. Grey literature

RESULT

The search yielded 102 articles, and 55 were screened which were independently assessed. 41 articles were eliminated with no full text articles and 14 articles were taken which has full text articles. Among these 4 studies were included in qualitative synthesis.

Figure 1 shows the flow diagram of the reports that were identified, screened, assessed for eligibility, excluded and included in the review.

Table 1 shows the characteristics of the intervention in the included studies. In all the 4studies, the effectiveness of aloe vera was compared with medicinal preparations. All the studies discussed differed individually from their sample used, age of the population and duration of intervention. All the 4 trials were performed in individuals with miRAS. Two of the trials were done 3 times a day for 7days, one trial for 4 times a day for 5days and one trial for 2 weeks.

Table 2 shows the outcome data about the effectiveness of aloe Vera in recurrent aphthous stomatitis in the included studies. The outcome and the results of the 4 clinical studies were mentioned in the table.

Table 3 shows the bias shown in all the studies, including in the study, which was categorized as high bias, low bias and unclear. The bias was categorized according to the Cochrane risk of bias for randomized controlled trials and pilot study.

TABLE 1: CHARACTERISTICS OF THE INTERVENTIONS IN THE INCLUDED STUDIES

AUTHOR	YEAR	SAMPLE USED	PATIENT CHARACTERISTICS	DURATION	NUMBER (CASE/CONTROL)
Ghada Mansour	2013	Aloe Vera and Myrrh (0.5% w/w) plus Mucoadhesive gel	Patients were 38 males and 52 females aged 18 – 36 years with 1 – 3 fresh ulcers (<48 hours duration)	4 times per day for 5 days	90 individuals with miRAS Group 1: 30 patients using Mucoadhesive gel with Aloe Vera Group 2: 30 patients using Mucoadhesive gel with myrrh Group 3: 30 patients using plain Mucoadhesive gel (placebo)
Elena Bardellini	2016	Faringel (Sodium bicarbonate, alginate, honey, Aloe Vera, chammonile) compared with hyaluronic acid	Children (5 – 14 years) with miRAS	3 times per day for 7 days	87 patients Group A: 44 patients treated with Faringel Group B : 43 patients treated with 0.2% hyaluronic acid
Bhalang K	2013	0.5% acemannan in carbopol, 0.1% Triamcinolone acetonide or carbopol	50 healthy individuals 180 individuals with recurrent aphthous ulcer	3 times per day for 7 days	Group A: 50 healthy individuals treated with 0.5% acemannan in carbopol Group B: 180 individuals with RAS treated with 0.1% Triamcinolone acetonide, 0.5% acemannan in carbopol or pure carbopol
Babaee N	2012	2% Aloe Vera oral gel or lubricant gel (2% normal saline) used as placebo	40 patients (aged between 15 – 35 years) with oral miRAS during the last two days	2 weeks	40 patients with miRAS (allocated with either Case group – Aloe vera gel or Control group – Placebo group

TABLE 2: OUTCOME DATA AS REPORTED IN INCLUDED STUDIES

AUTHOR NAME	YEAR	OUTCOME	RESULTS
Ghada Mansour	2013	76.6% of patients using Aloe gel showed complete ulcer healing, 80% of them revealed subsidence of erythema and exudation especially at day 6 visit, whereas 76.7% of myrrh treated patients revealed almost absence of pain at day 6. No side effects were encountered with the used of any of the 3 gels	The new formulated aloe and myrrh based gels proved to be effective in topical management of miRAS. Aloe was superior in decreasing ulcer size, erythema, and exudation; whereas myrrh resulted in more pain reduction
Elena Bardellini	2016	In both the groups there was a progressive reduction in ulcer extension with complete healing in both groups on day 10	Used of faringel allows faster reduction of ulcerative lesion compared to patients treated with hyaluronic acid
Bhalang K	2013	No allergic reactions or side effects to acemannan. Effectiveness of acemannan in reducing ulcer size and pain is superior to control but inferior to 0.1% triamcinolone acetonide	Acemannan can be used for treatment of oral aphthous ulcer who wished to avoid used of steroids although its effectiveness is comparatively lesser than triamcinolone acetonide
Babaee N	2012	The mean (±SD) of patients age was 29.25 ± 8.48 and 27.95 ± 7.96 years in the control and aloe vera gel treated groups. The duration of complete wound healing, pain score, wound size and inflammation zone diameter in the aloe vera treated group were significantly lower than the control group on specific time points after treatment	Aloe vera 2% oral gel is not only effective in decreasing recurrent aphthous stomatitis patients pain score and wound size but also decreases the aphthous wound healing period.

TABLE 3: BIAS ASSESSEMENT AS INCLUDED IN THE STUDIES

The bias is assigned as low risk - +, high risk- ++ and unclear - ?.

Author Name, year	Random sequence generation	Allocation concealment	Selective reporting	Incomplete outcome data	Blinding of participants and personnel	Blinding of outcome assessment
Ghada Mansour, 2013	+	++	+	+	+	+
Elena Bardellini, 2016	++	++	+	+	?	?
Bhalang K, 2013	?	?	+	+	?	?
Babaee N, 2012	++	++	+	+	+	+

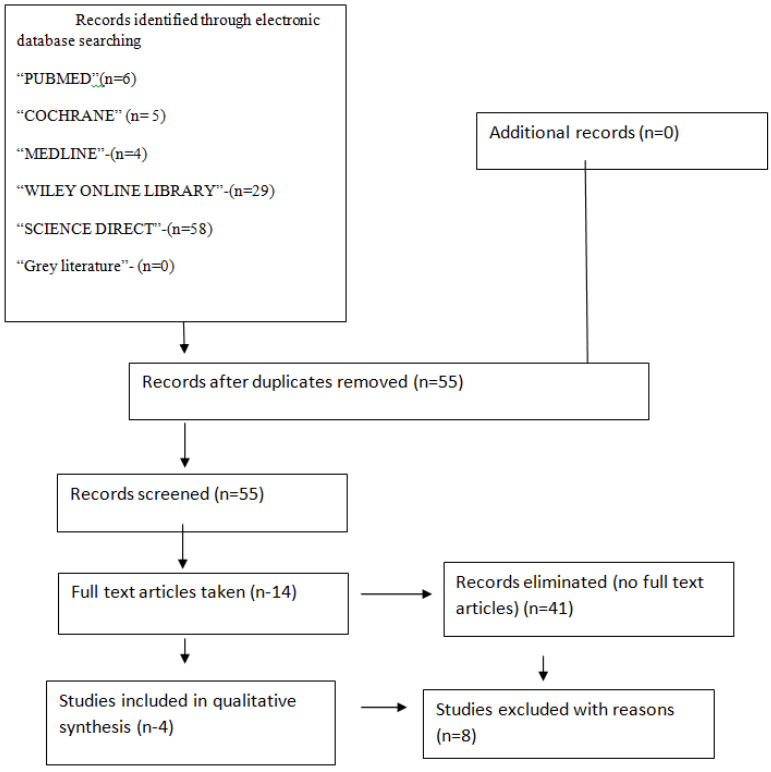

FIGURE 1: FLOW DIAGRAM SHOWING THE NUMBER OF STUDIES IDENTIFIED, SCREENED, ASSESSED FOR ELIGIBILITY, EXCLUDED AND INCLUDED IN THE SYSTEMIC REVIEW

DISCUSSION

Aloe Vera is one of the most widely used herbal medicine for various medical, cosmetic and neutraceutical applications. RAS is a common ulcerative disease of the oral mucosa causing discomfort to the patient and interfere with patients quality of life. In today's world, herbal medicines are preferred over pharmaceutical drugs; the reason being herbal medicines has no side effects, whereas side effects can be seen in some patient using pharmaceutical drugs. This systematic review found supportive results regarding the use of aloe Vera in recurrent aphthous stomatitis.This research yielded several studies which favour the use of aloe Vera in management of recurrent aphthous stomatitis. In all the 4 studies mentioned above, they have used aloe Vera as one of the intervention in treating recurrent aphthous stomatitis and suggested that aloe Vera may provide an alternative treatment for miRAS against pharmaceutical drugs. While its effectiveness is not comparable to medicinal preparations, the fact that aloe Vera does not cause any side effects to the patient has shown its safeness of this herbal medicine.

In our systematic review the effectiveness of aloe Vera has been reported in various studies. Ghada Mansour[2] has discussed the clinical efficacy of aloe Vera- and myrrh-based oral Mucoadhesive gels in the management of miRAS on patients with 1 to 3 fresh ulcers (< 48hrs) and concluded that both are proved to be effective in treating RAS with aloe Vera being superior in decreasing the ulcer size, erythema and exudation and myrrh resulted in more pain reduction. There were no side effects encountered in any of the patients using these gels.

Elena Bardellini[1] has compared Faringel (a solution composed of sodium bicarbonate, alginate, honey, aloe vera,chammonile) with hyaluronic acid in the treatment of minor recurrent aphthous stomatitis in children and the results showed that the use of faringel allows a faster reduction of the ulcerative lesion and pain level in comparison with hyaluronic acid.

Bhalang et al[6] has investigated whether acemannan (a mucopolysaccharides obtained from aloe Vera) caused any allergic reaction when used on human skin and he also measure the effectiveness of acemannan in the treatment of oral aphthous ulceration by comparing 0.5% acemannan in carbopol, pure carbopol and 0.1% triamcinolone acetonide. He concluded that acemannan can reduce the ulcer size significantly more than control. Even though its effectiveness is not comparable to that of triamcinolone acetonide, acemannan might be useful for patients who wish to avoid the use of steroid medication.

Babaee et al[7] has discussed the therapeutic effects of Aloe Vera gel on minor recurrent aphthous stomatitis using 2%aloe Vera gel or lubricant gel (2% normal saline) as placebo and concluded that aloe Vera 2% oral gel is not only effective in decreasing the recurrent aphthous stomatitis patients' pain score and wound size but also decreases the aphthous wound healing period to less than 7 days.

Maharjan et al[8] has discussed the biological properties and clinical effectiveness of aloe Vera and concluded that aloe Vera exhibits many pharmacological activities such as wound healing, anti-oxidant, anti-microbial, immune boosting, hypoglycaemic, and anti-diabetic. Thus it is a multipurpose medicine however further experiments are needed to find out the mechanism of the bioactive chemicals using modern instruments. Mangaiyarkarasi et al has discussed the benefits of Aloe Vera in dentistry and concluded that aloe Vera is quite economical which will reduce both medical cost and invalidity and more research is required on its healing properties, antibacterial, anti-inflammatory and its releasing pattern as a local drug delivery system. In all the studies, aloe Vera was used as one of the intervention for treating RAS.

CONCLUSION

Aloe Vera has played a significant role in the treatment of recurrent aphthous stomatitis and does not cause any side effects. However more research is required on its healing properties, antimicrobial, anti-inflammatory and its releasing pattern as a local drug delivery system.

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