The efficacy of amlexanox and triamcinolone acetonide in the treatment of recurrent aphthous ulcers.

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Abstract

Background: Recurrent aphthous stomatitis (RAS) is the most common oral mucosal disease characterised by chronic, ulcerative condition of the oral mucosa. **Material and Methods:** In this study we compared the efficacy of 5% Amlexanox with 0.1% Triamcinolone Acetonide in patients with RAS for pain relief and healing time. The patients were principally divided into 2 study groups, 30 in each group. Group A were treated by 5% Amlexanox, and Group B were given 0.1% Triamcinolone acetonide, topical application on the ulcer 3 times a day for 7 days. **Results:** The mean value of pain scores on the days after the treatment from the first day to the seventh day was significantly higher in amlexanox group than triamcinolone acetonide group ($P \leq 0.05$). The time of complete healing of ulcers was recorded in amlexanox group, the mean healing time of ulcers, reported by these 24 patients, was 4.17 ± 1.80 days (range 4-7). In triamcinolone acetonide group, the mean healing time of ulcers, reported by 30 patients with healed ulcers, was 2.24 ± 1.36 days (range 2-4). The difference was statistically significant ($P \leq 0.05$). **Conclusion:** Both amlexanox and triamcinolone acetonide are effective and safe in the treatment of aphthous ulcers.

Key words: Recurrent aphthous stomatitis, Amlexanox, triamcinolone acetonide, oral ulcer.

Introduction

Recurrent aphthous stomatitis (RAS) is the most common oral mucosal disease characterised by chronic, ulcerative condition of the oral mucosa without a fully recognized etiology. The term “aphthous” is derived from a Greek word “aphthae” which means ulceration.[1] Hippocrates used this and Kummel as ‘Mikulicz’s aphthae.’ It is more common in patients between 10-40 years of age.[2]

RAS is classified into 3 types, minor, major, and herpetiform aphthous ulcerations according to the diameter of the lesion. Minor RAS, which comprisesmore than 80%-90% of RAS cases, presents lesions of less than 1cm in diameter and heals within

7-14 days without scar formation. Major RAS lesions exceed 1cm in diameter and heal within 20-30 days with scarring. Herpetiform ulcers are characterized by recurrent crops of dozens of small ulcers throughout the oral mucosa, 1-3mm, which may coalesce into larger ulcers and heal up to 15 day.[3, 4]

RAS is characterized by the presence of painful, oval erosions or ulcers generally localized on the unattached oral mucosa of the lips, cheeks and tongue, which are surrounded by an erythematous halo. Nearly 5-25 % of the population is affected by RAS and more frequent in the age range of 10-40 years. It is a multifactorial disease and several predisposing and risk factors have been implicated in its pathogenesis. Etiopathogenesis remains poorly understood despite their high prevalence.[5] The exact pathogenesis of RAU remains unknown. Various causes of RAU have been reported in several studies and include genetic predisposition, drugs, foods, the presence of certain oral microbial communities, immunological factors, endocrinopathies, and psychological and hereditary factors.[6] Different studies have introduced different factors affecting the disease such as, immune disorders, hormonal changes, vitamin deficiency and so on. However, the etiology of this illness is unknown.[7, 8]

RAS is a difficult disorder to treat. There is no definite treatment for RAS and supportive treatment is performed aiming to control pain, accelerate healing and prevent recurrence.[9] All therapies are aimed to decrease the painful symptoms and duration of the ulcers.[10] Topical or systemic antibacterial such us chlorhexidine, anti-inflammatory, immunomodulatory, or symptomatic treatments are used however such treatments are not totally reliable.[11] Since the cause of the disease is not known, many drugs have been evaluated in an attempt to palliate the symptoms. Drugs used in the treatment of RAU are systemic corticosteroids, pentoxifylline, colchicine, dapsone, thalidomide, low-dose interferon-α and levamisole.[12] In this study we compared the efficacy of 5% Amlexanox with 0.1% Triamcinolone Acetonide in patients with RAS for pain relief and healing time.

Material and Methods

The patients who visited our dental hospital with a complaint of recurrent oral aphthous ulcers less than 1cm in diameter on the first day of the occurrence of the ulcer and between ages of 20 and 40 were included in the study. Patients willing to participate in the study and with clinically

diagnosed minor RAS noticed within 2 days of development of ulcer were included in the study. Patients having major RAS, traumatic ulcer, denture stomatitis or suffering from any systemic illness, patients under any medication (topical or systemic), and dental surgery during the previous one month were excluded. Pregnant or lactating women were also excluded from the study.

The current study included in all 60 healthy patients suffering with RAS, with an age group from 20 years and above. The patients were principally divided into 2 study groups, 30 in each group. Group A were treated by 5% Amlexanox (Trade name-Lexanox), and Group B were given 0.1% Triamcinolone acetonide (Trade name-Kenacort), topical application on the ulcer 3 times a day for 7 days. Both the groups were followed up on the first, fourth and seventh day. Written informed consent was obtained from all patients. Also ethical committee clearance was obtained from Institutional Ethics Committee.

Changes in pain scores, healing time, and side effects of the treatment were evaluated. At admission the patients were asked to evaluate the severity of pain by visual analog scale (VAS). Pain was numerically valued from 0 to 10 using visual analog scale (VAS). For patients, the number 0 and 10 were considered as no pain and the worst pain, respectively.After the treatment the pain severity and healing time of the ulcer was evaluated on the first, fourth, and the seventh day. Data were analyzed using SPSS 16 and t-test. The statistically significant level was accepted as a P value <0.05.

Results

The study group consisted of 48 men and 12 women with an average age of 23.52±3.50 years (20-40 years). Thirty patients received the amlexanox ointment and 30 patients received triamcinolone acetonide ointment. Table 1 shows the mean value of pain scores at admission and on the days after the treatment. The mean value of pain scores before the treatment was similar in both of the groups (P = 0.832).The mean value of pain scores on the days after the treatment from the first day to the seventh day was significantly higher in amlexanox group than triamcinolone acetonide group ($P \leq 0.05$).

On the seventh day after the treatment, the ulcers were completely reepithelialized in 24 patients (68.5%) in amlexanox group and in 30 patients (85.7%) in triamcinolone acetonide group. The difference was statistically significant ($P \leq 0.05$). Furthermore, the time of complete healing of ulcers was recorded in

Table1: Comparison of VAS score for the Amlexanox and Triamcinolone acetonide groups in different days

	Before the treatment	Day 1	Day 4	Day 7
Amlexanox Group	8.65 ± 0.45	7.25 ± 0.57	5.10 ± 0.38	1.55 ± 0.27
Triamcinolone acetonide Group	8.80 ± 0.32	6.70 ± 0.28	4.35 ± 0.20	1.30 ± 0.52
***P* value**	0.832	0.275	0.0488	0.040

amlexanox group, the mean healing time of ulcers, reported by these 24 patients, was 4.17 ± 1.80 days (range 4-7). In triamcinolone acetonide group, the mean healing time of ulcers, reported by 30 patients with healed ulcers, was 2.24 ± 1.36 days (range 2-4). The difference was statistically significant ($P \leq 0.05$)(Figure 1). Additionally, no patient reported any side effects from either of the groups.

Discussion

Recurrent aphthous ulcer (RAU) is one of the most common ulcerative diseases affecting the oral mucous membrane. RAS is a difficult disorder to treat. Symptomatic and supportive treatment should be provided initially.

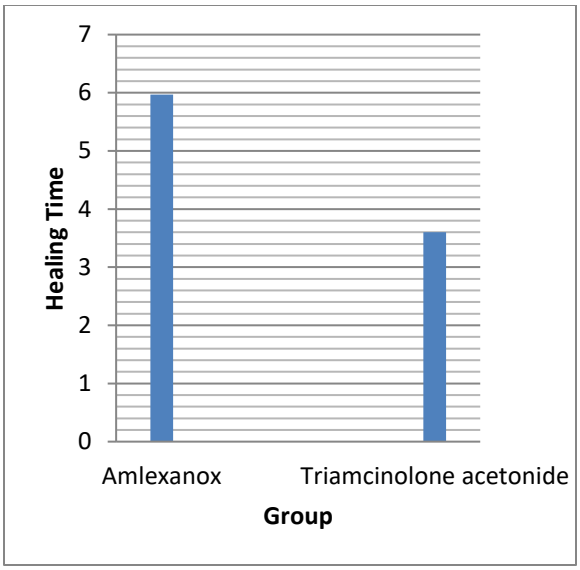

Figure1: The mean healing time in ulcers in amlexanox group and triamcinolone acetonide group.

Therefore, first choice of treatment for RAS patients is corticosteroids and analgesics. Topical treatments are preferred over systemic therapy due to fewer side effects

The present study evaluated the effect of amlexanox and triamcinolone acetonide in the treatment of recurrent aphthous stomatitis, pain severity and healing process on the first, fourth and seventh days of study. A total of 60 subjects were analyzed in the present study. The mean value of pain scores on the days after the treatment from the first day to the seventh day was significantly higher in amlexanox group than triamcinolone acetonide group ($P \leq 0.05$). Sharma R et al[13] showed that 0.1% Triamcinolone Acetonide and 5% Amlexanox is more

efficacious in the reduction of size, Number and Pain at day 8 and at day 10 as compared to single application of 20% Benzocaine gel, 100 mg Doxycycline Hyclate and the placebo, which was statistically significant.

Meng W et al[14] showed that amlexanox significantly reduced ulcer size (p= 0.038) and alleviate ulcer pain (P = 0.026) on 6th day of treatment. Abbasi F et al[15] showed no significant differences in pain score, tingling and lesion size between Amlexanox and Adcortyl groups. Reduction in the assessed variables was significant between days 1-3, 3-5, and 5-7 ($p < 0.001$) in both groups. Rahmani F et al[16] showed that the mean ulcer size on the fifth day (p=0.026, p=0.042, respectively) and VAS on the third and fifth days (p=0.011, p=0.013, respectively) were significantly less in Triamcinolone and Chitosan groups than Biogel and the no treatment episode. There were no significant differences between Chitosan and Triamcinolone groups in the average ulcer size and pain intensity in all the examination days. In our study the time of complete healing of ulcers was recorded in amlexanox group was 4.17 ± 1.80 days (range 4-7). In triamcinolone acetonide group, the mean healing time of ulcers was 2.24 ± 1.36 days (range 2-4). The difference was statistically significant ($P \leq 0.05$).

5% of Amlexanox oral paste is clinically beneficial in reducing the pain, erythema, exudation and size of the ulcer over a period of 6 days. Jijin MJ et al[17] proved that 5% amlexanox oral paste is effective in relieving pain associated with minor aphthous stomatitis. Nasry SA et al[18] showed that Amlexanox demonstrated a 29.8 +11.3 and 61.9+24.5 mean % of reduction in pain scores at day 2 and 5 respectively, and with a 22.2+10.5 and 43.4+15.8 mean % reduction in pain scores at day 2 and day 5. Also the highest mean % of reduction in ulcer size was 48.1+16.5 at day 2 and 77.8+28.7 at day 5. Darshan DD et al[19] showed that amlexanox 5% can reduce the frequency, duration and symptoms associated with the aphthous ulcers with no side effects attributed to the drug. In a study by Bhat S et al[20] amlexanox group showed marked reduction in ulcer size, significant reduction in pain, significant lower scores of erythema and exudation when compared to the placebo group. In 3 controlled clinical studies by Binnie WH et al[21] that evaluated 1,124 immunocompetent patients with mild to moderate aphthous ulcers, 5% Amlexanox oral paste (Aphthasol) was shown to accelerate healing of these ulcers. This was true both when treatment with 5% Amlexanox oral paste was compared to treatment with a vehicle and when treatment with the Amlexanox paste was compared to

no treatment. After 3 days complete resolution of pain was reported for 44% in paste group and 20% in patients with no treatment.

Minimal adverse experiences were observed by Khandwala A et al[22] and their data the data indicate that 5% Amlexanox paste (Aphthasol) is safe for the treatment of recurrent minor aphthous ulcers.

Study by Deshmukh RA et al[23] showed significant difference in size, pain, number, and duration of ulcers in triamcinolone acetonide gel within a period of 7 days, and these results were similar to our results.

Conclusion

Both amlexanox and triamcinolone acetonide are effective and safe in the treatment of recurrent aphthous stomatitis.

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Nil.

Conflicts of Interest

There are no conflicts of interest.

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