

Efficacy of Single Application of Topical Doxycycline Hyclate and Triamcinolone Acetonide in Denture Adhesive in the Management of Recurrent Aphthous Stomatitis: A Comparative Study

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Abstract:

Aim: To evaluate the efficacy of single application of topical doxycycline hyclate and single application of triamcinolone acetonide in the management of recurrent aphthous stomatitis for pain reduction.

Materials and Methods: A total of 30 patients were selected and divided into 2 groups (Group I and II) with 15 subjects belonging to each. Patients with aphthous ulcer were diagnosed on clinical examination and pain intensity was measured using a discrete visual analog scale (VAS) of 0–10 (with 1 mm division, where “0” is no pain and “10” is worst possible pain). Number of ulcers along with size and duration of each ulcer were recorded. Group I was treated with doxycycline hyclate (100mg) tablet crushed into fine powder and mixed with denture adhesive (fixon) and applied onto the lesion. Group II was treated with 0.1% triamcinolone acetonide gel mixed in denture adhesive and applied onto the lesion. A pain scale sheet was given to each patient to self-evaluate the daily status of pain scale on the day after treatment for about a week.

Results: Pain intensity on VAS scale in Group I was 4.29 before treatment and 2.29 after treatment. Similarly, in Group II was 3.62 before treatment and 2.15 after treatment. Pain reduction in VAS after treatment in 15 Group I patients was 47% after treatment on day 1. Moreover, in Group II was 41% after treatment on day 1. Group I had faster ulcer healing 2.89 ± 0.745 days when compared to Group II 5.15 ± 0.917 days with the P value of (<0.001).

Conclusion: Healing of the ulcer was significantly faster with doxycycline hyclate treatment compared to triamcinolone ointment with no adverse effects. Doxycycline is proved to be one of the modalities for the treatment of aphthous ulcer.

Keywords: Aphthous ulcer, denture adhesive, doxycycline hyclate, triamcinolone acetonide

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I. Introduction

Recurrent aphthous ulcers (RAUs) affect 20% of the population and are currently one of the most common oral disorders.[1] Recurrent aphthous stomatitis (RAS) is an inflammatory condition of unknown etiology characterized by recurrent, painful, single, or multiple ulcerations of the oral mucosa.[2] Most studies have failed to find the exact etiology and pathophysiology of RAS. Heredity, hematologic deficiencies, immune dysregulation, stress, local trauma, mechanical injury, hormonal disturbances, some foods, drugs, infections, smoking habits, and poor oral hygiene can be the predisposing factors.[3,4] It has been suggested that interstitial collagenases (matrix metalloproteinase-1 [MMP-1] and MMP-8) play a major role in tissue destructive events in RAU.[5-7] Various treatment modalities such as anti-inflammatory agents, steroids, sucralfate, tetracycline suspension, analgesics, anesthetics, antiseptics, and silver nitrate which are the standard topical treatment options that provide symptomatic relief. Beneficial results are obtained with topical or systemic steroids for some subjects. Several therapies are available either to cure or reduce the duration of recurrences but no single therapy has been shown to provide a satisfactory means for curing aphthous stomatitis, moreover, their clinical value remains unproven.[8-13] Since 1960, tetracycline has been used in the management of RAS based on its antimicrobial property. However, newer properties of doxycycline such as leukocyte suppression, inhibition of prostaglandin production, and inhibition of collagenase and gelatinase have further promoted its use in the management of RAU as an effective modality.[5,14-16] Recently, tissue adhesives have been used in the treatment of RAS, as it keeps the medication attached in close contact with the ulcer as long as possible.[17] Therefore, the aim of the present study is to compare the efficacy of single topical

application of doxycyclinehyclate with triamcinolone acetonide onlyonce as a new therapeutic regimen in the treatment of minor RAU for pain reduction.

II. Materials and Methods

The study was conducted in the Department of Oral Medicine and Radiology with approval from institutional ethical committee. This study included a total of 30 subjects which were divided into two groups each of 15 patients. In Group I: 15 patients received doxycyclinehyclate 100mg tablets (Fig. 1 a, b). In Group II: 15 patients received 0.1% triamcinolone acetonide paste (Fig. 2 a, b). The sample was selected randomly from those who came in Oral Medicine and Radiology Department. 16 females and 14 males were selected; with age ranging from 15 to 40 years but age group was not matched. Patients were selected on the basis of history and clinical examination. Healthy controls with a history of the duration of ulcers for more than 24 h and not exceeding 72 h with symptoms and ulcers with the characteristic clinical features of recurrent minor oral aphthous were included in the study. The exclusion criteria were (i) pregnant and lactating women, (ii) existing other oral mucosal diseases, (iii) hematologic abnormalities, (iv) history of hypersensitivity to tetracycline, (v) end-stage renal disease, or (vi) those taking any other medications for minor oral aphthous ulcer.

Clinical examination was carried out using sterile hand gloves and mask. A detailed case history, with patient's informed consent was taken. Medication was applied on the initial visit only. A diagnosis of aphthous ulcer was made when it occurred in the non-keratinized mucosa as a shallow crateriform ulcer covered by a whitish yellow pseudomembrane and presented with a round, regular border with a surrounding erythematous halo. On clinical examination, pain intensity using a visual analog scale (VAS) of 0–10 (with 1 mm division, where "0" is no pain and "10" is worst possible pain), number of ulcers, size of each ulcer (a graduated periodontal probe was used to measure the ulcer size at the maximum diameter of the ulcer), and the duration of each ulcer (the day of onset of the first prodromal symptom of each ulcer) were recorded. After complete clinical examination of the ulcer, pre-treatment photographs were taken before the start of treatment. The ulcer and the mucosa surrounding the ulcer were dried thoroughly. Cotton rolls were placed for isolation. In Group I, doxycycline hyclate was ground to fine powder using a glass mortar and pestle. An appropriate amount of the medicament was mixed with a pinch of denture adhesive and few drops of saline in a glass slab using a stainless steel cement spatula. Then, the final mixture was placed over the ulcer using a plastic instrument. Similarly, in Group II, 0.1% triamcinolone acetonide was mixed in denture adhesive and applied onto the lesion in a similar manner. After topically applying the medicament over the ulcer in each group it was allowed to dry within few minutes with the chip syringe, the patient was asked to refrain from eating or drinking for 2 h. The patient was recalled after 3 days following the treatment procedure. A pain scale sheet to record the daily status of pain was given at the initial visit. The patients were instructed to self-evaluate the pain scale sheet on the day after treatment and daily after that for 3 days and also to note any adverse effects with the medication. After 3 days, the patients were asked to return the pain scale record.

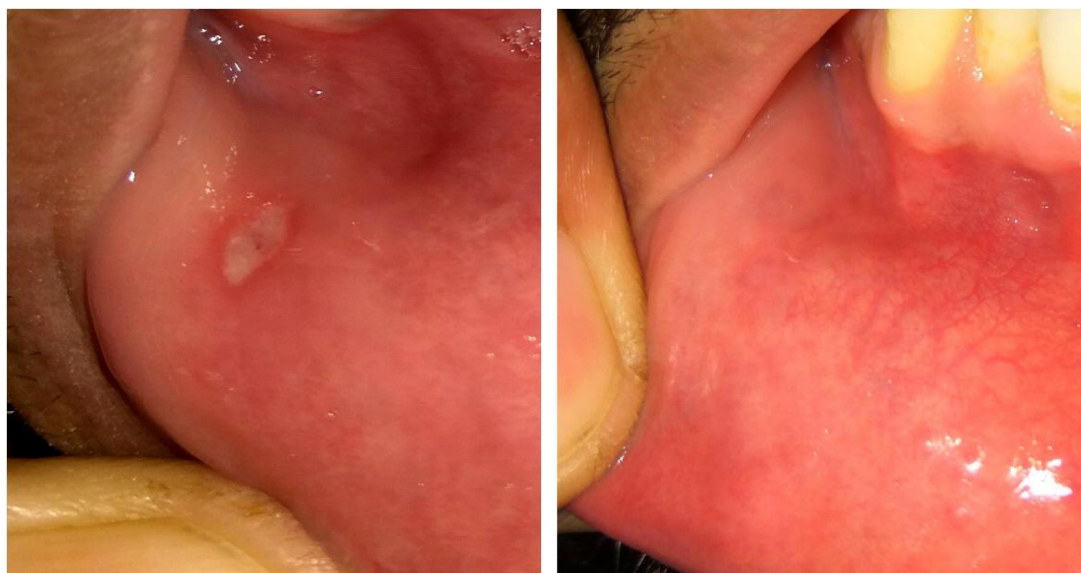


Figure 1: (a) Doxycycline hyclate group- pre-treatment, (b) doxycycline hyclate group- post-treatment



Figure 2: (a) triamcinolone acetonide group- pre-treatment, (b) triamcinolone acetonide group- post-treatment

III. Results

Data were tabulated, statistical analysis was done, and results were obtained. In the present study, out of 30 patients 16 were females and 14 were males with age ranging from 15 to 40 years. Out of 15 patients in Group I had 17 ulcers, out of which 2 patients had 2 ulcers. There were 15 ulcers in Group II patients. Pain intensity on VAS scale in 15 Group I patients was 4.27 ± 1.387 before treatment on day 1 and immediately after treatment was 2.29 ± 1.165 on day 1 and subsequently 1.15 ± 0.992 on day 2 and 0.55 ± 0.642 on day 3. Pain reduction in VAS- after treatment in 15 Group I patients was 47 % after treatment on day 1; 73.7 % on day 2; 88 % on day 3. The average number of days for individuals in Group I to heal ulcer was 2.89 ± 0.745 days. There was a statistically significant difference with the $P < 0.001$ noted in Group I in pain intensity by VAS scale and percentage of pain reduction. Similarly, in Group II, the pain intensity was 3.62 ± 1.6 before treatment and 2.15 ± 1.4 after treatment on day 1; 1.35 ± 0.818 on day 2; 0.40 ± 0.6 on day 3. Pain reduction in VAS- after treatment in 15 in Group II was 41 % after treatment on day 1; 63.3% on day 2; 90 % on day 3. The average number of days for individuals in Group II to heal ulcer was 5.15 ± 0.917 days. There was a statistically significant difference with the $P < 0.001$ noted in Group II in pain intensity by VAS scale and percentage of pain reduction. When Group I and II were compared together, there was no statistically significant difference in pain intensity by VAS scale and there was no statistically significant difference in pain reduction in ulcer healing between both groups. Days required for ulcer healing was significantly faster in doxycycline group when compared to triamcinolone group. None of the patients in our study reported any serious adverse effects because of the study drugs.

IV. Discussion

RAUs or aphthous stomatitis is a disorder characterized by recurring ulcers confined to the oral mucosa in patients with no other signs of disease. RAS is classified according to clinical characteristics: Minor ulcers, major ulcers (Sutton's disease, peradenitis mucosa necrotica recurrens), and herpetiform ulcers. Minor ulcers, which comprise over 80% of RAS cases, are less than 1 cm in diameter and heal without scars within a week. Major ulcers, are over 1 cm in diameter and take longer to heal over 10–14 days and often scar. Herpetiform ulcers are considered a distinct clinical entity that manifests as recurrent crops of dozens of small ulcers throughout the oral mucosa. [18] The first episodes of RAS most frequently begin during the second decade of life and may be precipitated by minor trauma, menstruation, upper respiratory infections, or contact with certain foods. The lesions are confined to the oral mucosa and begin with prodromal burning anytime from 2 to 48 h before an ulcer appears. [18] During this initial period, a localized area of erythema develops. Within hours, a small white papule forms, ulcerates, and gradually enlarges over the next 48–72 h. The individual lesions are round, symmetric, and shallow (similar to viral ulcers), but no tissue tags are present from ruptured vesicles. This helps to distinguish RAS from disease with irregular ulcers such as erythema multiforme, pemphigus, and pemphigoid. The buccal and labial mucosa are most commonly involved. Lesions are less common on the heavily

keratinized palate or gingiva.[18] A significant reduction in the pain intensity of RAU was found in the group of patients with doxycycline group as well as triamcinolone group when compared together. The intensity of the pain was statistically reduced on the very 1st day after treatment almost immediately after application of the medication. This indicates that treatment with doxycycline is as effective as triamcinolone in treating an aphthous ulcer. In the present study, pain relief was achieved with doxycycline treatment was effective compared with Gorsky *et al.*[19] conducted a crossover trial to assess the efficacy of 0.2% minocycline and 0.25% tetracycline oral rinses in patients with frequent episodes of RAS. Minocycline mouthwashes as compared with topical tetracycline rinses resulted in significantly improved pain control, by reducing the severity and duration of pain. Another study by Preshaw *et al.*[20] used sub-antimicrobial dose of doxycycline 20 mg to prevent the recurrence of RAS. In this study, we used powder of doxycycline mixed in denture adhesive mixed in saline in applied onto the ulcer. Vijayabala *et al.*[17] conducted a study on topical doxycycline hyclate powder mixed in denture adhesive was applied on an aphthous ulcer in which doxycycline hyclate patients had significantly less pain by day 1 ($P < 0.001$) and healed faster ($P < 0.001$) compared with placebo. In the present study, Group I patients had significantly less pain by day 1 and also ulcer healed faster when compared with Group II patient. Pain relief with doxycycline may be due to the recently recorded non-antimicrobial properties of doxycycline molecules. Recent studies indicate that MMPs may play an important role in tissue destruction in aphthous ulcers and the effect of tetracyclines helps to inhibit human MMP.[5,6] Doxycycline may also reduce the amount of some MMP proteins present in the tissue. An additional non-antimicrobial property of doxycycline that may be relevant to inflammation cell-mediated tissue destruction in RAU is their ability to suppress neutrophil function and to scavenge reactive oxygen species. In the present study, pain relief achieved with the triamcinolone acetonide mixed in denture adhesive group in a similar fashion as that of doxycycline group compared with the study by Miles *et al.*[21] where topical steroid triamcinolone acetonide combined with cyanoacrylate barrier was used as the local medication. From the present study, it was evident that the vehicle used in our study denture adhesive showed some beneficial effect with the fact that any topical medication in the oral cavity can be retained for a longer time with the help of tissue adhesive material used. The pain reduction in both groups was quite similar when both groups were compared together, the only difference being that the ulcer healed faster in doxycycline group when compared to triamcinolone acetonide group.

V. Conclusion

Healing of the ulcer was significantly faster for the doxycycline group compared to triamcinolone ointment. No significant difference in the speed of pain reduction between the doxycycline and triamcinolone ointment. The doxycycline was found to be equally effective in treating oral aphthous ulceration, with some advantage over the widely used preparation triamcinolone ointment. It appears advantageous because of its cost-effectiveness, single application, and faster symptomatic relief than other drugs.

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Conflicts of interest

There are no conflicts of interest.

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