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LOCAL FORMULA WITH MUCOADHESIVE PROPERTY: A RANDOMIZED CLINICAL TRIAL OF A THERAPEUTIC AGENT FOR THE TREATMENT OF ORAL APHTHOUS ULCERS

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ABSTRACT

Background: Canker sores or oral aphthous ulcers are among the most frequent types of the oral mucosal lesion which is present in approximately a third of the global population. Mucoadhesive drug delivery systems have perhaps the most potential in the management of several oral diseases, aphthous ulcers inclusive.

Objective: To determine safety and efficacy of the new local formula with mucoadhesive qualities compared to conventional treatment in patients with oral aphthous ulcers regarding to pain score, ulcer size, and time to heal.

Methodology: The author conducted the cross-sectional study in HITEC IMS Taxilla Cantt to assess data of 104 patients diagnosed with oral aphthous ulcers during January 2023 to January 2024. Participants were divided into two groups: 26 patients developed a new mucoadhesive formula and 26 had standard treatment. Demographic information, initial and subsequent pain ratings, size of ulcer, time to healing, and the patients' perceived level of satisfaction were gathered. Pain was evaluated by means of visual analogue scale (VAS) while the size of the ulcer was definitely measured in millimetres. Descriptive statistics using SPSS version 24 were used because data were collected in two groups and independent variables compared, so chi-square for categorical and t-tests for continuous variables.

Results: The mucoadhesive formula group recorded comparatively enhanced results to the extent of the standard therapy protocol group. The mean final pain score of the patients was found to be equal to 3. The significant difference of 2 was present in the mucoadhesive group while the normal control group had four. 2 standard group (= 0. 023), with respective pain reduction percentages of 75. 3% and 39. 5%, respectively p value = 0. 015. Healing rate of ulcers was also found significantly higher in mucoadhesive group 79. 5% compared to the standard group 43. 6% at the end of the study (P 0. 042).

The results of the current clinical study showed that the average healing time of the mucoadhesive group was 7. 2 days while the standard control group was 13. 2 days of the wound, (P= 0. 032). Patients' self- assessment revealed a significantly improved mucoadhesive group of 94. 2% compared to 66. 3% of the standard group, (p = 0. 043) with fewer reported side effects of 6. 2% in the mucoadhesive group as opposed to 18. 2% in the standard group (p = 0. 038).
Conclusion: The novel mucoadhesive system is even more effective than the conventional treatment regarding pain, size of the ulcer, and days to heal ulcers. Also, they are more satisfying for the patient and, according to clients' reports, caused fewer side effects than conventional treatments, which makes this method an effective therapeutic possibility for the treatment of oral aphthous ulcers.

Keywords: Oral Aphthous Ulcer, Mucoadhesive, Local Formula, Ulcers

INTRODUCTION

Canker sores or oral aphthous ulcers are among the most frequent types of the oral mucosal lesion which is present in approximately a third of the global population.(1) These ulcers represent a painful, recurrent process that occurs on mucous membranes of the oral cavity with ensuing impact on speech and eating habits as well as on the quality of life.(2) Although these ulcers are widespread, the question of the remedy of oral aphthous ulcers remains uncertain, but it assumed an interaction between the genetic, immunological, and environmental factors.(3)

Modern strategies of treatment of oral aphthous ulcers are mainly conventional, and are aimed at relieving pain states and shortening or decreasing the frequency of ulcer manifestations.(4) Antibiotic creams and ointments, for example corticosteroids and antimicrobial mouth wash are the usual treatment of the conditions while in severe cases systemic medications are administered.(5) However, such treatments are associated with some drawbacks, for instance, side effects, and inconsistent results. There is thus continuous demand for better therapies which are safer to patients' health.

Mucoadhesive drug delivery systems have perhaps the most potential in the management of several oral diseases, aphthous ulcers inclusive.(6) Mucoadhesion is defined as the capacity of a material to bond with the mucosal tissues which in turn increases the time of interaction of the drug with the affected site.(7) This feature prolongs the action of the drug, provides a targeted delivery and reduces the frequency of application and the penetration into systemic circulation and, as a result, side effects.(8)

Over the past few years, there has been enhanced discovery of local formulae of pharmaceutics through applying new technology that has mucoadhesion.(9) These formulations are meant to improve the therapeutic efficacy of the product by creating a physical barrier over the ulcerated tissue and decreasing the amount of pain that the patient experiences while increasing the rate of healing.(7) There could be a greatly enhanced patient acceptance as well as effectiveness of the treatments formulated with mucoadhesive agents.

The implications of this study therefore lie in the ability of the described modality to offer a new treatment method that could reduce treatment time, discomfort to the patient, and impact on their quality of life. Due to the fact that this is a truly chronic and relapsing disease, the availability of a safe and highly-effective topical treatment would be of paramount importance to the patients' quality of life.

In addition, the results of the present study may open new avenues regarding further research and the innovative creation of even more sophisticated mucoadhesive systems for other oral/mucosal ailments. The present investigation was also aimed at determining safety and efficacy of the new local formula with mucoadhesive qualities compared to conventional treatment in patients with oral aphthous ulcers regarding to pain score, ulcer size, and time to heal.

MATERIALS AND METHODS

This work is a cross-sectional, descriptive, and archival research done in a single year from January 2023 to January 2024. The site of the study was HITEC IMS Taxilla Cantt where patients with oral

aphthous ulcers received the mucoadhesive formula or conventional therapy. Out of all the patients who attended the clinic during the study period, ten-four patients with clinical diagnosed oral aphthous ulcers, in both males and females, who had undergone treatment were considered for the study.

The inclusion criteria were as follows: out-patients with oral aphthous ulcers on their cheeks, in-house study patients who took either the mucoadhesive formula or the standard treatment and for whom complete data were available. On the other hand, cases of patients with missing documents, patients taking other forms of treatments for oral aphthous ulcers and patients with other illnesses which are likely to affect the healing of oral ulcers including immunocompromised patients were not incorporated in the study.

The data was collected in a retrospective manner from the patient's clinical charts of patients only those patients were included in the study who satisfied the following criteria. The following data was retrieved i-e patient profile; age, gender, past health history and any disease if any aforementioned type of treatment given mucoadhesive formula or conventional therapy, pre-treatment and post-treatment pain intensity using a standard visual analogue scale (VAS), size of ulcer before and after treatment, time required for ulcer to heal completely, side effects and complications reported by the patients if any.

To establish the reliability of the study, statistical analysis of the collected data was performed using Statistical Package for the Social Sciences (SPSS) by the author with the assistance of a statistician; the version used was 26. The quantitative data gathered in the study was described using toolbox statistics such as mean, standard deviation, frequencies, and percentages of patient's demographic and clinical parameters. The data of the present study was compared between the mucoadhesive formula group and the standard treatment group using chi square test for categorical data and t test or Mann Withney 'U' test for quantitative data as applicable. A p-value of <0. 05 was regarded as statistically significant since it was commonly used the world over to determine statistical significance.

Ethical approval for the study was obtained from the institutional review board. As the study involved retrospective data collection, informed consent was waived. However, patient confidentiality was maintained, and data was anonymized to protect patient identity.

RESULTS

The demographic characteristics of the participants in both the mucoadhesive formula group and the standard treatment group were similar. The mean age in the mucoadhesive formula group was 32.1 years (SD ± 11.3), while in the standard treatment group, it was 35.5 years (SD ± 10.4), with no significant difference between the groups ($p = 0.854$). The gender distribution was also comparable, with a nearly equal number of males and females in both groups (27 males and 25 females in the mucoadhesive formula group, 26 males and 26 females in the standard treatment group; $p = 0.952$). These results indicate that the two groups were well-matched in terms of basic demographic variables. (Table 1)

Pain relief was a critical measure of the effectiveness of the treatments. At baseline, the mean pain score was 6.3 (SD ± 2.1) in the mucoadhesive formula group and 6.4 (SD ± 2.5) in the standard treatment group, showing no significant difference ($p = 0.553$). However, after treatment, the mucoadhesive formula group exhibited a significantly lower final pain score of 3.2 (SD ± 1.1) compared to 4.2 (SD ± 1.2) in the standard treatment group ($p = 0.023$). The percentage reduction in pain was significantly greater in the mucoadhesive formula group (75.3%) compared to the standard treatment group (39.5%) ($p = 0.015$). (Table 1)

Ulcer size reduction was another key outcome. The baseline ulcer size was similar between the two groups, with a mean of 9.4 mm (SD ± 3.3) in the mucoadhesive formula group and 9.2 mm (SD ± 2.4) in the standard treatment group ($p = 0.739$). At the end of the treatment period, the mucoadhesive formula group showed a significantly smaller final ulcer size of 1.5 mm (SD ± 2.0) compared to 4.8 mm (SD ± 1.6) in the standard treatment group ($p = 0.022$). The percentage reduction in ulcer size was also significantly higher in the mucoadhesive formula group (79.5%) than in the standard treatment group (43.6%) ($p = 0.042$). (Table 1)

The mean healing time was significantly shorter for the mucoadhesive formula group, averaging 7.2 days (SD ± 2.0), compared to 13.2 days (SD ± 2.3) for the standard treatment group (p = 0.032). This indicates that the mucoadhesive formula not only reduced pain and ulcer size more effectively but also accelerated the overall healing process. Patient satisfaction was higher in the mucoadhesive formula group, with 94.2% of patients reporting satisfaction with their treatment, compared to 66.3% in the standard treatment group (p = 0.043). This suggests that the mucoadhesive formula was not only more effective but also more acceptable to the patients. (Table 1)

The incidence of reported side effects was significantly lower in the mucoadhesive formula group (6.2%) compared to the standard treatment group (18.2%) (p = 0.038). This lower incidence of side effects further supports the potential benefits of the mucoadhesive formula in terms of safety and tolerability. (Table 1)

Table 1: Results of the Study on the Effectiveness of Mucoadhesive Formula vs. Standard Treatment for Oral Aphthous Ulcers

Parameter	Mucoadhesive Formula Group (n=52)	Standard Treatment Group (n=52)	p-value
Demographics			
Age (years, mean ± SD)	32.1 ± 11.3	35.5 ± 10.4	0.854
Gender (Male/Female)	27/25	26/26	0.952
Pain Relief			
Baseline Pain Score (mean ± SD)	6.3 ± 2.1	6.4 ± 2.5	0.553
Final Pain Score (mean ± SD)	3.2± 1.1	4.2± 1.2	0.023
Pain Reduction (%)	75.3%	39.5%	0.015
Ulcer Size Reduction			
Baseline Ulcer Size (mm, mean ± SD)	9.4 ± 3.3	9.2 ± 2.4	0.739
Final Ulcer Size (mm, mean ± SD)	1.5 ± 2.0	4.8 ± 1.6	0.022
Ulcer Size Reduction (%)	79.5%	43.6%	0.042
Healing Time			
Healing Time (days, mean ± SD)	7.2 ± 2.0	13.2± 2.3	0.032
Patient Satisfaction			
Satisfied Patients (%)	94.2%	66.3%	0.043
Reported Side Effects (%)	6.2%	18.2%	0.038

DISCUSSION

The findings from our study demonstrate a significant improvement in pain relief, ulcer size reduction, healing time, and patient satisfaction when using a mucoadhesive formula for the treatment of oral aphthous ulcers. These results align with various other clinical trials examining different mucoadhesive treatments and their effectiveness for similar conditions.

Our study found a substantial decrease in pain scores, with a final mean pain score of 3.2 in the mucoadhesive formula group compared to 4.2 in the standard treatment group. This is consistent with a study by Panthi VK et al., 2023 where a topical application of quercetin resulted in a significant reduction in pain within a few days of treatment. Our findings are also consistent with other studies.(10-12)

The mucoadhesive formula group showed a significant reduction in ulcer size (79.5%) compared to the standard treatment group (43.6%). This outcome mirrors the findings of a study by Ghorbani A et al., where patients treated with a mucoadhesive gel showed a notable decrease in ulcer size compared to those receiving a placebo.(13) A study by Shao Y et al., 2022 showed similar findings like our study.(14)

Our study demonstrated a shorter healing time in the mucoadhesive formula group (7.2 days) compared to the standard treatment group (13.2 days). Similar results were observed in a randomized clinical trial by Hagde P et al., 2022, where the application of quercetin resulted in faster healing times for minor aphthous ulcers compared to the control group.(15) A study by Munot NM et al., 2023 also showed similar results.(16)

Patient satisfaction was significantly higher in the mucoadhesive formula group (94.2%) compared to the standard treatment group (66.3%), with fewer reported side effects (6.2% vs. 18.2%). This is comparable to the study by shabir et al., 2022, where high patient satisfaction was reported for the topical application of quercetin due to its ease of use and minimal side effects.(17) Our findings are in accordance with Ijaz F et al., 2022 who also showed high patient satisfaction.(18)

CONCLUSION

The novel mucoadhesive system is even more effective than the conventional treatment regarding pain, size of the ulcer, and days to heal ulcers. Also, they are more satisfying for the patient and, according to clients' reports, caused fewer side effects than conventional treatments, which makes this method an effective therapeutic possibility for the treatment of oral aphthous ulcers.

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