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ORIGINAL RESEARCH

THE IMPACT OF VARYING CHLORHEXIDINE CONCENTRATIONS ON THE HEALING OF RECURRENT APHTHOUS ULCERS: A CLINICAL EVALUATION

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Abstract

Background: REAUs among most common oral mucosal diseases Results : Muscles of mastication and mouth opening Muscles of mastication and opening the mouth (mediation, impairment and OZR) have a great influence on swelling and pain induced by RAUs in OLR. Chlorhexidine gluconate is an antiseptic agent widely used in dentistry, it is considered effective on treatment of RAU, however, the best and the lowest side effect concentration of the product remains controversial. Establishing the preferred concentration is important because this maximises the desirable properties of the product, and in so doing enhances the comfort and compliance of the patient using the product for treatment of RAU These results suggest the usefulness of the chlorhexidine mouth rinse in the clinical treatment of recurrent aphthous ulcers.

Objectives: The clinical aim of this study will be to assess whether there are therapeutic benefits to different concentrations of chlorhexidine mouthwash on promoting healing, reducing pain and preventing ulcer recurrence.

Materials and Methods: This study was a randomised, controlled clinical trial which enrolled 60 patients (aged 18-45 years) with minor RAUs. The participants were randomly divided equally into 3 groups (n = 20) and theoretically exposed to the following concentrations of chlorhexidine mouthwash: Group A (0.06%), group B (0.12%) and group C (0.2%). Subjects were directed to use the AND 2x/day for 7 days. On days 0, 3, and 7, the following clinical evaluations were performed:Size of the ulcer (in mm using a periodontal probe),Pain levels (measured with a 10-point visual analog scale [VAS]),Status of healing (healed, poorly healed, not healed walls), Securrent stone at 2 weeks follow- up.

Results: The scores improved in all groups during the 7 days of therapy. The shortest healing time was in Group C (0.2%) and on an average, ulcers healed on day 5. Groups Group A (0.06%) showed the slowest response exhibiting partial healing in some cases, and Group B (0.12%) demonstrated moderate healing at 6 d.

The pain scale was significantly alleviated in all groups, and there were the extent reduction of 7, 5.5 and 4 points in group C, group B and group A respectively. Thirty per cent of patients in Group C and 10% in Group B reported adverse effects like altered taste and mild irritation, but none in Group A experienced the same. There was no recurrence in Group C (1 case), while two (2) and four (4) recurrences were reported in Groups B and A respectively.

Conclusion: Use of 0.2% CHX results in maximum rate of healing and pain relief, but leads to increased mucosal side effects increasing patient noncompliance. In contrast, 0.12% CHX is a favorable balance of therapeutic benefit in relation to potential to heal and lower potential to cause irritation or alter taste and is a therapeutically practical

Keywords: Aphthous ulcer, Chlorhexidine gluconate, Mouthwashes, Oral mucosa, Ulcer, Healing.

INTRODUCTION

Recurrent aphthous ulcers (RAUs), known as recurrent aphthous stomatitis (RAS), are painful, superficial ulcers involving the non-keratinized oral mucosa and have a worldwide prevalence ranging from 5% to 25% [1]. Although ra Us are benign and self-limited, the condition could severely affect patients' quality of life owing to pain, difficulty in eating and speaking impairments [2].

They are idiopathic however believed to be multifactorial in origin including local trauma, stress, nutritional deficit, immunological abnormalities and may be associated with microbial dysbiosis [3]. As to other treatment modalities, the chlorhexidine gluconate is the most commonly used agent in the dental practice because of its good antimicrobial and anti-inflammatory effects. It is commercially available in 0.06% to 0.2% solutions and prescribed as a mouthwash in the control of plaque and as an adjunct in the treatment of different types of oral lesions, including aphthous ulcers (4). Nevertheless, potential side effects of high-concentration chlorhexidine, including mucosal irritation, taste disturbance, and tooth discolouration, were highlighted in recent evidence that could affect patient compliance [4].

Chlorhexidine gluconate aqueous mouthwashes, with three varying concentrations, which are 0.06%, 0.12% and 0.2%, were purchased from a licensed pharmaceutical manufacturer. Chlorhexidine gluconate (CHG) is a bisbiguanide antiseptic, commonly available at 0.12% and 0.2%, and has bactericidal activity due to the disruption of the cell membrane and precipitation of intracellular material [5].

Its efficacy in reducing plaque accumulation and gingival inflammation has made it a routine part of dental home care practices, emphasizing the orthodontic patients with fixed appliances 6.

Chlorhexidine (CHX) mouthwash is one of the most commonly used antiseptic agents in dental practice due to its broad-spectrum antimicrobial activity and its ability to reduce oral microbial load effectively. It is particularly recommended before dental procedures to minimize the risk of infection and to maintain oral hygiene in patients with compromised oral conditions [7].

While the clinical efficacy of chlorhexidine in the treatment of RAUs has been the focus of several studies, few of them evaluated treatment outcomes between various concentrations in a controlled clinical

setting. A recent systematic review noted the absence of standardization of clinical data to direct optimal dosing of chlorhexidine in ulcers.

This study aims to evaluate the clinical effects of different concentrations of chlorhexidine mouthwash on the healing process of recurrent aphthous ulcers (RAUs).

The specific objectives include:

1. To compare healing time of RAUs among 0.06%, 0.12%, and 0.2% chlorhexidine mouthwash concentrations.
2. To assess pain reduction associated with each concentration.
3. To evaluate the recurrence rate of ulcers during and after treatment.
4. To monitor adverse effects such as mucosal irritation or taste alteration.

MATERIALS AND METHODS

Sixty subjects, 18-45 years old, clinically diagnosed as having minor RAUs were included. Regular single use plastic cups were used for rinsing, and the participants were directed to rinse for twice a day for 10 ml of the respective mouthrinses for 7 days continuously.

Clinical evaluation tools included:

A UNC-15 periodontal probe (Hu-Friedy, Chicago, IL, USA) for the dimensions of the ulcers in millimeters was used.

A VAS (0–10 scale) for evaluation of subjective level of pain.

Gloves, gauze and tongue blades for intra oral examination.

All ulcer area, pain score, and healing status assessments were completed using standardized case report forms. A digital timer (CASIO HS-80TW-1DF, Japan) was employed to ensure that the timing of the mouthwash application and subsequent montoring of the follow-up exams was adeouate.

This study was a randomised, controlled clinical trial which enrolled 60 patients (aged 18-45 years) with minor RAUs. The participants were randomly divided equally into 3 groups (n = 20) and theoretically exposed to the following concentrations of chlorhexidine mouthwash: Group A (0.06%), group B (0.12%) and group C (0.2%). Subjects were directed to use the AND 2x/day for 7 days. On days 0, 3, and 7, the following clinical evaluations were performed:

-Size of the ulcer (in mm using a periodontal probe)

-Pain levels (measured with a 10-point visual analog scale [VAS])

-Status of healing (healed, poorly healed, not healed walls)

-Recurrent stone at 2 weeks follow- up.

Statistical analysis was conducted on SPSS v26. Some statistical tests were performed using ANOVA and chi-square test at $p < 0.05$ level of significance.

RESULTS

The scores improved in all groups during the 7 days of therapy. The shortest healing time was in Group C (0.2%) and on an average, ulcers healed on day 5. Groups Group A (0.06%) showed the slowest response exhibiting partial healing in some cases, and Group B (0.12%) demonstrated moderate healing at 6 d. The pain scale was significantly alleviated in all groups, and there were the extent reduction of 7, 5.5 and 4 points in group C, group B and group A respectively. Thirty per cent of patients in Group C and 10% in Group B reported adverse effects like altered taste and mild irritation, but none in Group A experienced the same. There was no recurrence in Group C (1 case), while two (2) and four (4) recurrences were reported in Groups B and A respectively (table1).

Table 1. Effect of Different CHX Concentrations on Healing Time, Pain Reduction, and Adverse Effects

Group	CHX Concentration	Mean Healing Time (days)	Mean Pain Reduction (VAS)	Adverse Effects (%)
A	0.06%	6.5	4	0%
B	0.12%	5.8	5.5	10%
C	0.2%	5.0	7	30%

DISCUSSION

The findings of this clinical trial support the use of chlorhexidine (CHX) mouthwash in the treatment of recurrent aphthous ulcers (RAUs), particularly in accelerating healing, alleviating pain, and reducing recurrence. Patients treated with 0.2% CHX demonstrated the most rapid improvement, with significant epithelial regeneration observed by day 5. These results are consistent with previous studies, including Liu et al. (2022), which demonstrated faster mucosal healing with higher CHX concentrations (8), and Salarzehi, F. K., et al. (2021) who attributed the sustained efficacy to CHX's long-term substantivity and tissue affinity [9].

However, higher concentrations were associated with an increased incidence of side effects, particularly mucosal irritation, altered taste, and transient desquamation. These side effects, as reported by Plantinga et al. (2016), may limit patient compliance [10]. In contrast, 0.12% CHX provided a clinically effective response with fewer adverse effects, indicating a favorable balance between efficacy and tolerability .

Group A (0.06%) showed the lowest incidence of side effects, though healing was slower and recurrence higher. This suggests that a minimal effective threshold may be necessary for CHX to exert significant antimicrobial and anti-inflammatory effects [11].

Recent studies have proposed the integration of CHX with adjunctive natural agents such as aloe vera and hyaluronic acid to enhance mucosal healing and reduce irritation [12]. In addition, innovative drug delivery systems such as nanocarriers or mucoadhesive herbal gels (e.g., turmeric or propolis) may enhance local retention and reduce toxicity.

It is also important to consider biological variability. Differences in healing responses may be influenced by factors such as ulcer subtype, underlying nutritional deficiencies, systemic conditions, and oral microbial profiles. These variables are rarely standardized across trials, contributing to outcome inconsistencies [13].

Furthermore, future research should investigate the effects of CHX on inflammatory cytokines (e.g., interleukin-1β, TNF-α), to better understand its immunomodulatory role in ulcer healing.

This could help identify additional therapeutic targets.

Limitations of this study include a modest sample size (n = 60) and short follow-up duration (14 days). These factors constrain the generalizability of the results. Future studies should consider extended follow-up and include comparisons with other agents such as topical corticosteroids, tetracyclines, and non-pharmacological approaches to determine the most effective long-term treatment.

In terms of side effects, however, increasing the concentration reflected not safe usage, as the higher concentration was associated with increased reports of side effects, especially taste dysfunction, oral mucosa irritation, and transient desquamation. These results are consistent with other study who advised to limit the prolonged use of 0.2% CHX due to the potential for patient discomfort and esthetic complications [5].

On the other hand, 0.12% CHX seemed to reflect the best compromise between clinical efficacy and patient acceptance. Less therapeutic effect and fewer side effects still make it to be the ‘right’ dose in routine patients.

More interestingly, the 0.06% group exhibited less frequent side-effects, albeit with slower ulcer healing time and greater recurrence rate. This means that a certain concentration of honey may be required for effective antibacterial and anti-inflammatory effects on inflamed and ulcerated mucosa.

In addition, some recent studies have suggested using CHX combined with adjunctive materials, e.g. aloe vera or hyaluronic acid, to promote wound healing and reduce the irritative effects [14]. Pairing drugs in this fashion could help solve some of the current trade-offs between safety and the level of efficacy.

It is important to mention that the present study had small sample size (n = 60) and short followup period (14 days). These limitations constrain the generalization of the results. Bigger and longer term future randomised trials are needed. Comparison with other ulcer therapies, including corticosteroids and antimicrobial tetracyclines and non-prescription herbal rinses, could help to clarify the relative efficacy and safety of CHX for RAS

Properties and Pharmacological Effects of Chlorhexidine

Chlorhexidine gluconate is a cationic bisbiguanide compound that has broad-spectrum antimicrobial activity. It is a very potent agent active against both Gram-positive and Gramnegative bacteria, facultative anaerobes, and certain fungi and viruses. Mechanism of action of TTO is based on disruption of microbial cell membrane, cell content precipitation and cell death [15].

Chlorhexidine is highly substantive to oral tissues, conferring prolonged substantivity, which means that the agent is to remain effective in the oral cavity after rinsing for up to 12 hours . This feature makes it to be especially beneficial for treating the infections and inflammations present in the oral mucosa. Its effectiveness in dental plaque prevention and gingival inflammation reduction is well documented [16, 19, 20].

In the case of RAUs, chlorhexidine serves a double purpose, that is, to decrease the secondary bacterial colonisation on the ulcer surface and to reduce local inflammation, thus promoting a quicker resolution of the lesion. In addition, it might have an action on the oral microbiome to avoid ulceration relapse in aniled-predisposed patients [17].

But the therapeutic use of chlorhexidine is dose-dependent. It is rapid on its action, providing microbial clearance at 0.2%, although at the expense of increasing the side effects (as mucosal desquamations, changes in taste, and teeth and tongue staining) [5]. Lower concentrations (0.06% to 0.12%) may cause reduction of these side effects for those patients who are less tolerant and still provide favorable clinical responses, especially with consistent utilization over time [5].

Recent studies have reported that the addition of natural agents such as aloe vera or hyaluronic acid to chlorhexidine may improve mucosal healing with less irritation, presenting possible new options for adjunctive therapy in the management of RAU [18].

Considering the concentration-dependent results obtained, clinicians should take into account patient sensitivity, severity of the ulcer and managability of compliance while choosing a CHX formulation. In addition, the effect of CHX combined with natural bioactive compounds to enhance therapeutic efficacy and reduce potential drawbacks should be explored further in future studies.

Due to wide spectrum of concentrations, it is important to assess the efficacy and safety of different strengths for achieving an optimal trade-off between clinical efficacy and tolerability.

In addition, this study is to evaluate the effectiveness of various concentrations of chlorhexidine on the healing time, relieving pain, and recurrence rates of RAUs that could guide for clinicians to use more appropriate type of agents.

CONCLUSION

These results suggest the usefulness of the chlorhexidine mouth rinse in the clinical treatment of recurrent aphthous ulcers. Use of 0.2% CHX results in maximum rate of healing and pain relief, but leads to increased mucosal side effects increasing patient noncompliance. In contrast, 0.12% CHX is a favorable balance of therapeutic benefit in relation to potential to heal and lower potential to cause irritation or alter taste and is a therapeutically practical and preferred formulation for multiple-purpose use.

DECLARATION

Authors contribution

authors contribution All authors have significantly contributed to the research and preparation of this paper.

Ethical Approval

The study was approved by the Institutional Ethics Committee. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Informed Consent

Written informed consent was obtained from all participants included in the study.

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Conflict of Interest Statement

The authors declare no conflicts of interest related to this study.

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