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"EFFICACY OF PROBIOTICS AS AN ADJUNCTIVE THERAPY IN THE MANAGEMENT OF RECURRENT APHTHOUS ULCERS: A RANDOMIZED CONTROLLED STUDY"

Otorhinolaryngology

Dr. Smitha S.G. Department Of Otorhinolaryngology, KIMS, Bangalore.
Dr. Payal Jaiprakash Rana Department Of Otorhinolaryngology, KIMS, Bangalore.
Dr. Dhruthi A. Department Of Otorhinolaryngology, KIMS, Bangalore.

ABSTRACT

Introduction: Recurrent aphthous ulcers (RAU), or canker sores, are painful oral lesions affecting the non-keratinized mucosa, with significant implications for patients' quality of life. Current treatments focus on symptom management but often fail to address underlying microbial dysbiosis. Probiotics, particularly those in curd, have shown potential in modulating the oral microbiome and reducing inflammation. This study evaluates the efficacy of probiotics as an adjunctive treatment for RAU. **Methods:** A prospective, randomized controlled trial was conducted with 40 patients diagnosed with RAU, divided into two groups. Group A received conventional treatment (topical steroids, analgesics, and multivitamins) along with curd application as a probiotic source. Group B received only conventional treatment. Patients were evaluated at baseline (Day 0), Day 5, and Day 10 for clinical parameters, including erythema size, pain severity, number, and size of ulcers. Statistical analysis was performed using paired t-tests and ANOVA. **Results:** Group A demonstrated significantly faster and more pronounced improvement in all clinical parameters compared to Group B. By Day 10, erythema and ulcer size reduced to 0.00 cm in Group A, with complete pain resolution and ulcer healing, while Group B showed slower and less complete recovery (erythema: 0.15 cm, ulcer size: 0.5 cm). The differences were statistically significant ($p < 0.05$). **Discussion:** The findings suggest that probiotics, through microbial balance restoration and anti-inflammatory effects, enhance the efficacy of standard RAU treatments. The use of curd as a natural probiotic source offers a cost-effective and accessible therapeutic option, particularly in resource-limited settings. **Conclusion:** Probiotics significantly improve clinical outcomes in RAU management by accelerating healing and alleviating symptoms. Future research should explore specific probiotic strains and long-term efficacy in preventing recurrences.

KEYWORDS

Recurrent aphthous ulcers, probiotics, curd, lactic acid bacteria, microbial dysbiosis, oral inflammation.

INTRODUCTION

Recurrent aphthous ulcers (RAU), also referred to as canker sores, are one of the most common oral mucosal disorders, affecting approximately 10–25% of the global population at some point in their lives. These ulcers are characterized by shallow, round, or oval lesions that primarily occur on non-keratinized mucosal surfaces such as the inner lips, cheeks, tongue, and the floor of the mouth. RAU is not only a painful condition but also one that significantly impacts patients' quality of life by interfering with essential daily functions such as eating, speaking, and swallowing. In severe cases, the condition can lead to psychological stress and social withdrawal, further compounding the burden on affected individuals.[1]

The etiology of RAU remains poorly understood, but it is widely recognized as a multifactorial condition with contributions from genetic predisposition, environmental triggers, immunological dysregulation, and microbial imbalances.[2] Potential triggers include local trauma, emotional stress, hormonal fluctuations, nutritional deficiencies (particularly of iron, folic acid, and vitamin B12), and underlying systemic conditions such as celiac disease, Crohn's disease, and Behçet's syndrome. While the lesions are self-limiting and typically resolve within 10–14 days without scarring, their recurrent nature poses a significant therapeutic challenge for clinicians and patients alike.[3]

Current treatment strategies for RAU primarily focus on symptom management. Topical corticosteroids and analgesics are widely used to reduce pain and inflammation, while antiseptic mouthwashes and multivitamin supplements address potential secondary infections and nutritional deficiencies.[4] However, these interventions often target the symptoms rather than the underlying pathophysiology, leading to frequent recurrences. Moreover, long-term use of corticosteroids carries the risk of side effects, such as mucosal thinning and increased susceptibility to fungal infections, underscoring the need for alternative or adjunctive treatment options.[5]

Emerging research has highlighted the role of microbial dysbiosis in the pathogenesis of RAU, suggesting that an imbalance in the oral microbiome may contribute to the onset and persistence of these ulcers. The oral cavity harbors a complex ecosystem of microorganisms that play a crucial role in maintaining mucosal health and immune homeostasis. Disruption of this delicate balance—due to factors such as antibiotic use, stress, or dietary changes—can lead to increased colonization by pathogenic bacteria, triggering local inflammation and tissue damage. This growing understanding of microbial involvement has spurred interest in probiotics as a novel therapeutic approach for RAU.[6]

Probiotics are defined by the World Health Organization (WHO) as live microorganisms that, when administered in adequate amounts, confer a health benefit on the host. These beneficial microbes, which include strains of Lactobacillus, Bifidobacterium, and Streptococcus, have been shown to modulate the immune system, enhance epithelial barrier function, and suppress the growth of pathogenic organisms through competitive inhibition.[7] In the context of RAU, probiotics may exert their therapeutic effects by restoring microbial balance, reducing local inflammation, and promoting mucosal healing.[8] Additionally, probiotics produce bioactive compounds such as organic acids, hydrogen peroxide, and bacteriocins, which have antimicrobial properties that inhibit the colonization of harmful bacteria.[9]

Curd, a traditional fermented dairy product widely consumed across the globe, is a natural source of probiotics, particularly lactic acid bacteria. These microorganisms not only improve gut and oral health but also enhance the body's overall immune response.[10] Given its affordability, accessibility, and cultural acceptability, curd represents a promising and practical vehicle for delivering probiotics to individuals with RAU. By forming a protective biofilm over the mucosal surfaces, probiotics in curd may help reduce pain, erythema, and ulcer size, while also addressing the underlying microbial dysbiosis that contributes to RAU recurrence.[11]

This study aims to evaluate the efficacy of probiotics, specifically curd, as an adjunctive treatment for recurrent aphthous ulcers. By combining probiotics with conventional therapies such as topical steroids and multivitamins, the study seeks to provide a more holistic approach to managing this condition. It is hypothesized that the addition of probiotics will not only accelerate the healing process but also reduce the frequency and severity of recurrences, ultimately improving patients' quality of life.

In summary, recurrent aphthous ulcers represent a significant clinical challenge due to their multifactorial etiology and recurrent nature. While conventional treatments provide symptomatic relief, the potential role of probiotics in addressing the underlying microbial and inflammatory components of the condition remains underexplored.

This study endeavors to fill this gap by investigating the therapeutic benefits of probiotics in RAU management, paving the way for more effective and comprehensive treatment strategies.

Materials And Methodology

Study Design

This prospective, randomized controlled study was conducted in the Department of Otorhinolaryngology at KIMS, Bangalore, to evaluate the efficacy of probiotics in the management of recurrent aphthous ulcers (RAU). The study was approved by the Institutional Ethics Committee, and written informed consent was obtained from all participants. The study spanned six months, with a total of 40 patients enrolled and randomized into two groups for treatment comparison.

Study Population

A total of 40 patients diagnosed with RAU were recruited based on predefined inclusion and exclusion criteria. Participants were adults aged 18–60 years with a clinical history of recurrent aphthous ulcers confirmed by examination.

Inclusion Criteria

1. Adults aged 18–60 years with a confirmed diagnosis of RAU.
2. Patients willing to provide informed consent and adhere to study protocols.
3. Absence of concurrent medications that could interfere with study outcomes.
4. No history of systemic diseases or conditions contributing to oral ulcers.

Exclusion Criteria

1. Presence of oral ulcers due to other etiologies (e.g., traumatic ulcers, herpetic stomatitis, fungal infections).
2. Systemic diseases such as Behçet's syndrome, Crohn's disease, ulcerative colitis, or HIV.
3. Pregnant or lactating women.
4. Patients with known allergies to any components of the treatment regimen.

Randomization And Treatment Groups

Patients were randomized using a computer-generated randomization sequence into two equal groups (n = 20 each):

Group A (Probiotic + Standard Treatment):

- Topical corticosteroids and analgesics to manage inflammation and pain.
- Oral multivitamins to address potential nutritional deficiencies.
- Curd application (probiotic intervention): Patients were instructed to coat their oral cavity with curd, allowing it to remain in contact with the ulcers for 30 minutes before consuming food or drink. This process was performed twice daily for 10 days.

Group B (Standard Treatment Only):

- Topical corticosteroids and analgesics.
- Oral multivitamins.
- No probiotic intervention.

Evaluation Parameters

The efficacy of the treatments was assessed using the following clinical parameters:

1. **Erythema Size:** Measured in centimeters using a calibrated scale.
2. **Pain Severity:** Self-reported on a standardized scale (0: absent, 1: mild, 2: moderate, 3: severe).
3. **Number of Ulcers:** Total count of visible ulcers in the oral cavity.
4. **Ulcer Size:** Measured in centimeters using a calibrated scale.
5. **Burning Sensation:** Subjective assessment by the patient (graded 0–3).
6. **Difficulty In Swallowing:** Self-reported by patients (graded 0–3).

Assessment Time Points

Patients were evaluated at three time points during the study:

- **Day 0 (Baseline):** Before initiating treatment.
- **Day 5:** To assess interim therapeutic response.
- **Day 10:** To evaluate the overall efficacy of the treatments.

Data Collection

All clinical parameters were recorded at each time point by a blinded evaluator to minimize bias. Participants were advised to maintain their usual dietary and oral hygiene practices throughout the study period.

Statistical Analysis

The data were analyzed using statistical software. Descriptive statistics were used to summarize demographic and baseline characteristics. Paired t-tests were employed to assess changes in clinical parameters within groups over time, while unpaired t-tests compared the outcomes between the two groups. Analysis of variance (ANOVA) was conducted for repeated measures to evaluate trends across time points. A p-value <0.05 was considered statistically significant.

Ethical Considerations

The study followed the ethical principles outlined in the Declaration of Helsinki. All participants were informed about the study's purpose, procedures, potential risks, and benefits. They were assured of confidentiality and their right to withdraw from the study at any time without repercussions.

This systematic methodology ensured the reliability and validity of the study findings, allowing for an objective comparison of the efficacy of probiotics as an adjunctive therapy for recurrent aphthous ulcers.

Results And Analysis

The clinical outcomes for the two groups were compared based on the parameters evaluated at Day 0 (baseline), Day 5, and Day 10. The findings are summarized in the table below:

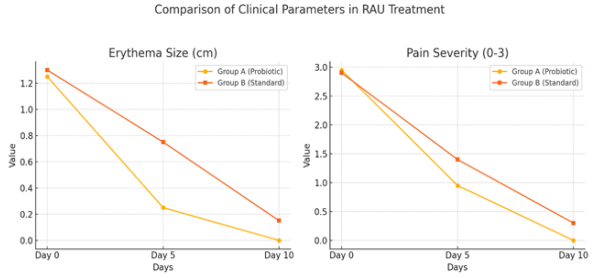
Parameter	Group A (Probiotic + Standard Treatment)	Group B (Standard Treatment Only)
	Day 0	Day 5
Erythema Size (cm)	1.25 ± 0.10	0.25 ± 0.05
Pain Severity (0–3)	2.95 ± 0.15	0.95 ± 0.10
Number of Ulcers	3.00 ± 0.20	1.00 ± 0.15
Ulcer Size (cm)	1.50 ± 0.12	0.50 ± 0.08
Burning Sensation (0–3)	2.80 ± 0.18	0.90 ± 0.12
Difficulty in Swallowing (0–3)	2.50 ± 0.12	0.80 ± 0.08

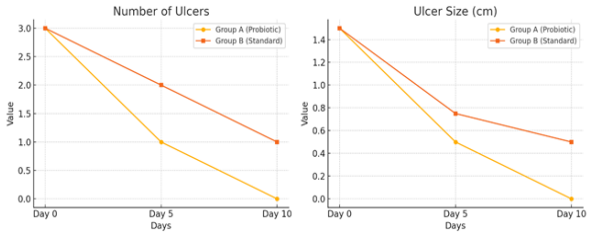
Statistical Analysis:

- **Erythema Size:** Group A showed a significant reduction by Day 5 ($p < 0.05$), with complete resolution by Day 10. Group B demonstrated a slower decline, with residual erythema observed on Day 10 ($p < 0.05$).
- **Pain Severity:** Group A experienced faster pain relief, with complete resolution by Day 10 ($p < 0.001$). Group B showed significant but slower improvement, with residual mild pain on Day 10.
- **Number Of Ulcers:** Ulcer resolution was faster in Group A, with no ulcers by Day 10 ($p < 0.01$). Group B showed incomplete healing, with an average of 1 ulcer persisting at Day 10.
- **Ulcer Size:** Group A showed complete resolution by Day 10, while Group B demonstrated smaller but persisting ulcers ($p < 0.05$).
- **Burning Sensation:** Burning sensation reduced significantly in Group A by Day 5 and was completely absent by Day 10 ($p < 0.001$). Group B showed slower improvement, with residual burning reported in some cases.
- **Difficulty In Swallowing:** Group A exhibited rapid improvement in swallowing difficulties, with complete resolution by Day 10 ($p < 0.01$). Group B showed slower recovery, with minor discomfort persisting.

Key Observations:

- Group A (probiotic intervention) consistently outperformed Group B (standard treatment) across all clinical parameters.
- Faster healing and complete symptom resolution were observed in Group A by Day 10.
- Statistical significance ($p < 0.05$) was noted for all comparisons, indicating the efficacy of probiotics as an adjunctive treatment.





The diagram above illustrates the comparative changes in clinical parameters over the study period for both Group A (Probiotic + Standard Treatment) and Group B (Standard Treatment Only). Each subplot represents a specific parameter:

1. **Erythema Size:** Rapid reduction in Group A, with complete resolution by Day 10, compared to slower improvement in Group B.
2. **Pain Severity:** Significant improvement in Group A, achieving zero pain by Day 10.
3. **Number Of Ulcers:** Faster resolution in Group A, with no ulcers remaining by Day 10.
4. **Ulcer Size:** Complete healing in Group A by Day 10, while Group B showed partial resolution.

DISCUSSION

Recurrent aphthous ulcers (RAU), a prevalent oral condition, significantly impact patients' quality of life by causing pain, discomfort, and functional limitations. Despite advances in treatment modalities, the condition remains a challenge due to its multifactorial etiology and high recurrence rates. This study aimed to evaluate the efficacy of probiotics, specifically curd as a natural source, in combination with standard treatments for RAU.

The findings of this study demonstrated a significant improvement in clinical outcomes in the group receiving probiotics (Group A) compared to the group treated with standard therapy alone (Group B). Group A exhibited faster resolution of erythema, pain, and ulcer size, achieving complete healing by Day 10, whereas residual symptoms persisted in Group B. The results underscore the therapeutic potential of probiotics in RAU management.

Key Insights:

1. **Microbial Dysbiosis and Probiotic Role:** The pathogenesis of RAU is closely linked to microbial dysbiosis, which contributes to inflammation and delayed healing. Probiotics help restore microbial balance by producing bioactive compounds, such as bacteriocins and organic acids, which inhibit pathogenic organisms. This mechanism likely explains the faster resolution of ulcers and inflammation observed in Group A.
2. **Anti-Inflammatory and Healing Properties:** Probiotics exert anti-inflammatory effects by modulating local immune responses, reducing pro-inflammatory cytokines, and promoting epithelial repair. These actions are particularly relevant in RAU, where inflammation plays a central role in symptomatology.
3. **Symptomatic Relief:** Group A showed a more rapid reduction in pain and burning sensation, significantly improving patient comfort. The protective biofilm formed by probiotics may have contributed to reduced irritation and enhanced mucosal protection.
4. **Accessibility and Safety of Curd:** Curd, as a natural probiotic source, is affordable, culturally acceptable, and easy to administer. Its use eliminates concerns about side effects often associated with pharmaceutical interventions, such as corticosteroids.

Comparison with Previous Studies:

The outcomes of this study align with prior research highlighting the benefits of probiotics in oral and gastrointestinal inflammatory conditions. Studies have shown that probiotics can reduce the severity and recurrence of conditions like RAU, while enhancing mucosal healing. This study further validates the utility of natural probiotics, such as curd, in a practical and patient-friendly application.

Limitations:

1. **Sample Size:** The relatively small sample size may limit the generalizability of the results.
2. **Strain-Specific Analysis:** The study did not analyze specific probiotic strains in curd, which could provide more targeted therapeutic insights.
3. **Short-Term Follow-Up:** A longer follow-up period is needed to assess the impact of probiotics on RAU recurrence rates.

CONCLUSION

Probiotics, specifically curd as a natural source, significantly enhance the management of recurrent aphthous ulcers (RAU) by accelerating healing, reducing inflammation, and addressing microbial dysbiosis. Patients receiving probiotics alongside standard treatment demonstrated faster and complete resolution of symptoms compared to those receiving standard treatment alone. Probiotics offer a safe, cost-effective, and accessible adjunctive therapy for RAU, with the potential to improve patient outcomes and quality of life. Future studies should focus on validating these findings with larger sample sizes and exploring the long-term benefits of probiotics in preventing RAU recurrence.

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